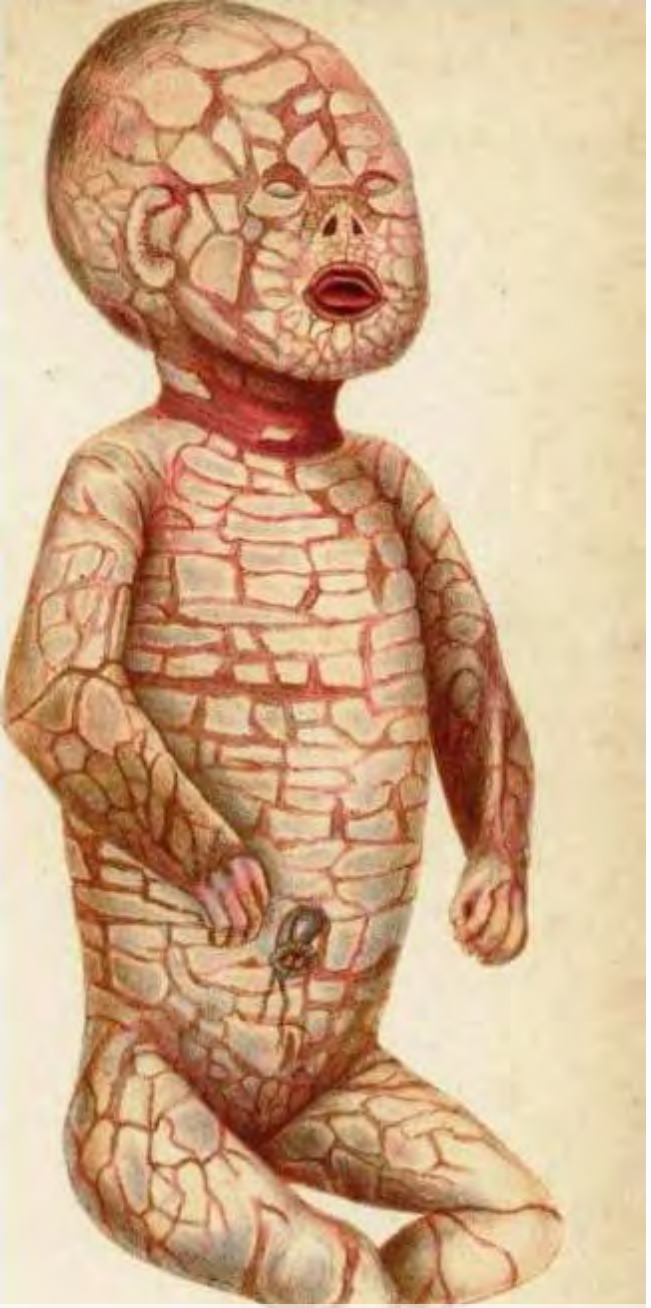
18th Summer Academy of Dermatopathology
Graz, July 6 – 10, 2026

You want' see this in adults:

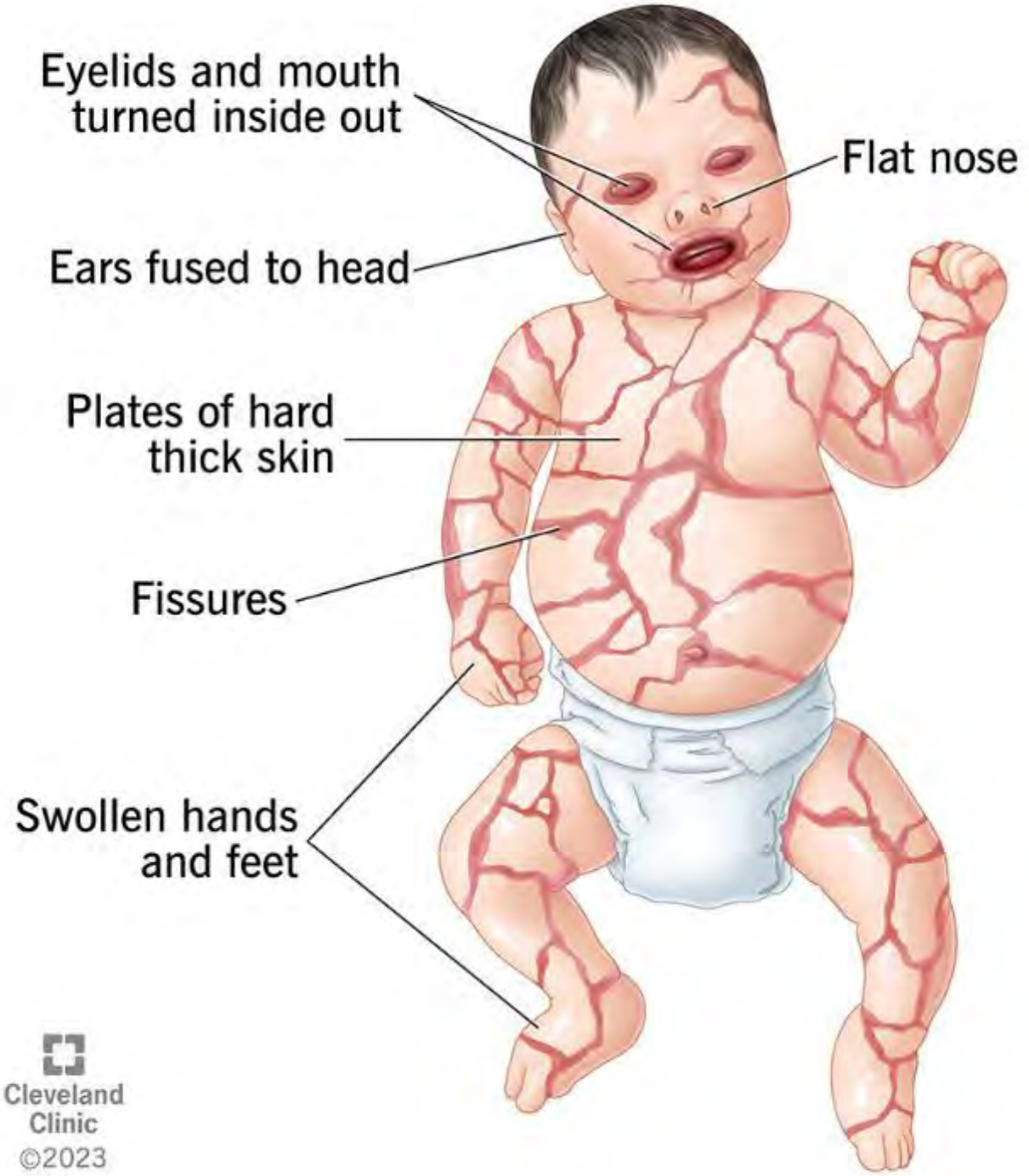
selected cases in neonates, children and teen-agers

Lorenzo Cerroni

(with some help from Antonio Torrelo)



J Bland Sutton: A Case of General Seborrhœa or “Harlequin” Fœtus. Med Chir Trans 1886;69:291–296



Harlequin ichthyosis

Genetic mutation in the *ABCA12* gene, transmitted in an autosomal recessive manner, causing very low level or absence of the ABCA12 protein.

The ABCA12 protein has an important role in transporting lipids to the epidermis, and is crucial for the formation of the epidermal barrier.

dermatopathology

Dermatopathology 2026, 13, 9

MDPI

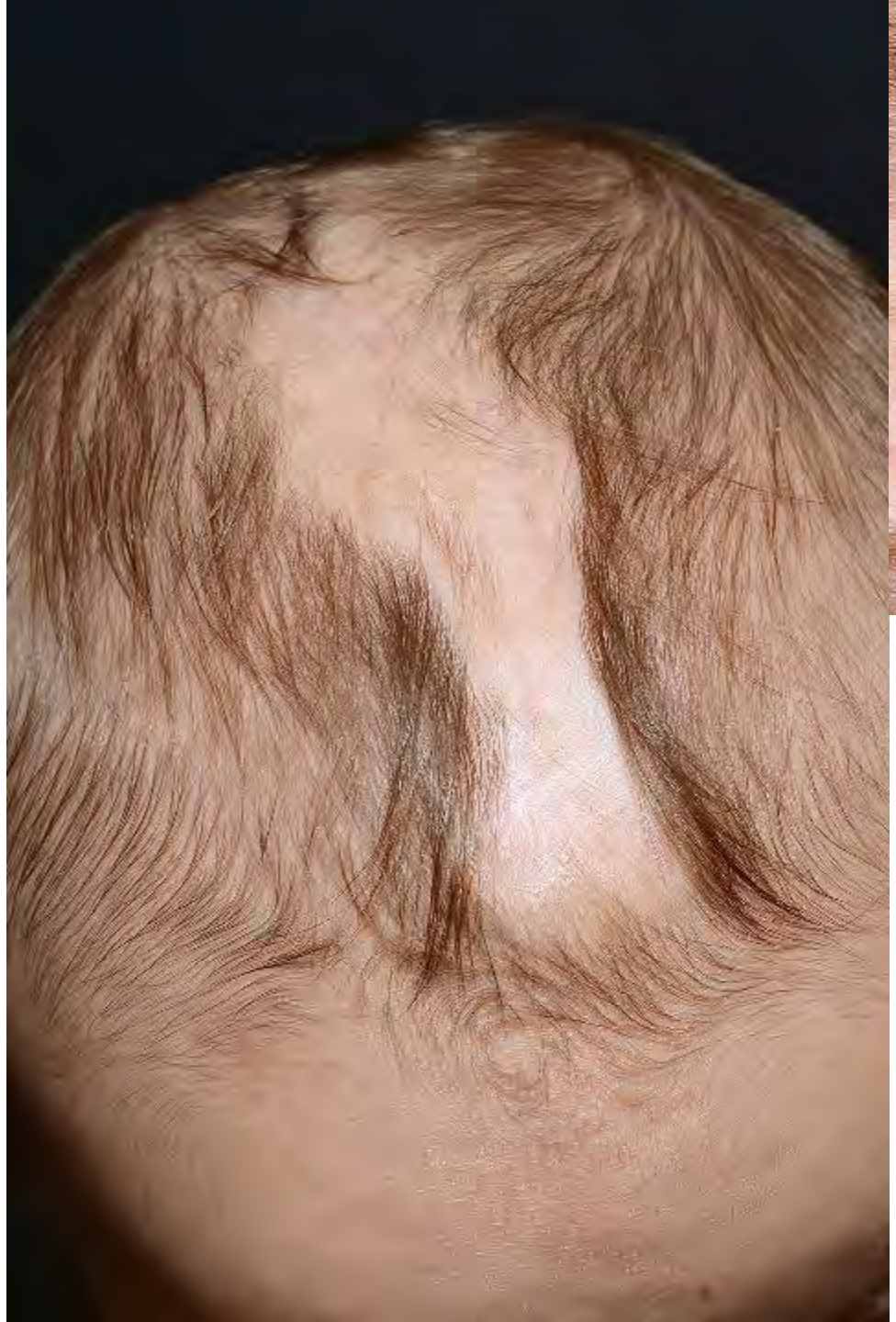
Article

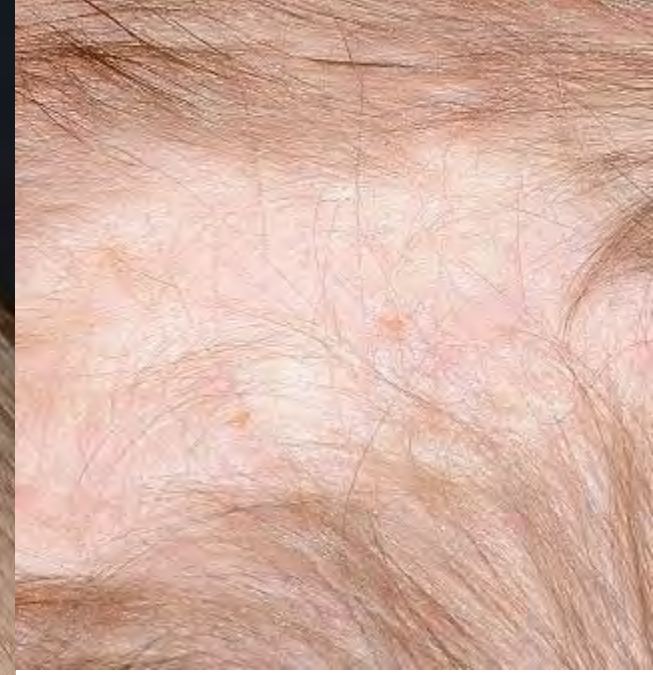
Defining Histological Patterns in Inherited Ichthyoses: Toward a Diagnostic Algorithm Based on 66 Confirmed Cases

Kira Süßmuth [1,*], Vinzenz Oji [2], Jacqueline Bodes [2], Isabelle Jochum [1], Florian Muhs [2], Katalin Komlosi [3], Ingrid Hausser [4], Matthias Schmuth [5], Heiko Traupe [2], Judith Fischer [3] and Dieter Metze [2]

Patient ID	Sex	Age	Biopsy Site	Diagnosis (Gene); (Mutation); (Diagnostic Method)	Cutaneous and Extracutaneous Symptoms	Histology							
						SC	SG	Acanthosis	Inflammation	FHK	AHK	Other Findings	Pattern(s)
36	m	15	upper limb	harlequin ichthyosis, overlap lamellar ichthyosis (*ABCA12*) (c.2140C>T(Arg714*); 2341T>A(Cys781Ser)); (*ABCA12*, Exon 17: c.2140C>T, p.(Arg714*) (Class 5); *ABCA12*, Exon 18: c.2341T>A, p.(Cys781Ser) (Class 4)); (NGS)	severe erythroderma and scaling; clinical overlap of lamellar ichthyosis with harlequin ichthyosis	+, OK, focal PK, compact	+	++/+++, regular	++	n.a.	normal	neutrophils in SC; BV: dilatated, kissing vessels	II
37	m	20	upper limb	harlequin ichthyosis (*ABCA12*) (c.3829+3A>G, Spleiß-Mutation, Intron 26); c6722_6723delGA (p.Arg2241lefs*4)) (NGS)	severe erythroderma and scaling	+, OK, focal PK, compact	−−	++, regular	++	n.a.	n.a.	neutrophils in SC; BV: dilatated, kissing vessels, suprapapillary thinning, papillomatosis	I

1. Orthohyperkeratosis with a reduced or absent stratum granulosum
2. Orthohyperkeratosis and a well-developed stratum granulosum
3. Hyperkeratosis with ortho- and parakeratosis with preserved or prominent stratum granulosum
4. Epidermolytic hyperkeratosis
5. Perinuclear vacuoles and binucleated keratinocytes
6. Psoriasis-like features

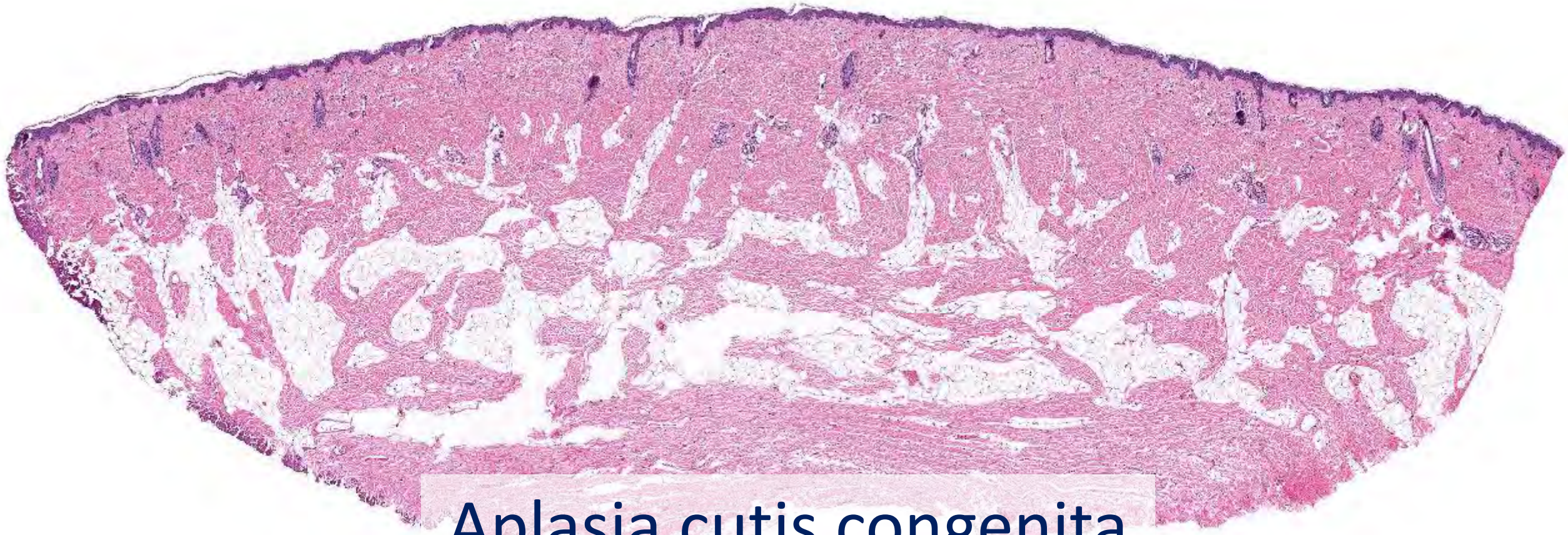




M, 1

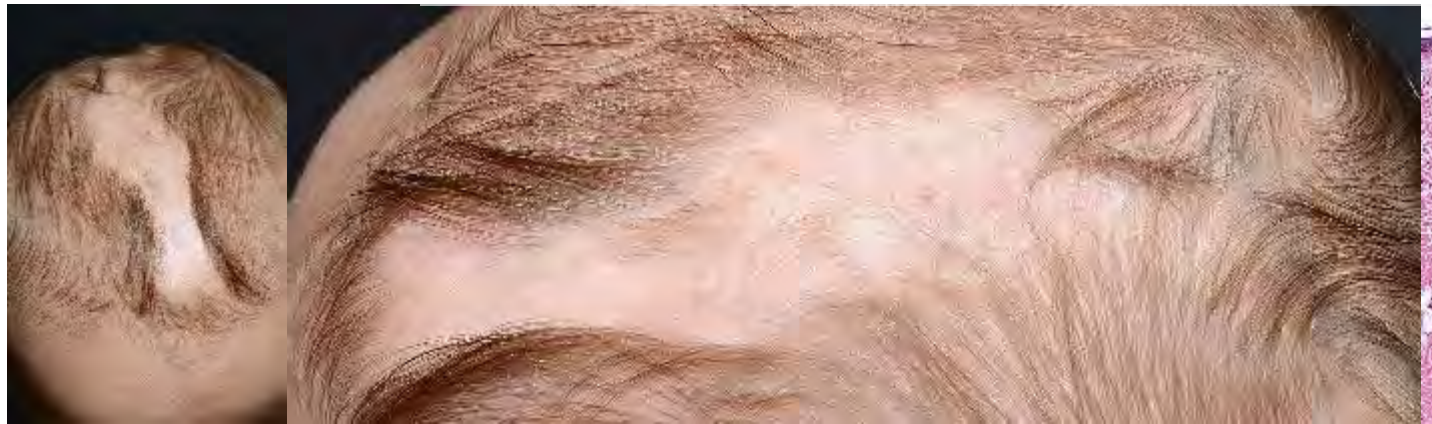
An area without hairs is present on the scalp since birth; no other symptoms.

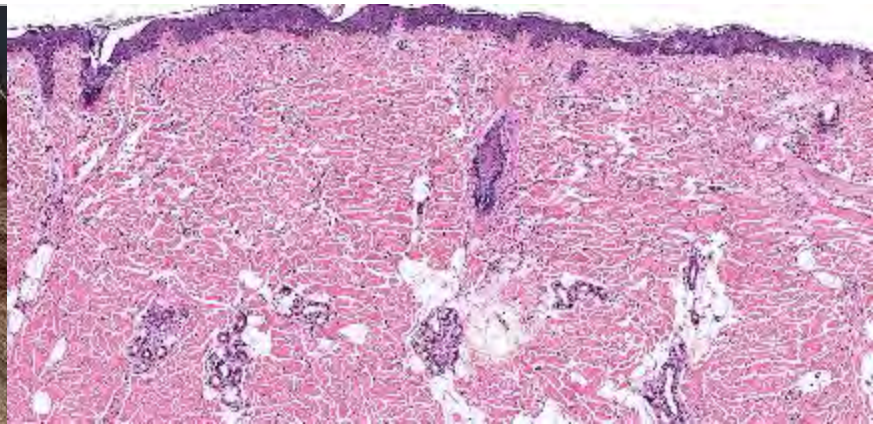
Pediatric surgeons plan to excise the area in 2 sessions; the first biopsy is taken.

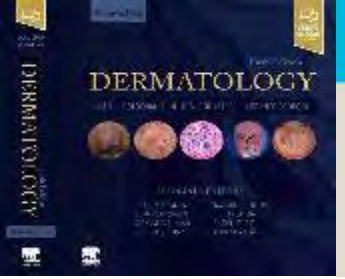


Aplasia cutis congenita

without other anomalies







Developmental Anomalies 64

Richard J. Antaya and Julie V. Schaffer

CLASSIFICATION SCHEME FOR APLASIA CUTIS CONGENITA (ACC)

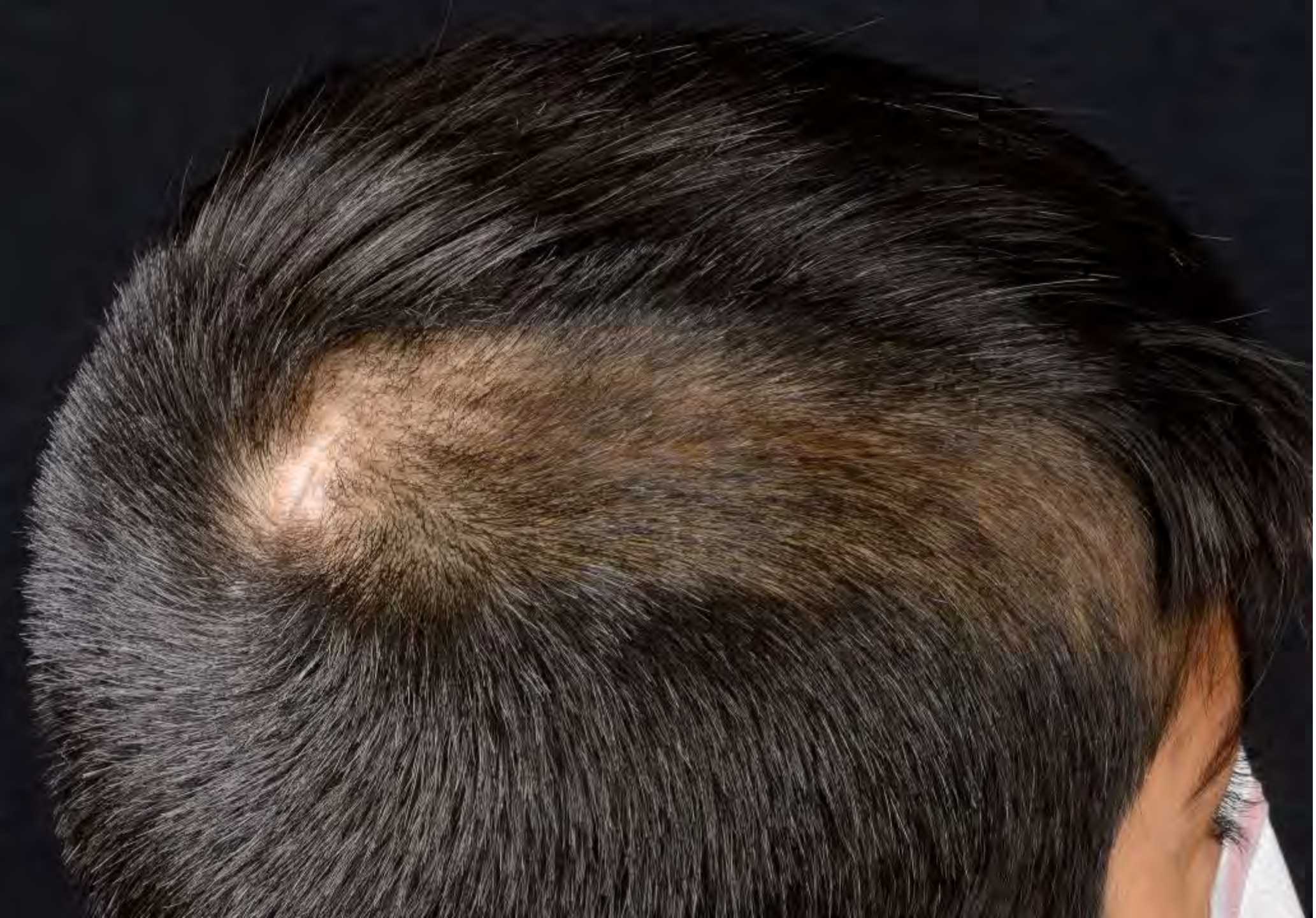
	Inheritance (Gene)	Features	Associated abnormalities
Group 1: Scalp ACC without multiple anomalies	Sporadic > AD	Usually at the vertex Membranous Hair collar	**No associated abnormalities** **Isolated abnormalities** (most often associated with membranous ACC): cleft lip and/or palate, tracheoesophageal fistula, high myopia and cone-rod dysfunction, patent ductus arteriosus, intestinal lymphangiectasia, omphalocele, polycystic kidneys, double cervix and uterus, intellectual disability, temporal triangular alopecia
	Often AD (*BMS1*)	Usually at the vertex Irregular and scar-like	
Group 2: Scalp ACC associated with Adams–Oliver syndrome	AD (*ARHGAP31*, *DLL4*, *NOTCH1*, *RBPJ*) AR (*DOCK6*, *EOGT*)	Midline scalp Often large, irregular lesions Skull defect Dilated scalp veins	**Adams–Oliver syndrome:** terminal transverse limb defects (e.g. reductions, syndactyly, nail dystrophy), cutis marmorata telangiectatica congenita, cardiac malformations, CNS abnormalities
Group 3: Scalp ACC associated with epidermal and sebaceous nevi (and, occasionally, congenital melanocytic nevi)	Sporadic due to mosaic RASopathy (e.g. *HRAS*, *KRAS*)	Scalp, often unilateral Membranous	**Epidermal nevus or nevus sebaceus**, usually in proximity to the ACC **Large congenital melanocytic nevus:** in a few reports* **Ipsilateral ophthalmologic abnormalities:** corneal opacities, scleral dermoids, eyelid colobomas, retinal dystrophy **CNS abnormalities:** intellectual disability, seizures
Group 4: ACC overlying embryologic malformations	Variable	Scalp, often with a hair collar if overlying a neural tube defect Lumbosacral Chest, abdomen	**Cranial malformations:** cephalocele, heterotopic brain or meningeal tissue, congenital midline porencephaly, holoprosencephaly, craniosynostosis, vascular malformation/aplasia/arteriovenous fistula **Spinal malformations:** occult dysraphism, myelomeningocele **Thoracic malformations:** sternal cleft **Abdominal malformations:** omphalocele, gastroschisis **Multiple malformations associated with generalized, lethal ACC ("systemic" ACC):** corneal opacities, choanal atresia, hypoplastic lungs, absent greater omentum, intestinal malrotation & atresias, hepatosplenomegaly, skull defects, syndactyly, anonychia
Group 5: ACC associated with fetus papyraceus, placental infarcts, or other ischemic events	Sporadic	Scalp, chest, flanks, axillae and/or extremities (see Fig. 64.19) Multiple, symmetric Stellate/angulated configuration	**Associated fetus papyraceus** due to second-trimester death of twin/triplet or fetal reduction of higher-order pregnancies **Placental infarction**, single umbilical artery **Duodenal, ileal, and/or biliary atresias with intestinal infarction** Intracranial hemorrhage/CNS abnormalities
Group 6: ACC associated with epidermolysis bullosa (EB)	AD or AR, depending on EB type	Lower extremities ("Bart syndrome") or large areas of the extremities, trunk, and scalp	**EB simplex (EBS; especially *KLHL24*-related), junctional EB (JEB), and dystrophic EB:** blistering of skin and/or mucous membranes, skin fragility, nail dystrophy **If more widespread (most often in JEB or EBS with pyloric atresia):** ureteral stenosis, renal abnormalities, arthrogryposis, abnormal ears and nose; may have intrauterine/neonatal death (*ITGB4*, *PLEC*)
Group 7: Localized ACC, presumably due to prenatal physical insult	Sporadic	Extremities, e.g. forearm, pretibial area	**Volkmann contracture or radial dysplasia** (with ACC on the forearm) **Amniotic band sequence** (see text)
Group 8: ACC caused by specific teratogens, maternal conditions, or intrauterine infections	Sporadic	Scalp with drugs Any site with congenital infections	**Methimazole (thiamazole), carbimazole:** imperforate anus, oral malformations **Misoprostol** **Low-molecular-weight heparin** **Valproic acid** **Maternal antiphospholipid syndrome** **Intrauterine varicella, herpes simplex or rubella infection:** signs of these infections
Group 9: ACC associated with malformation syndromes	Variable	Variable	See Table 64.4

*Referred to as "SCALP" syndrome (sebaceous nevus, CNS malformations, ACC, limbal dermoid, pigmented nevus).

Histologic features of membranous aplasia cutis include an atrophic flattened epidermis, replacement of the dermis by loose connective tissue, and an absence of adnexal structures.

Findings in other types of ACC vary but lesions that have healed generally show scarring, a lack of adnexa, and in some cases fragmented elastic tissue.

Although histologic examination may occasionally be helpful, the diagnosis of ACC is primarily clinical.



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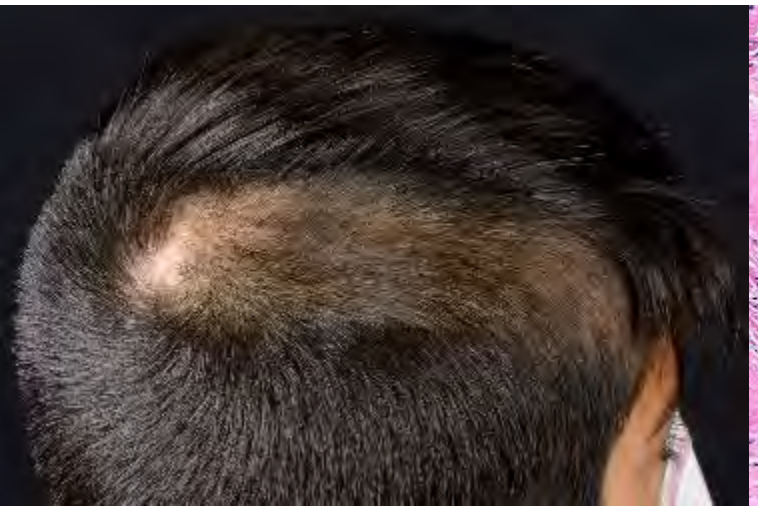
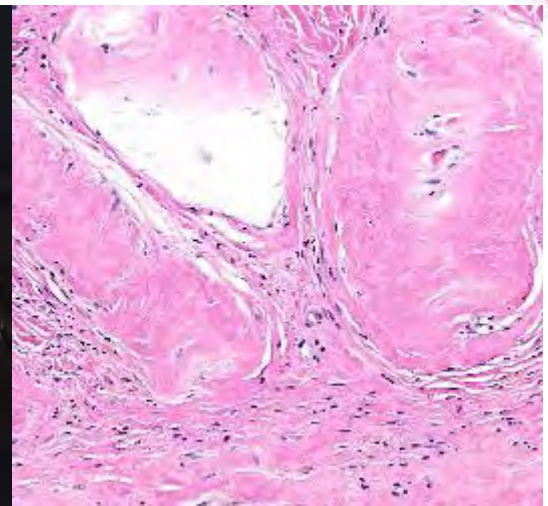
According to the parents scalp lesion for approximately 1 year.

No history of previous trauma.

A biopsy is taken.

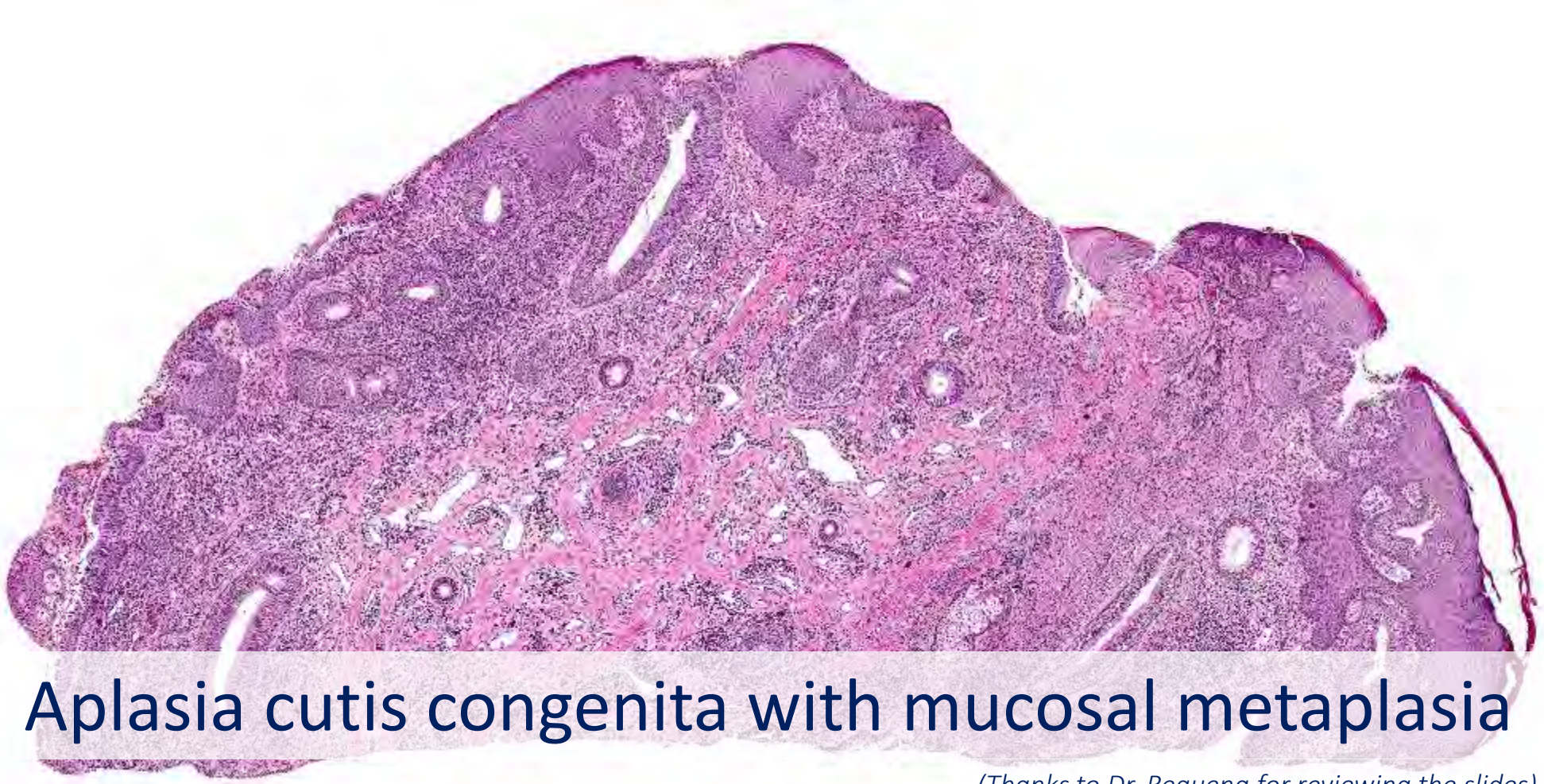


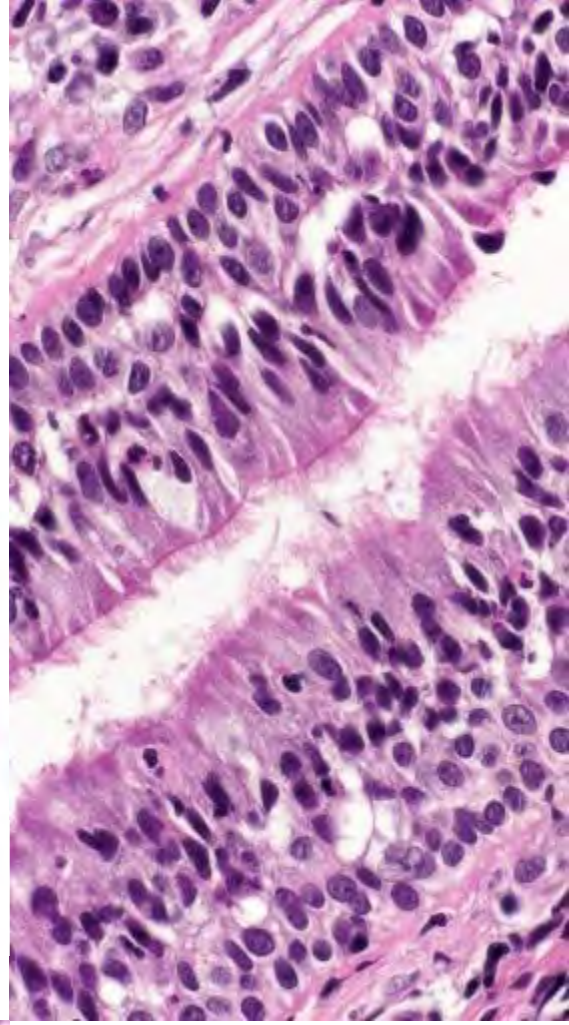


Early linear scleroderma

(en coupe de sabre)

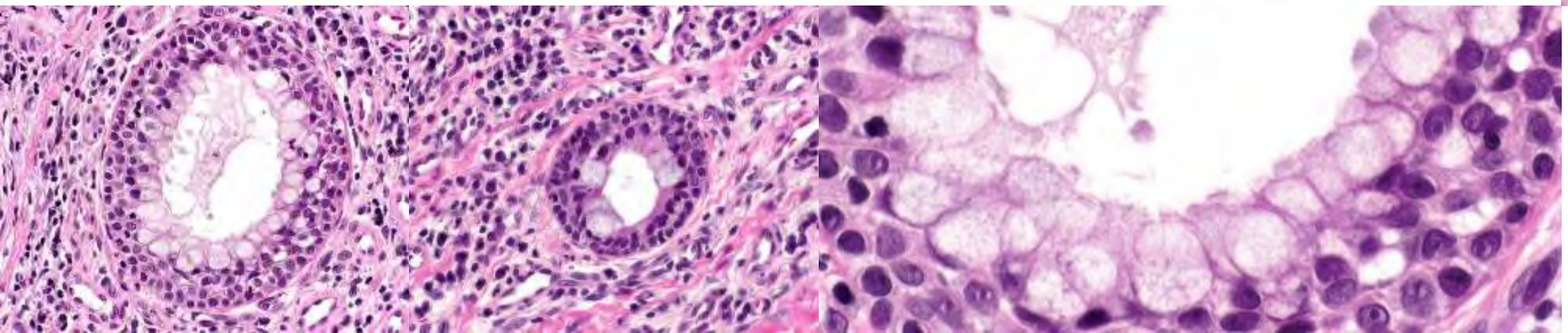
ANA: 1:320





Aplasia cutis congenita with mucosal metaplasia

(Thanks to Dr. Requena for reviewing the slides)



F, 1

Congenital "wound" on the right lower leg.

A biopsy is taken.

A Case of Aplasia Cutis Congenita, Type VII

[illegible] Lee, M.D., [illegible] Yun, M.D., [illegible] Lee, M.D.,
[illegible] Kim, M.D., Young Ho Won, M.D., Seung-Chul Lee, M.D.

Department of Dermatology, Chonnam National University Medical School, Gwangju, Korea

Aplasia cutis congenita (ACC) is a rare congenital defect in which localized or widespread areas of the skin are absent at birth. In the majority of cases, it is limited to the scalp especially on the vertex although other areas of the body may also be involved. Other congenital malformations can be associated with ACC. We present herein the case of a new born male with unilateral absence of skin on the extensor surface of the right lower leg. There was no associated malformation or skin disease such as blistering or nail abnormality. According to the classification outlined by Frieden, the condition was diagnosed as type VII aplasia cutis congenita. The treatment of this large ulcer was conservative, wet dressing and prophylactic topical antibiotics. On follow up after 2 years showed that the patient was nearly cured of the ulcer and had only minimal scar formation.
(Ann Dermatol (Seoul) 20(2) 70~73, 2008)

Key Words: Aplasia cutis congenita, Leg, Unilateral

INTRODUCTION

Aplasia cutis congenital (ACC) is defined as a localized or widespread absence of skin at birth. As it was first described by Cordon in 1767, the lesions usually appear as circular, oval, sharply outlined ulcer, which result in scarring after they are healed. Almost 80% of aplasia cutis appears in the scalp regions, and only about 10~15% of ACC involve other areas of the body. In some cases, the lesions can be a sign of embryonic malformation, chromosomal abnormality, or ectodermal dysplasia. Moreover, associations with epidermolysis bullosa, intrauterine infection, or specific teratogens has been described. Defects of the skin limited to the lower limbs are very rare. The defects are usually presented as ulcerations, membranous lesions, or areas of atrophic scarring.

We report an unusual case of ACC with full thickness skin defect located only on the right lower leg.

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CASE REPORT

A newborn male presented with a large ulcer on the right leg which had been present since birth. There was no significant antenatal or family history. The mother had no specific disease or drug history prior to or during the pregnancy. He was born through normal vaginal delivery at 39 weeks' gestation with a weight of 3.4 kg. On physical examination, a large ulcer was found, with a length of about 20 cm on the right leg from the knee area to the medial dorsal foot (Fig. 1). The toenails, teeth and mucosa of the mouth were not affected, and there was no blistering anywhere on the body. The routine laboratory results were within normal limits and the serologic analysis for TORCH yield negative results. A punch biopsy taken from the ulceration on the thigh 5 days after birth showed the absence of epidermis and adnexal structures as well as proliferation of blood vessels in the dermis (Fig. 2). There was no evidence of a hemangioma

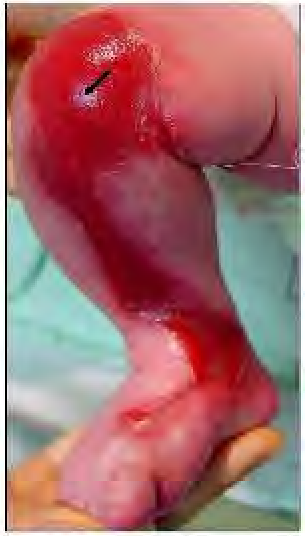

Fig. 1. Large ulcer about 20 cm length along the right leg without nail dystrophy. On the day of birth. Arrow indicates biopsy site.

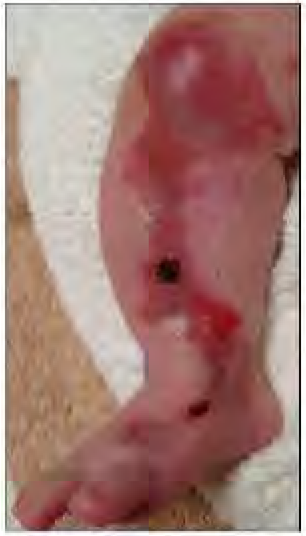

Fig. 3. Clinical features 15 days after birth. New hyper-proliferative granulation tissue has appeared and blood clots were observed.

Clinical review

Aplasia cutis congenita: A clinical review and proposal for classification

Ilona J. Frieden, M.D. *Oakland and San Francisco, CA*

Aplasia cutis congenita is a condition in which localized or widespread areas of skin are absent at birth. Several distinct clinical subtypes occur, characterized by the location and pattern of skin absence, the presence of associated malformations, and the mode of inheritance. The disorder is seen most frequently on the scalp, often as a solitary lesion without other anomalies. Scalp lesions can be seen in association with limb reduction defects and in association with epidermal and organoid nevi. Lesions may overlie overt or occult embryologic malformations. A form of aplasia cutis congenita occurs in association with placental infarcts or the in utero death of a twin fetus. The condition may be associated with epidermolysis bullosa, specific teratogens or intrauterine infections, or it may occur in the presence of chromosomal abnormalities, ectodermal dysplasias, or other syndromes of malformation. A classification for aplasia cutis congenita is proposed. (J AM ACAD DERMATOL 14:646-660, 1986.)

Aplasia cutis congenita, or congenital absence of skin, is a heterogeneous group of disorders in which localized or widespread areas of the skin are absent at birth. More than 500 cases have been described since the entity was first reported by Cordon[1] in 1767.

Diagnosis is primarily clinical. The histologic appearance varies. At birth, ulcerated lesions may show complete absence of all layers of skin, occasionally extending to the bone or dura. Healed lesions often demonstrate flattened epidermis, proliferation of fibroblasts in a loose connective tissue stroma, newly formed capillaries, and complete absence of adnexal structures.[2,3] Most cases of aplasia cutis congenita have not been studied histologically. In Demmel's review[3] of 351 cases, only forty-eight had histologic examination. The heterogeneous appearance of lesions, including the in utero healing of some lesions,[2] further contributes to the difficulty of defining aplasia cutis congenita. In some instances, obstetric trauma or fetal scalp electrodes are erroneously believed to cause areas of aplasia cutis congenita, further delaying the diagnosis.[4,5] At present, the diagnosis rests with the clinician who, observing eroded, absent, or scarred areas of skin at birth, recognizes the condition. In many cases, especially familial, diagnosis is retrospective when characteristic scarring is observed later in life.[6,7]

Many authors have speculated about the cause of aplasia cutis congenita. The amniogenous theory proposed that amniotic adherences to the fetal skin might tear off, leaving absent areas of skin.[3] Evidence against this as a unifying theory was the finding of normal placentas in most examined cases.[3] Intrauterine trauma was also proposed as a cause of aplasia cutis congenita, but there is a history of trauma in only a minority of cases.[3,8] Ingalls[12] observed that in many cases of aplasia cutis congenita in which cutaneous defects ap-

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Presented in part at the 43rd Annual Meeting of the American Academy of Dermatology, Washington, D.C., Dec. 1-6, 1984.

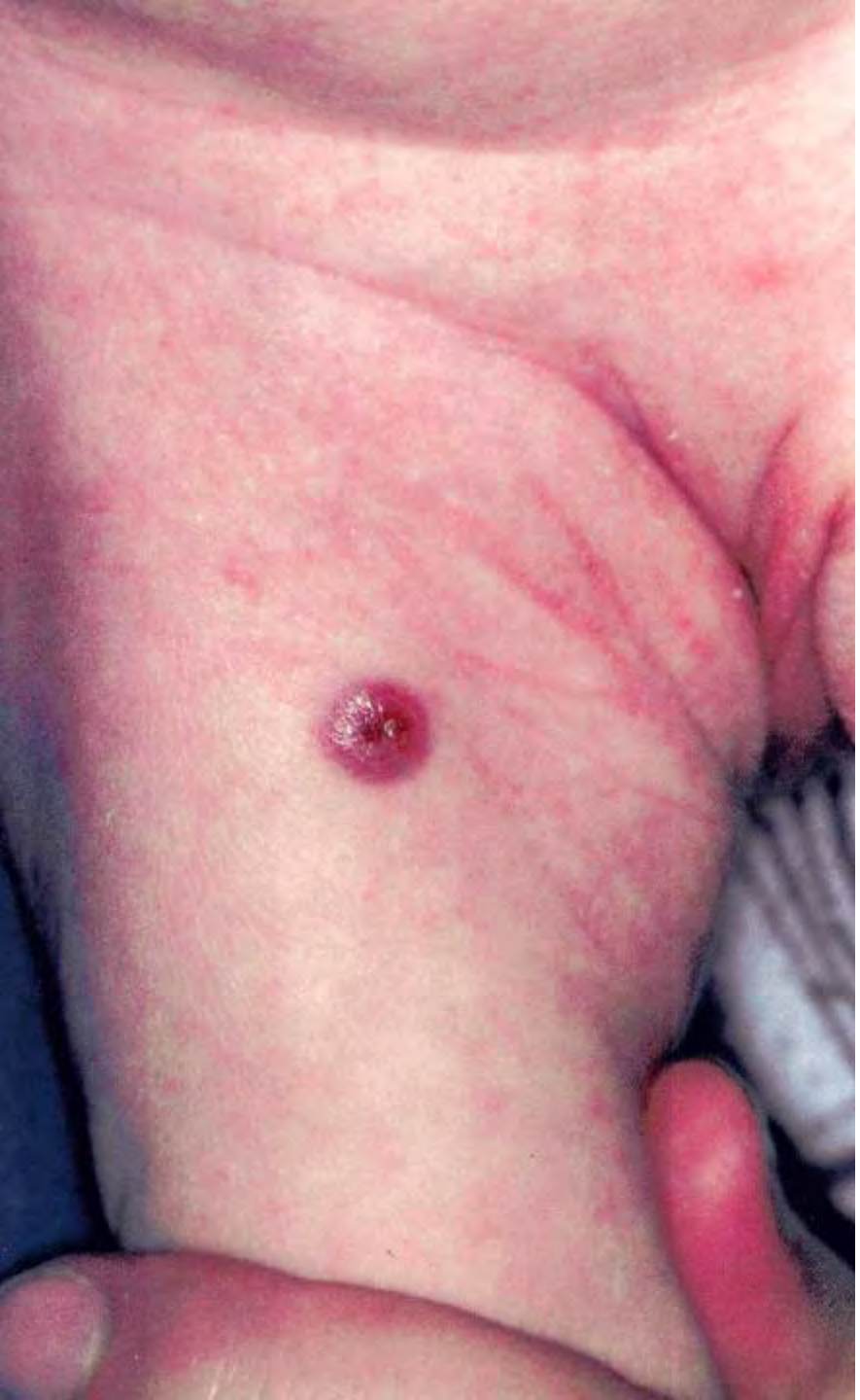
Reprint requests to: Dr. Ilona J. Frieden, Department of Dermatology, Kaiser Permanente Medical Center, 280 W. MacArthur Blvd., Oakland, CA 94611.

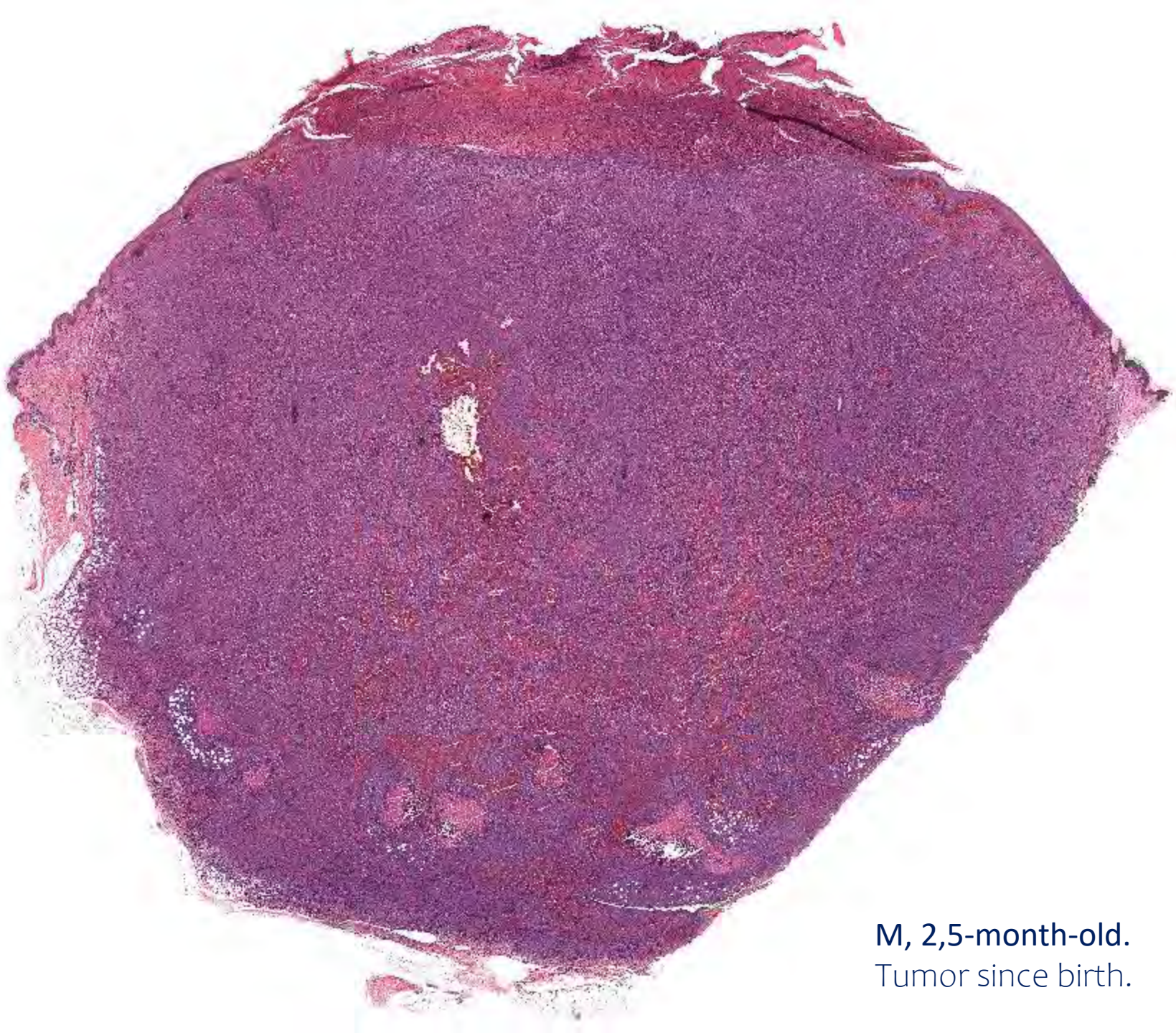
[1]Cordon M. Extrait d'une lettre au sujet de trois enfants de la même mère nés avec partie des extrémités dénuée de peau. J Med Chir Pharmacie 26:556-557, 1767.

Table 1. Proposed classification for aplasia cutis congenita

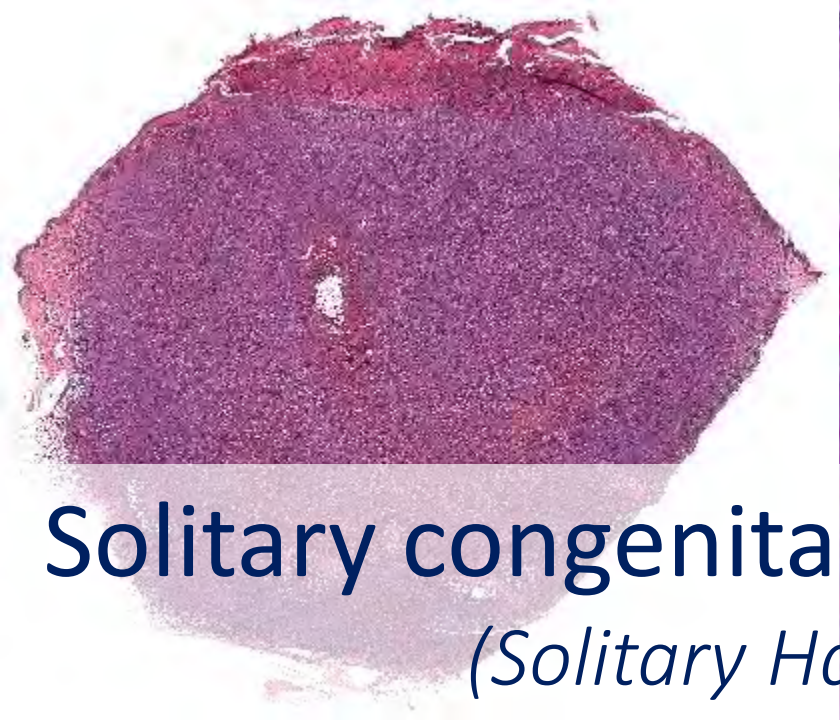
Category	Body area affected	Associated abnormalities	Inheritance
Group 1: scalp ACC without multiple anomalies	Scalp, usually vertex	Cleft lip and palate; tracheo-esophageal fistula; double cervix and uterus; patent ductus arteriosus; omphalocele; polycystic kidney; mental retardation; cutis marmorata telangiectatica congenita	Autosomal dominant or sporadic
Group 2: scalp ACC with associated limb abnormalities	Midline scalp	Limb reduction abnormalities; 2-3 syndactyly; clubfoot; nail absence or dystrophy; skin tags on toes; persistent cutis marmorata; encephalocele; woolly hair; hemangioma; heart disease; cryptorchidism; postaxial polydactyly (1 family)	Autosomal dominant
Group 3: Scalp ACC with associated epidermal and organoid nevi	Scalp, may be asymmetric	Corneal opacities; scleral dermoids; eyelid colobomas; psychomotor retardation, seizures	Sporadic
Group 4: ACC overlying embryologic malformations	Abdomen, lumbar skin, scalp; any site	Meningomyeloceles; spinal dysraphia; cranial stenosis; congenital midline porencephaly; leptomeningeal angiomatosis; ectropion of ear; omphalocele; gastroschisis	Depends on underlying condition
Group 5: ACC with associated fetus papyraceus or placental infarcts	Multiple, symmetric areas, often stellate or linear, on scalp, chest, flanks, axillae, and extremities	Single umbilical artery; developmental delay; spastic paralysis; nail dystrophy; clubbed hands and feet; amniotic bands	Sporadic
Group 6: ACC associated with epidermolysis bullosa (EB):			
Blistering, usually localized, without multiple congenital anomalies	Extremities	Blistering of skin and/or mucous membranes; absent or deformed nails; metatarsus varus; congenital absence of kidney (seen in cases of recessive, dystrophic EB; dominant, dystrophic EB; and EB simplex)	Depends on EB type; may be autosomal dominant or recessive
Widespread skin fragility with congenital anomalies	Large areas on extremities and trunk	Pyloric or duodenal atresia; abnormal ears and nose; ureteral stenosis; renal abnormalities; arthrogryposis; amniotic bands; nail dystrophy	Autosomal recessive
Group 7: ACC localized to extremities without blistering	Pretibial areas; dorsal aspects of hands and feet; extensor areas of wrists	None	Autosomal dominant or recessive
Group 8: ACC caused by specific teratogens	Scalp (with methimazole); any area (with varicella and herpes simplex infections)	Imperforate anus (methimazole); signs of intrauterine infection with varicella and herpes simplex infections	Not inherited
Group 9: ACC associated with malformation syndromes	Scalp; any location	Trisomy 13; 4p− syndrome; many ectodermal dysplasias; Johanson-Blizzard syndrome; focal dermal hypoplasia; amniotic band disruption complex; XY gonadal dysgenesis	Varies, depending on specific syndrome

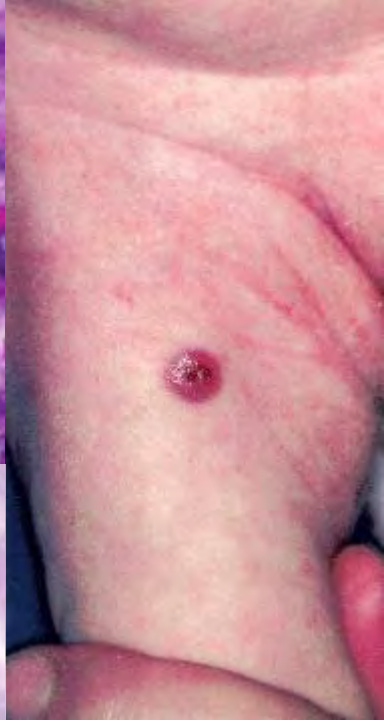
ACC, Aplasia cutis congenita; EB, epidermolysis bullosa.





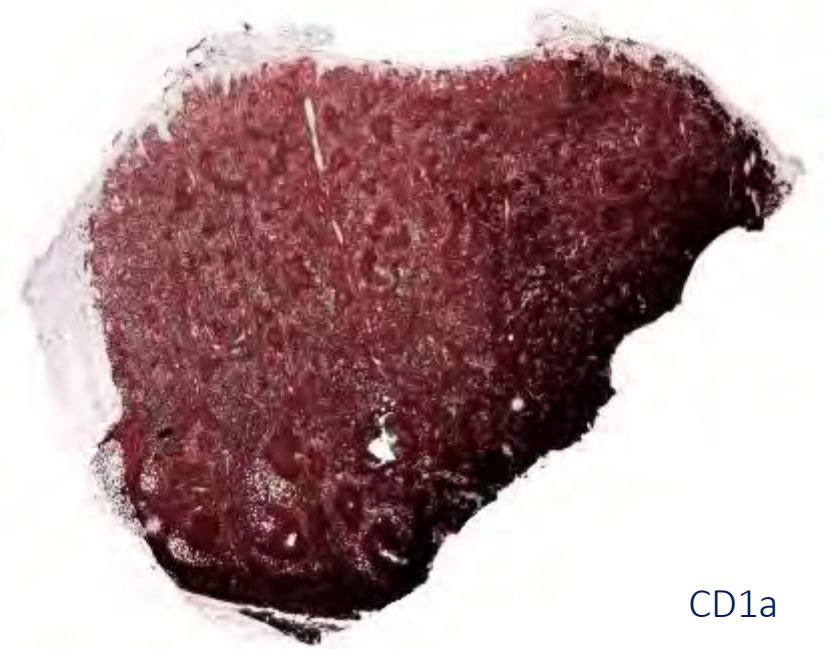
M, 2,5-month-old.
Tumor since birth.



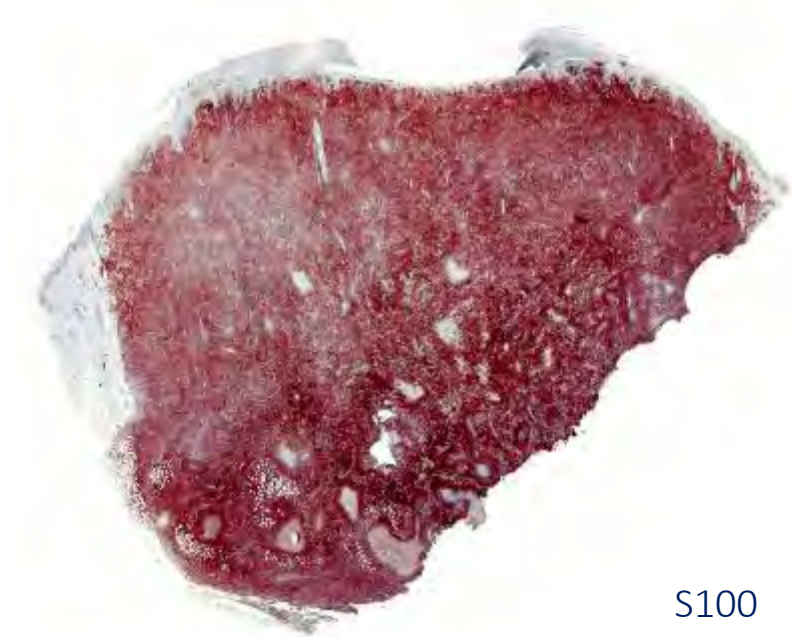


Solitary congenital Langerhans cell histiocytosis

(Solitary Hashimoto-Pritzker disease)



CD1a



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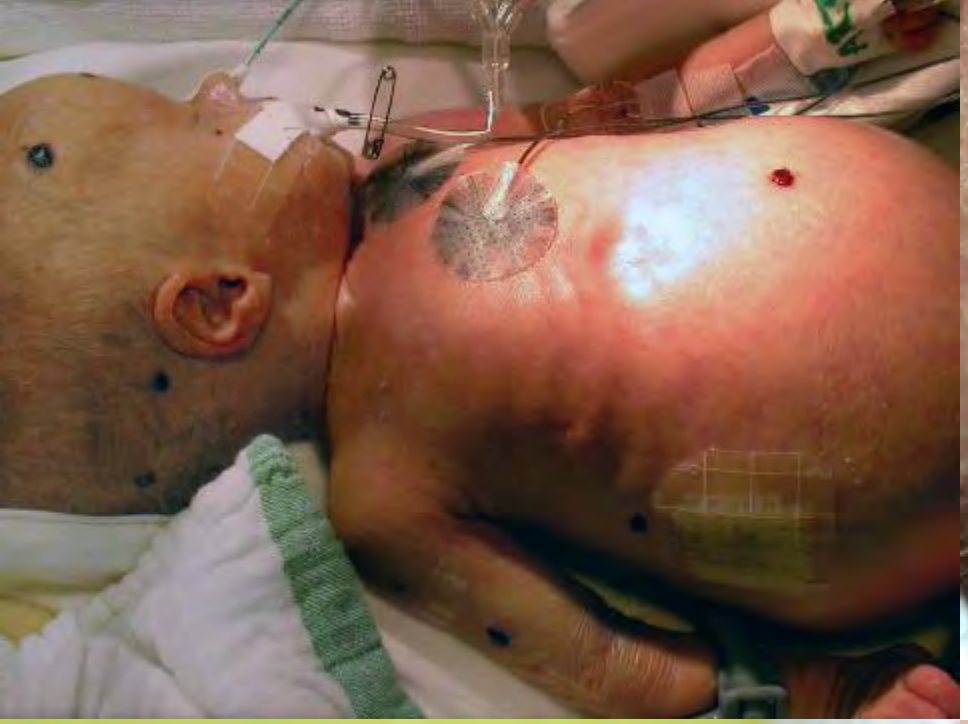
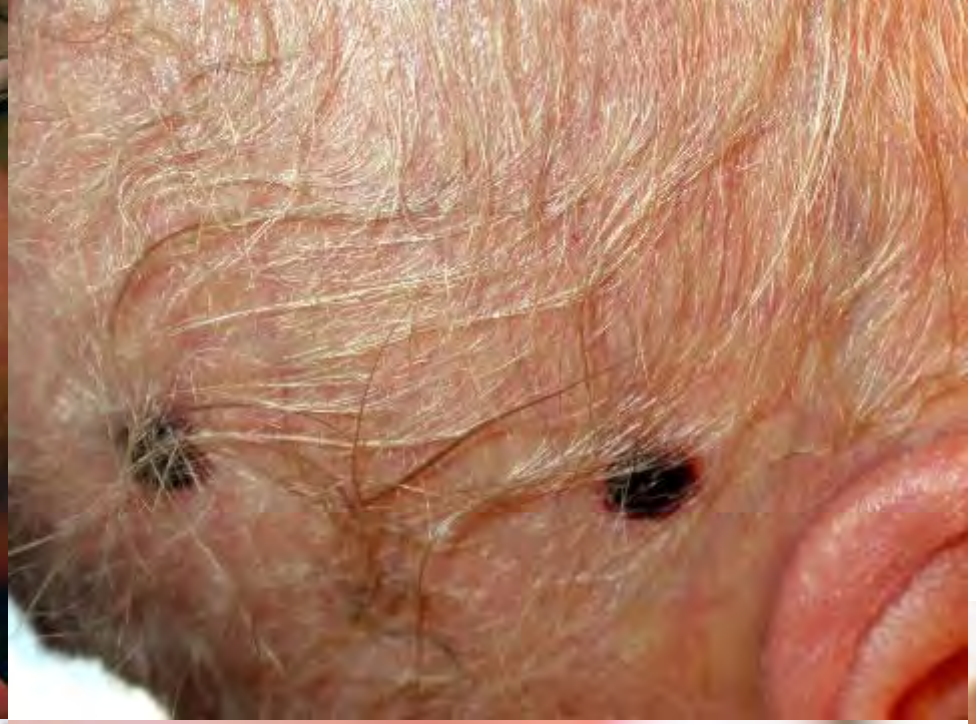




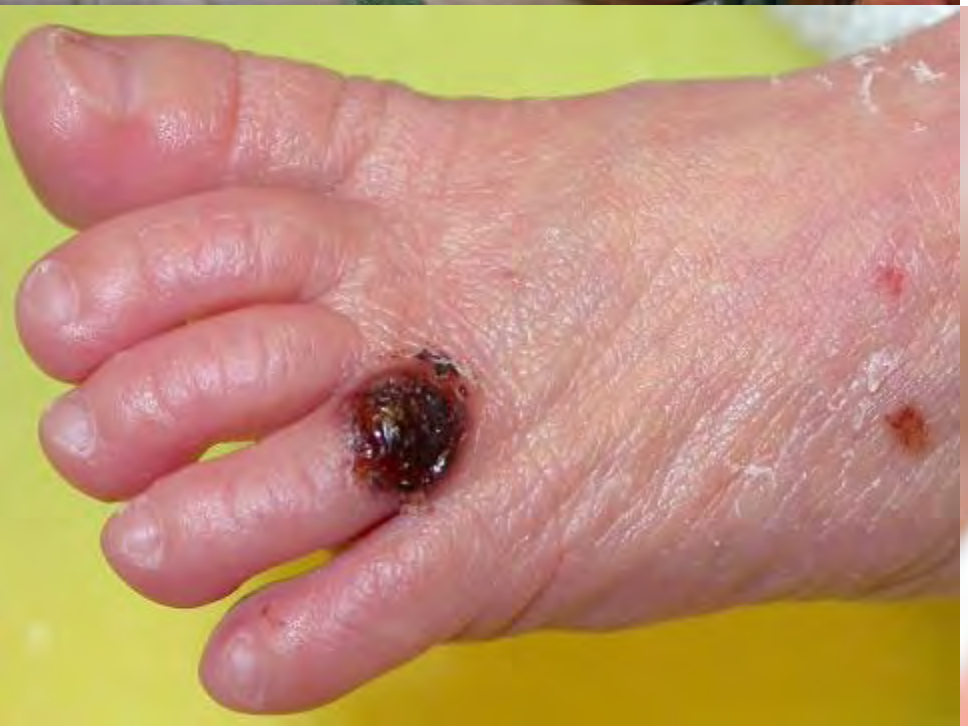
Female newborn

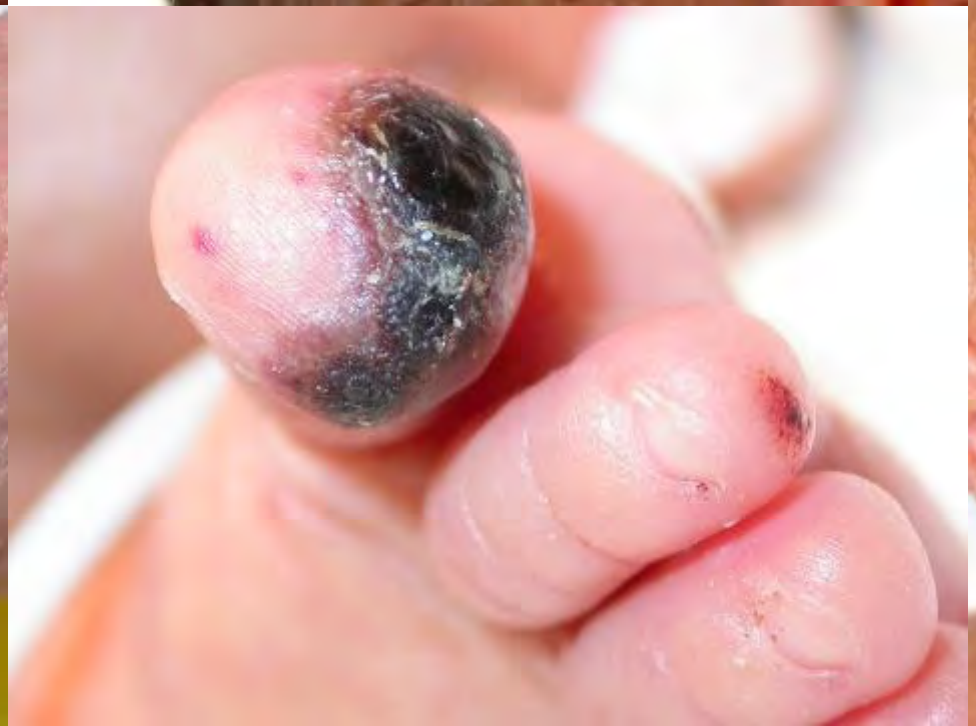
3th pregnancy of a 27-year-old woman (previously 2 healthy children).

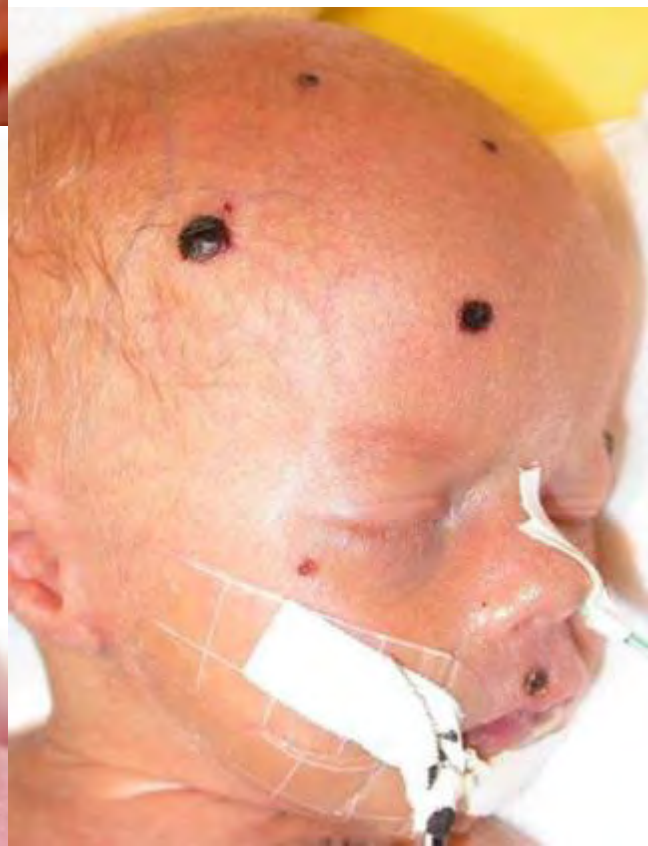
Premature delivery (34th week; 48 cm; 2348 g).

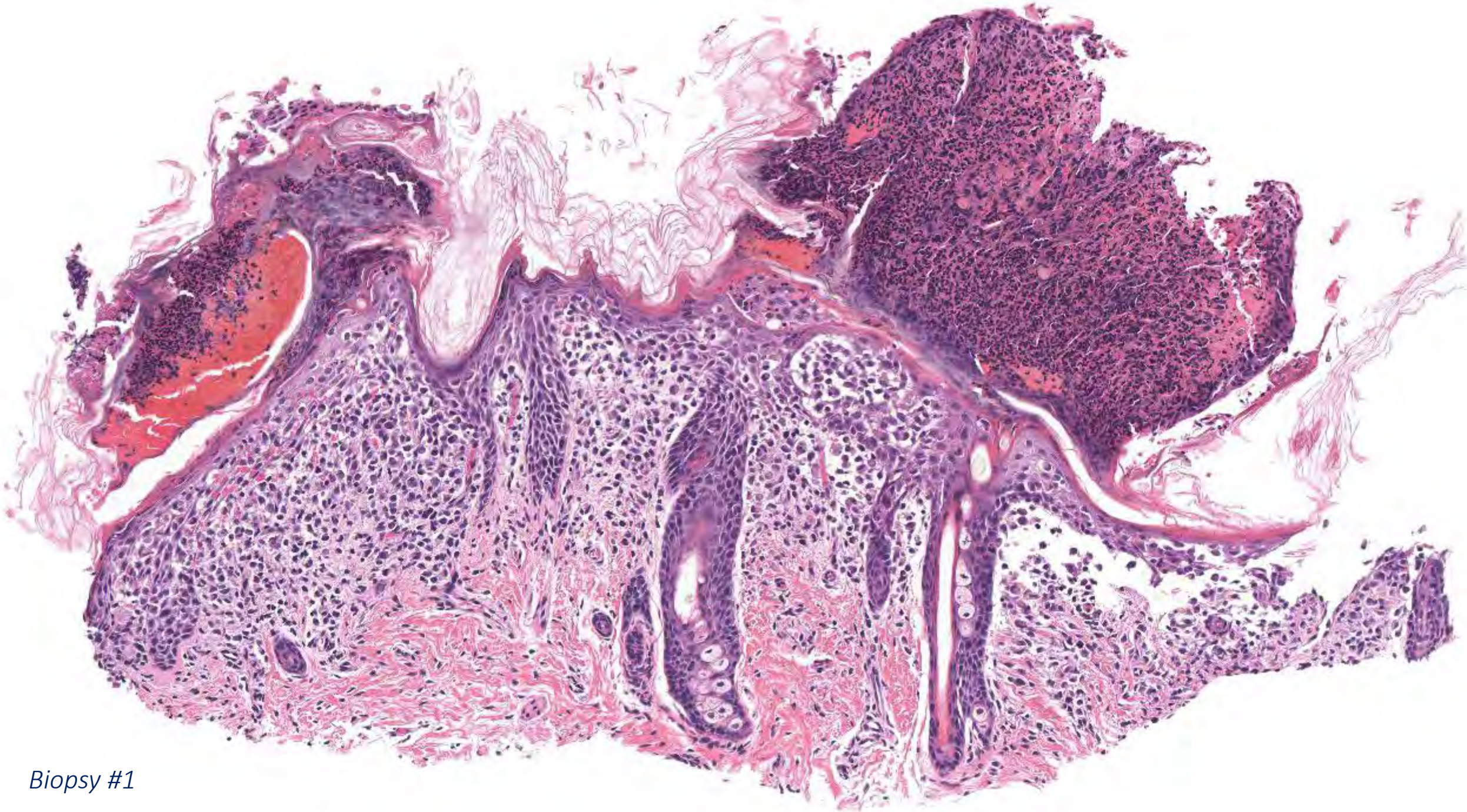
Ascites, hepatomegaly, splenomegaly; mild anemia, leukopenia, thrombocytopenia (41.000).

Two biopsies are taken.









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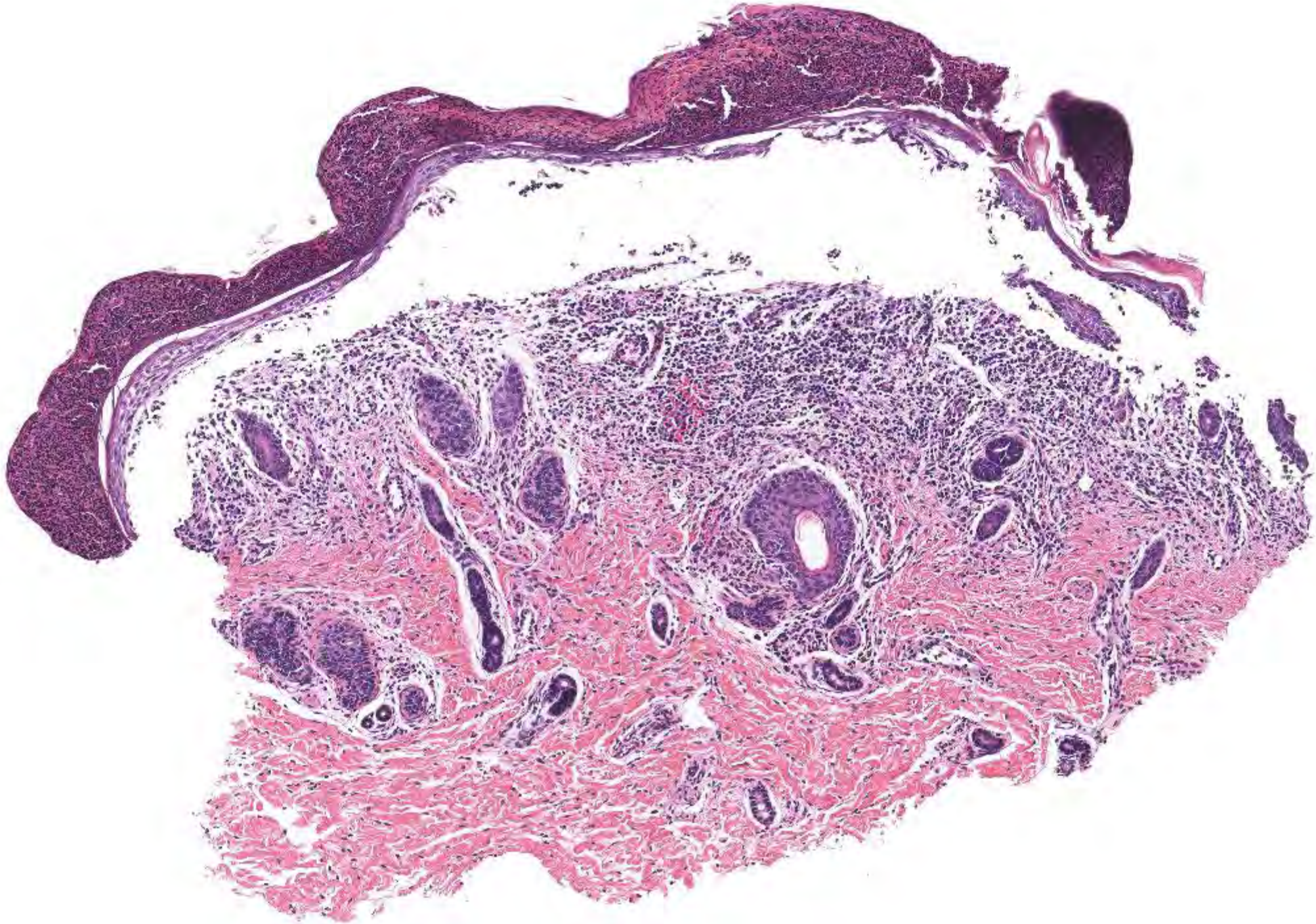

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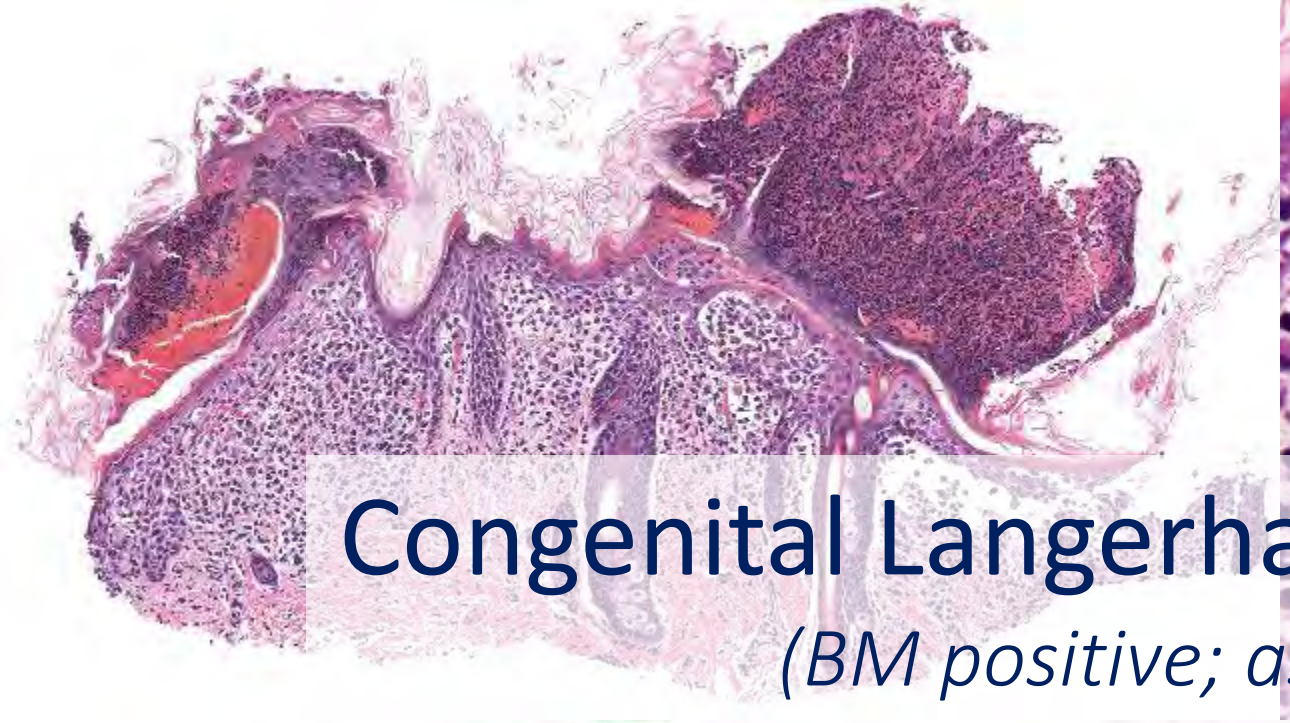
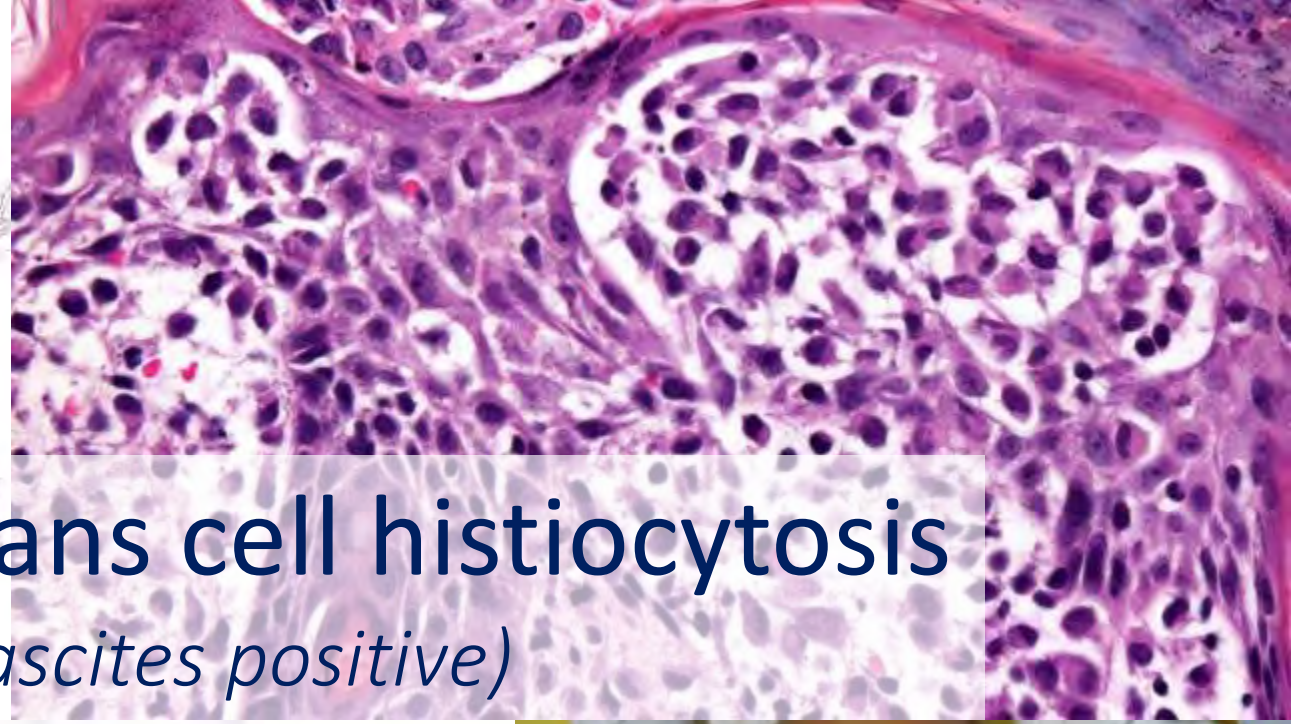
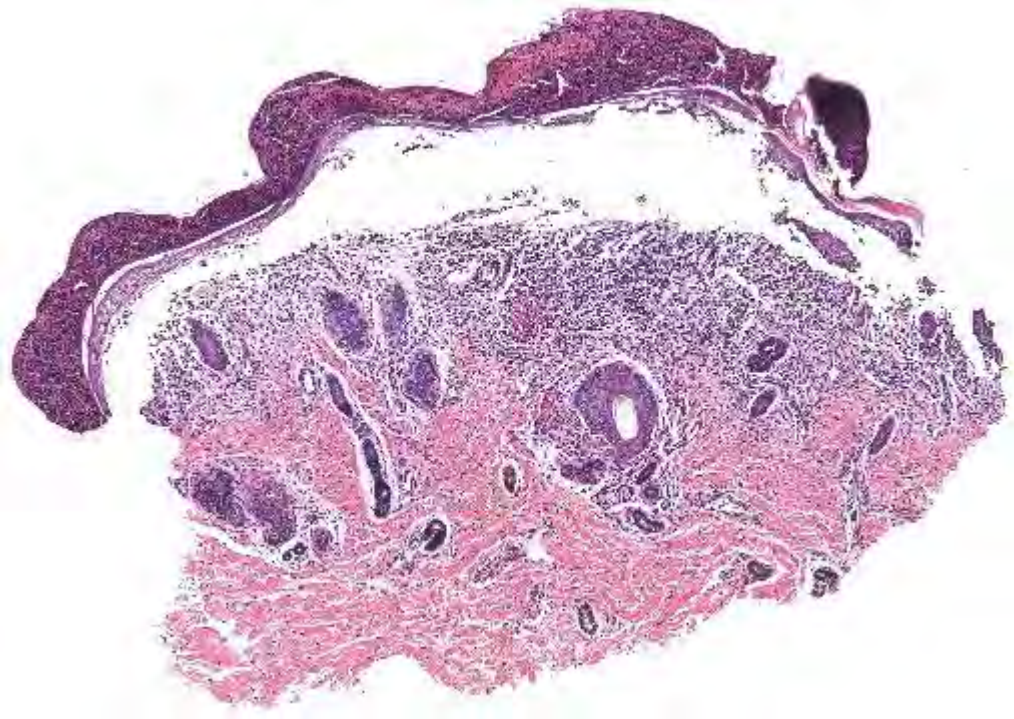
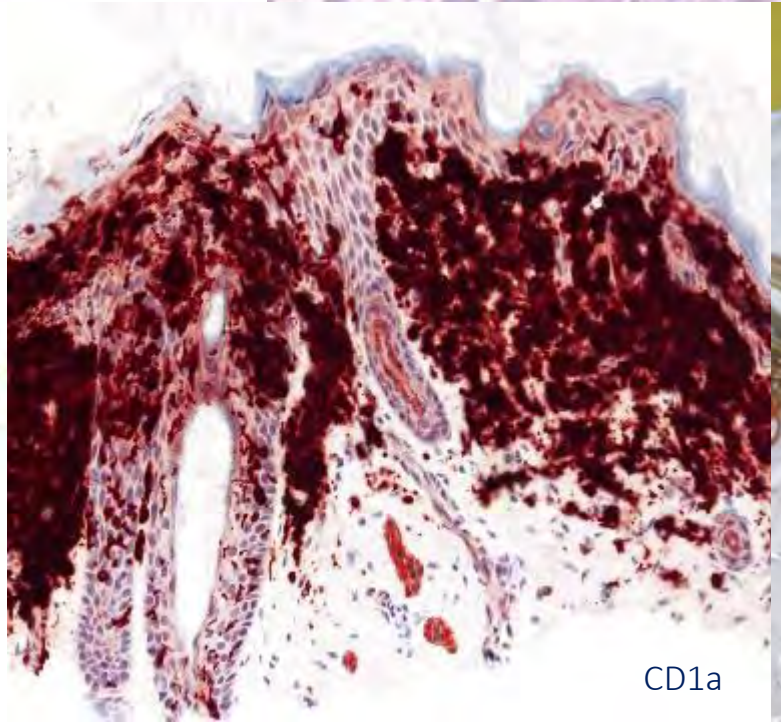




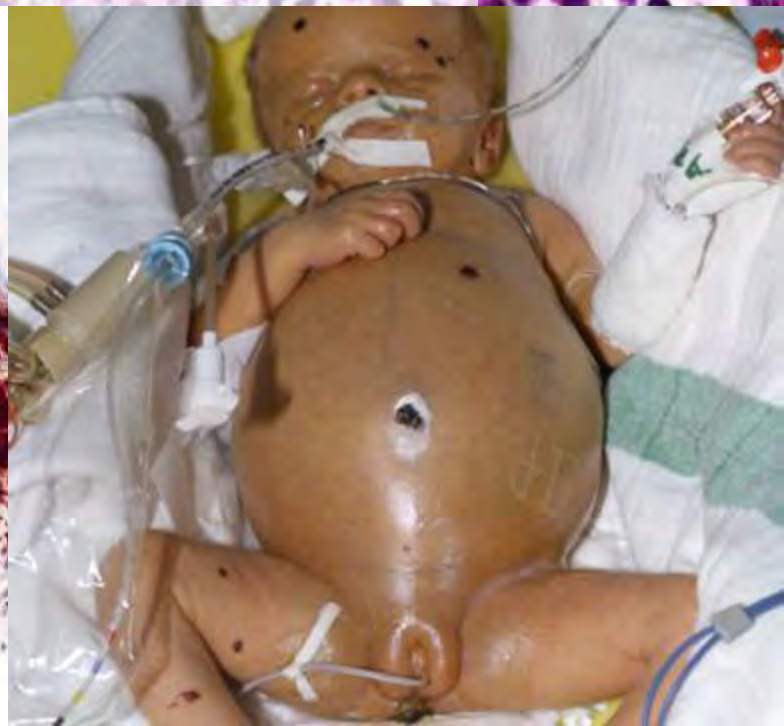
Congenital Langerhans cell histiocytosis

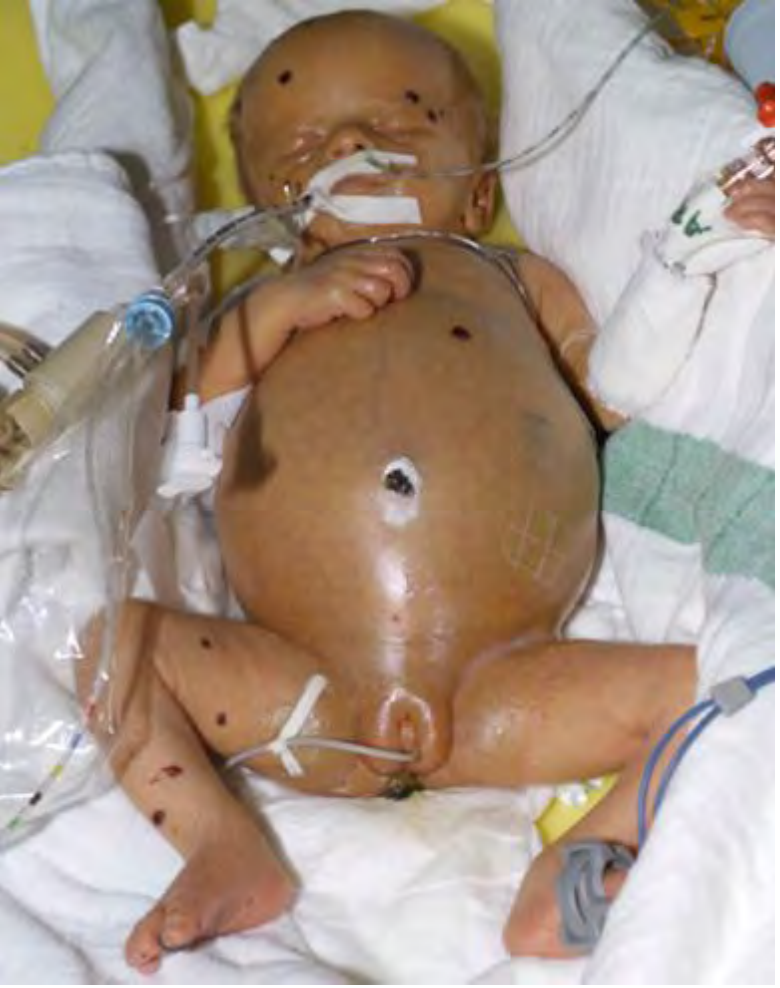
(BM positive; ascites positive)

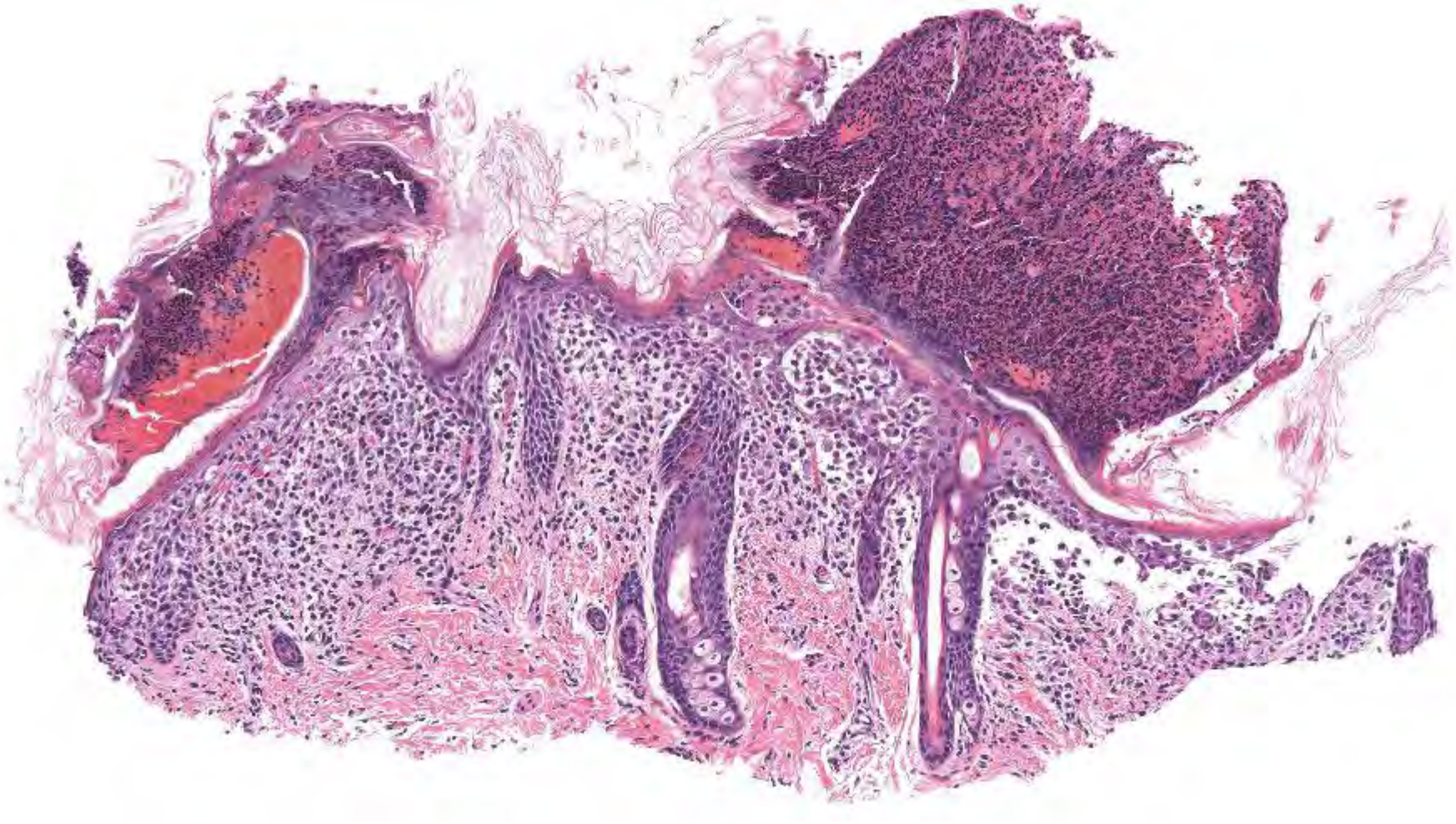




CD1a







Chemotherapy (LCH III protocol: prednisolone, vinblastine). Marked reduction of the ascites and hepatomegaly, almost complete resolution of all skin lesions with post-inflammatory hyperpigmentation already after the 1st cycle. Further management with mercaptopurine, prednisolone and vinblastine for a total of 12 months.

Congenital self-healing reticulohistiocytosis (Hashimoto-Pritzker disease): Ten-year experience at Dallas Children's Medical Center

Payal Kapur, MD, Christof Erickson, MD, Dinesh Rakheja, MD, K. Robin Carder, MD, and Mai P. Hoang, MD
Dallas, Texas

11 patients with Hashimoto-Pritzker disease

M:F=4:7; 10 cases at birth; 1 case at 1 month

7 cases with solitary lesions

4 cases with multiple lesions

8 patients with skin involvement in LCH

M:F=3:5; 1 case at birth (age range 0-6y)

7 patients alive w/o disease

1 patient died after liver Tx

Neonatal and Early Infantile Cutaneous Langerhans Cell Histiocytosis

Comparison of Self-regressive and Non–Self-regressive Forms

Objectives: ... **Design:** ... **Setting:** ... **Patients:** ... **Main Outcome Measures:** ... **Results:** ... **Conclusions:** ...

21 patients with self-regressing LCH

M:F=10:11; 15 cases at birth

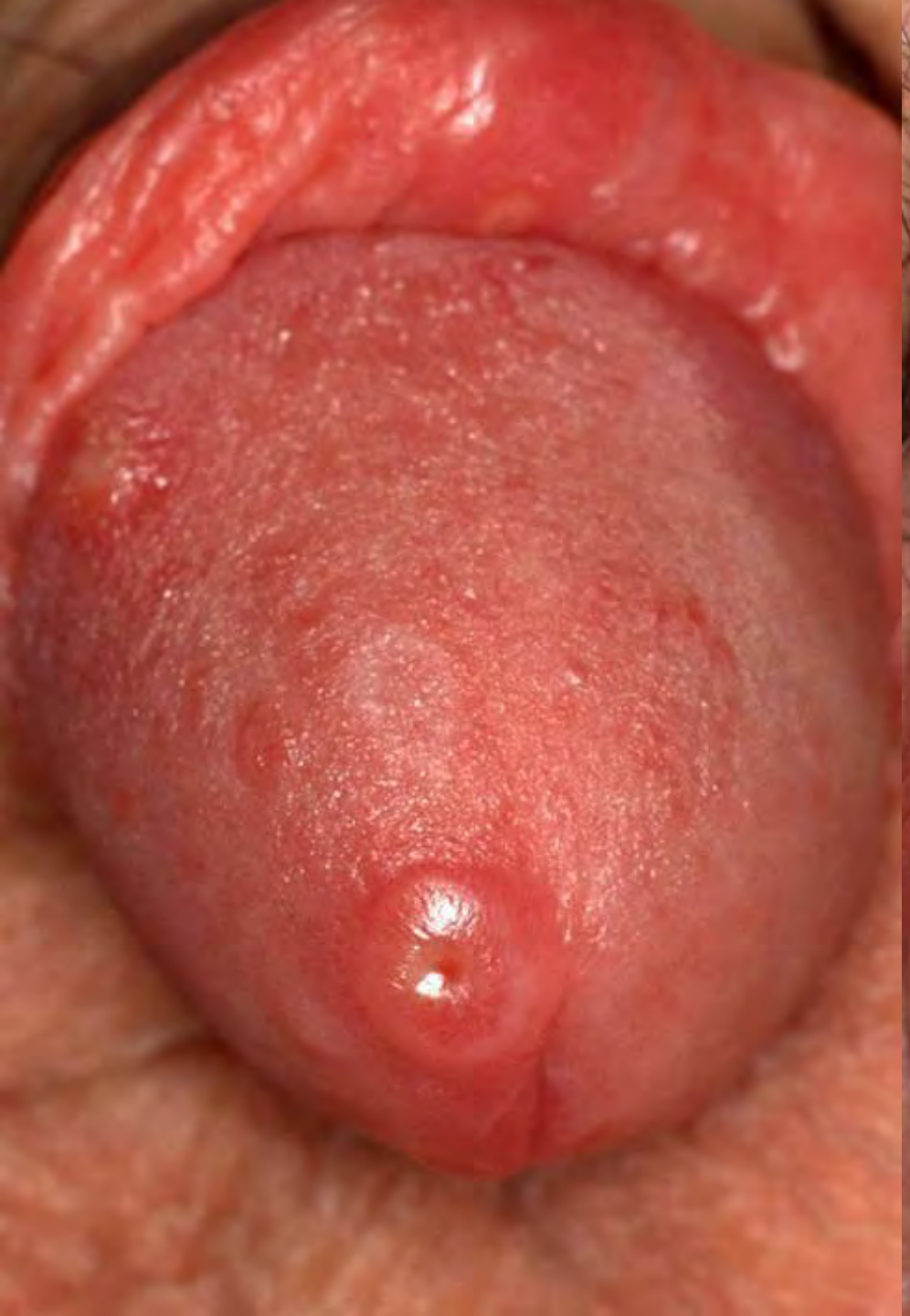
4 cases with solitary lesions

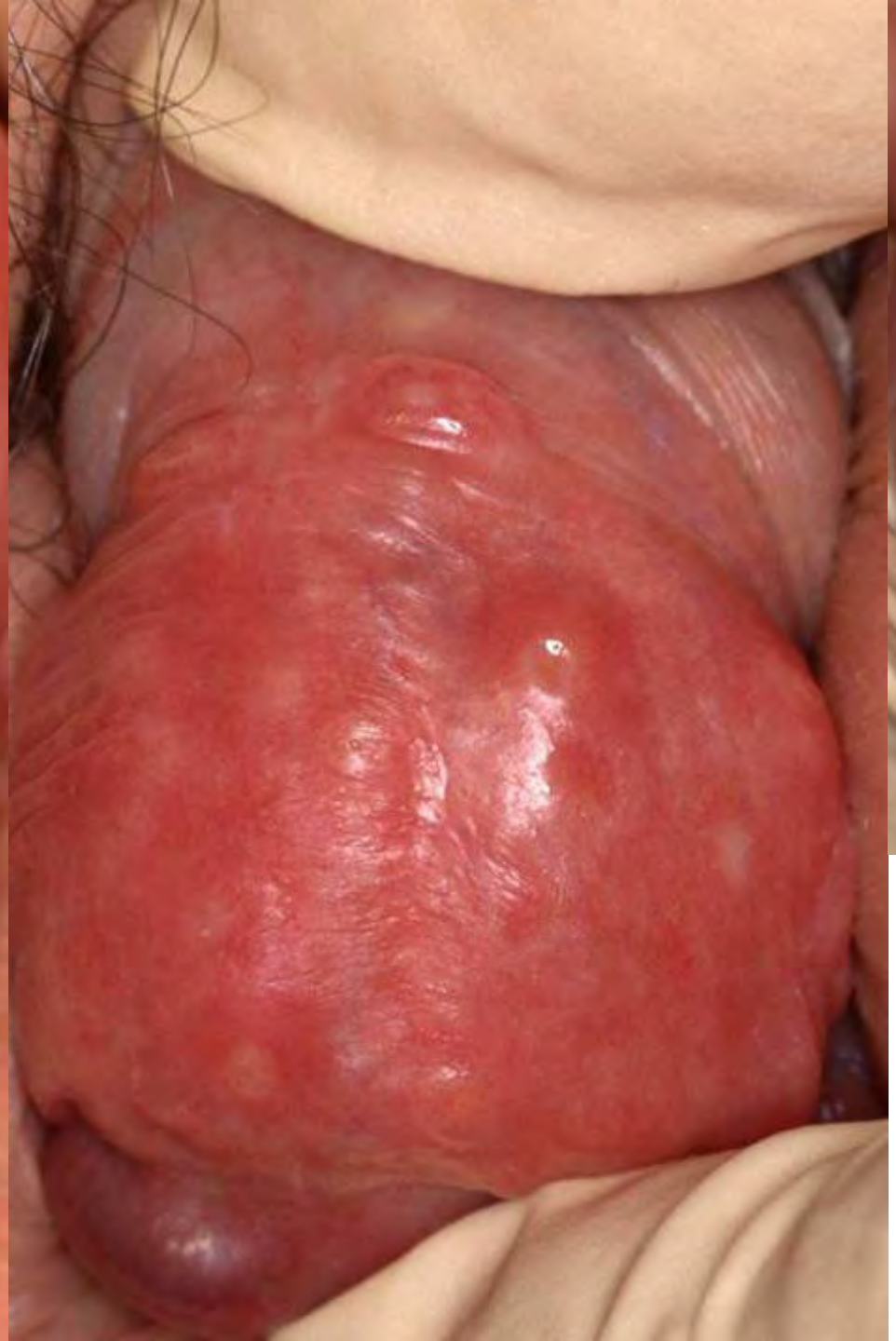
17 cases with multiple lesions

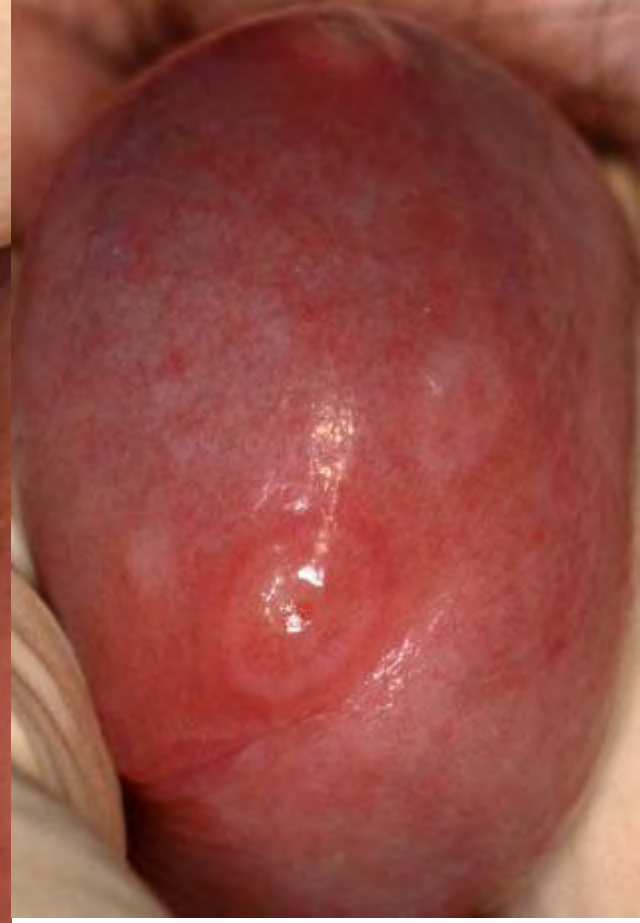
10 patients with non-self-regressing LCH

M:F=5:5; 1 case at birth

No case presenting with a solitary lesion



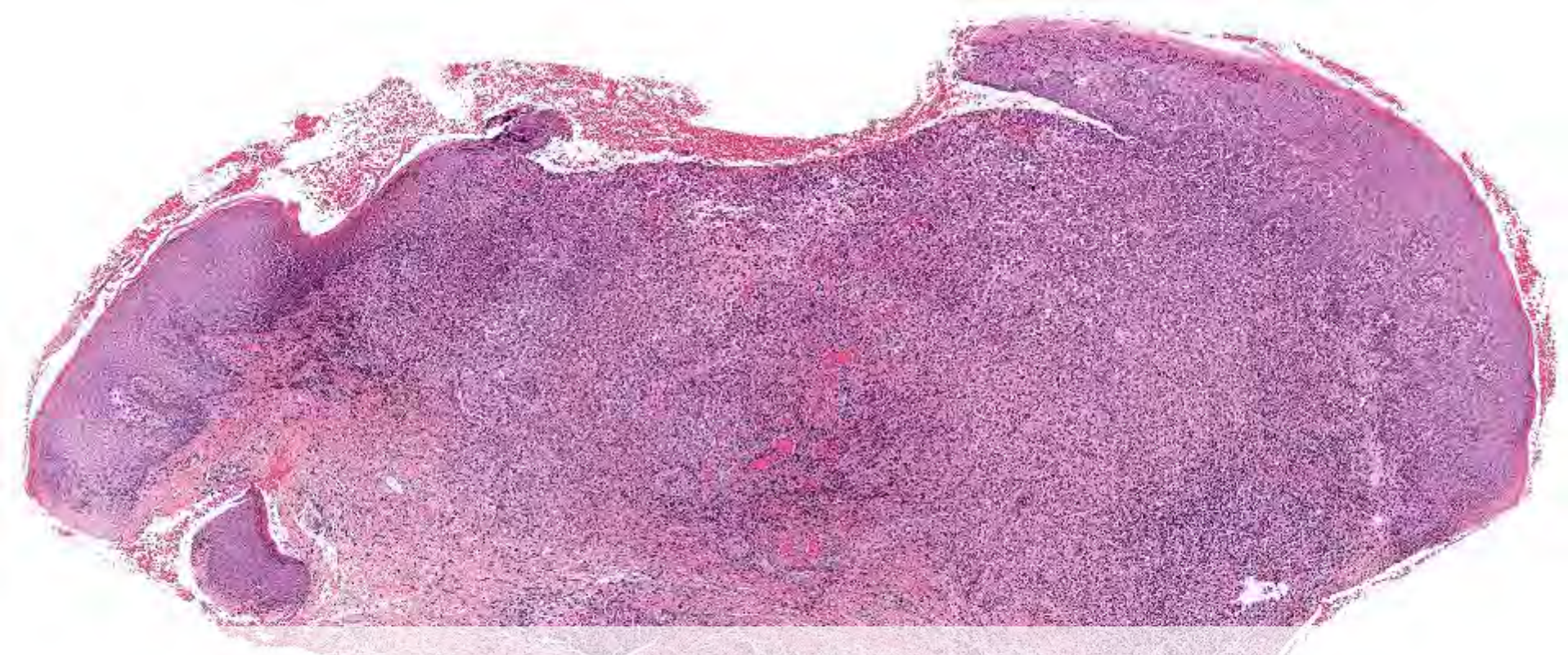


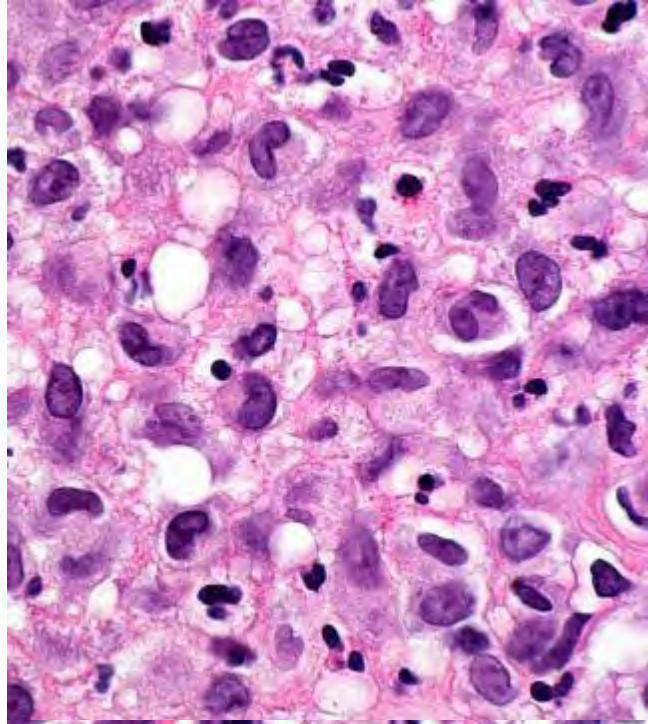


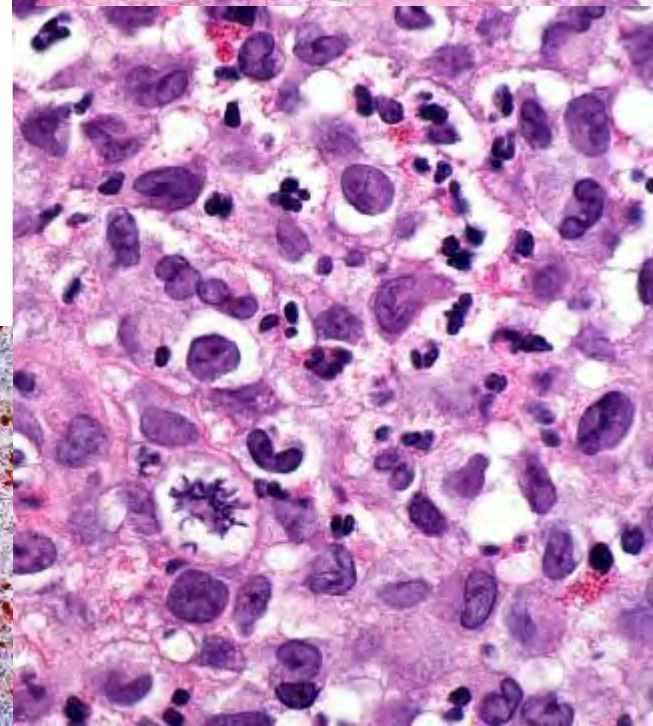
M, 15

According to the patient eroded papules and small vesicles on the glans penis and preputium for a few weeks.

A biopsy is taken.

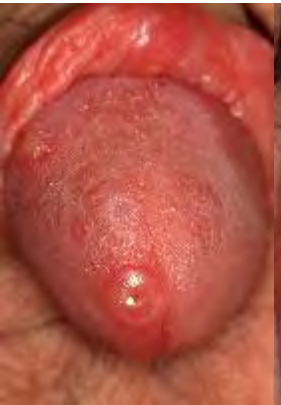


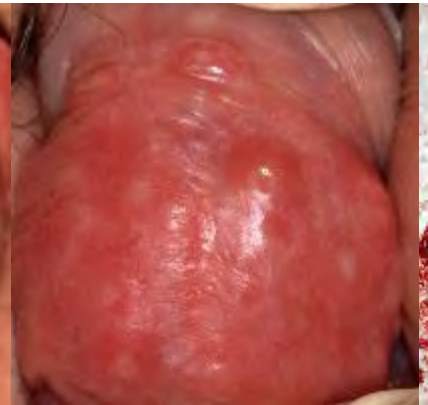


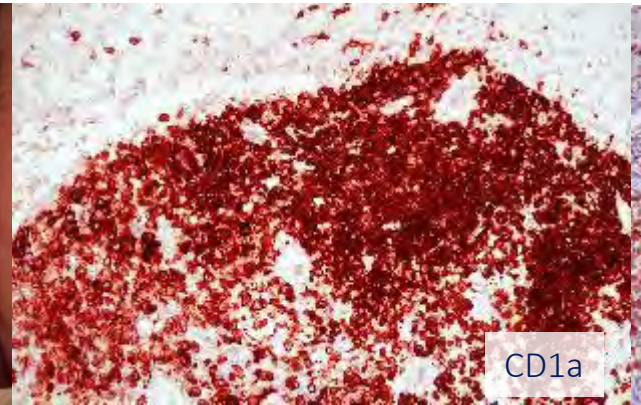


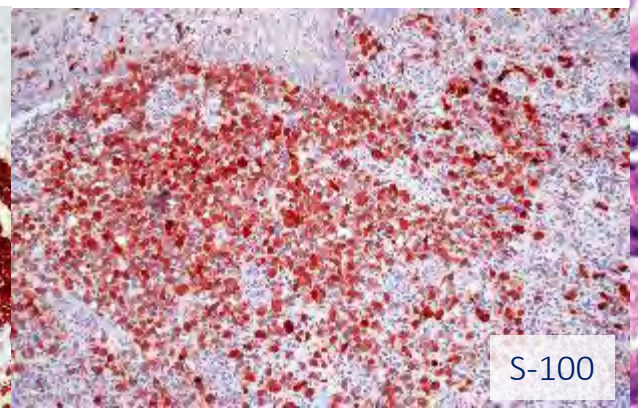
Localized Langerhans cell histiocytosis

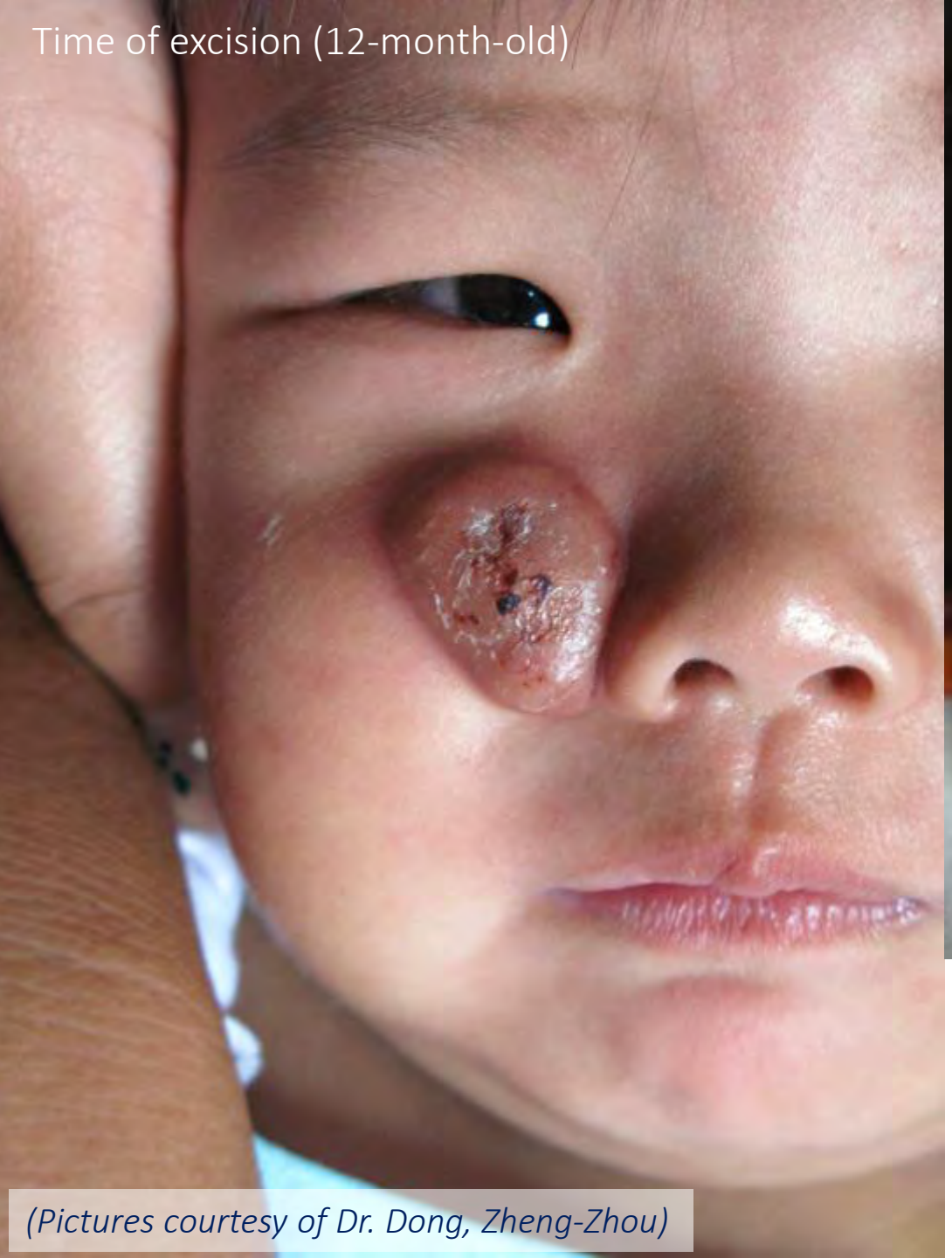
(Staging investigations negative; subsequently developed lung involvement; managed with systemic steroids, mercaptopurine and methotrexate for 4 years: alive and well 16 years after first diagnosis)

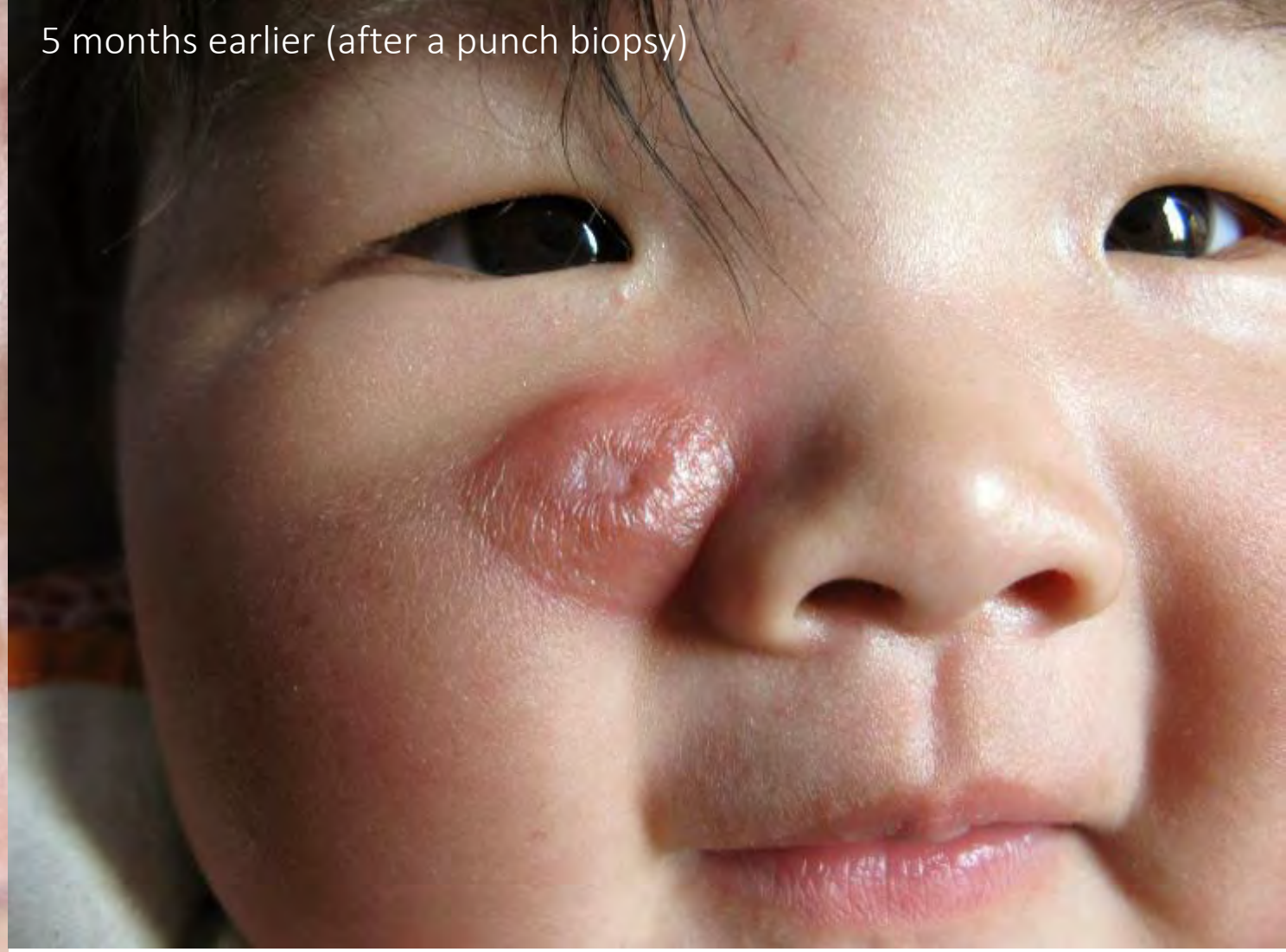








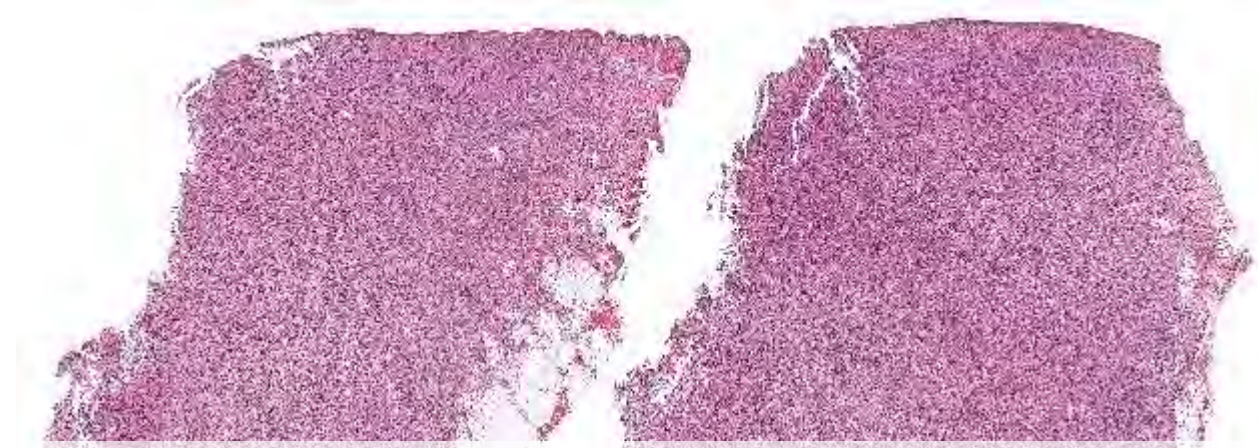


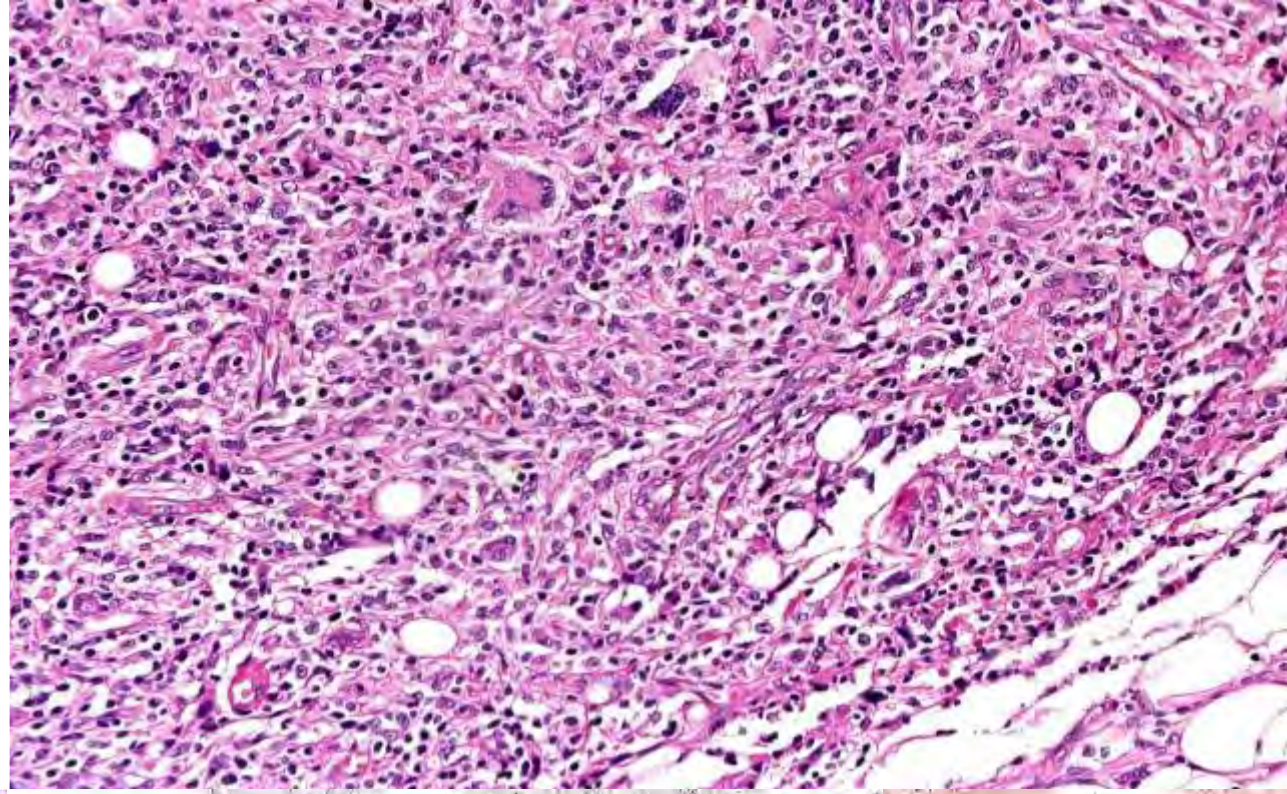


(Pictures courtesy of Dr. Dong, Zheng-Zhou)

F, 12-month-old

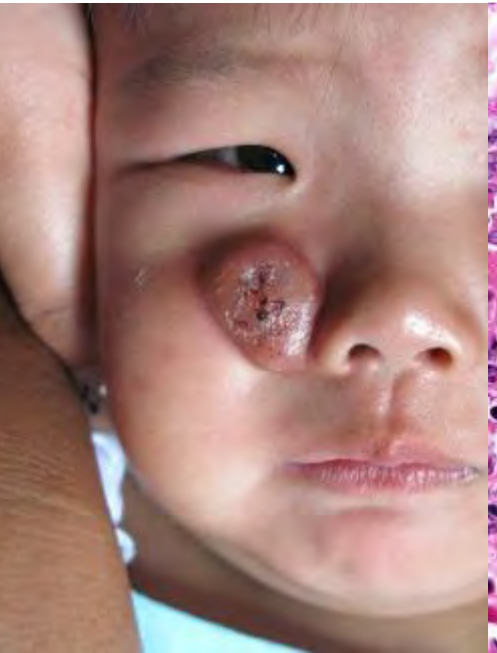
A 4 mm large papule was present at birth on the right cheek. A punch biopsy at the age of 7 months was interpreted as juvenile xanthogranuloma. Continuous growth over the following months. Complete excision at the age of 12 months.

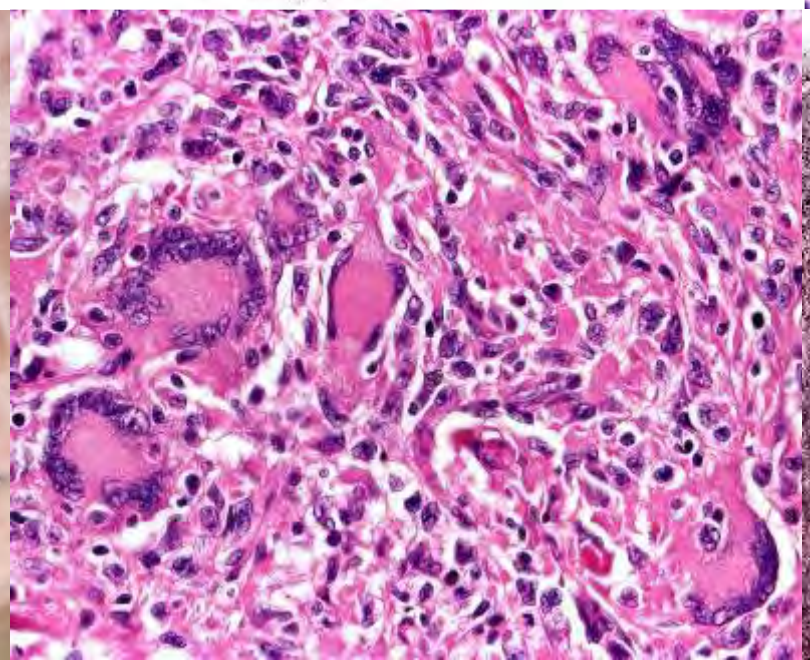


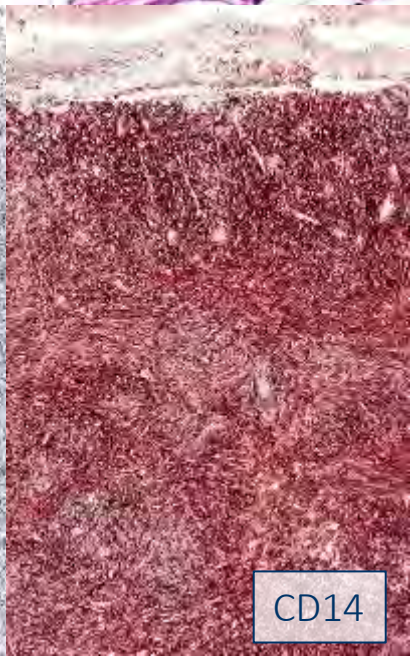


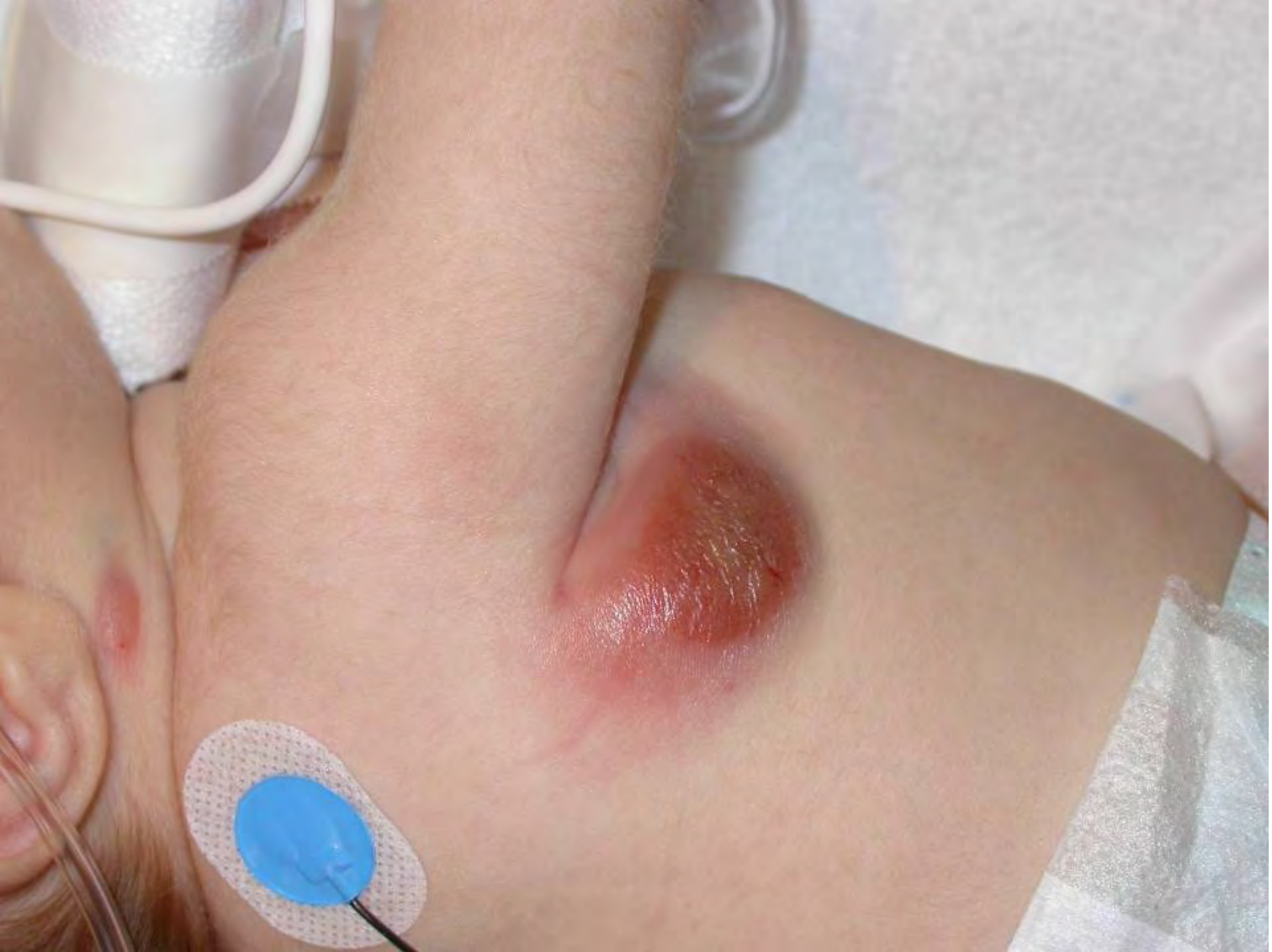
Rapid growing congenital juvenile xanthogranuloma

No evidence of extracutaneous disease at follow-up









Female newborn

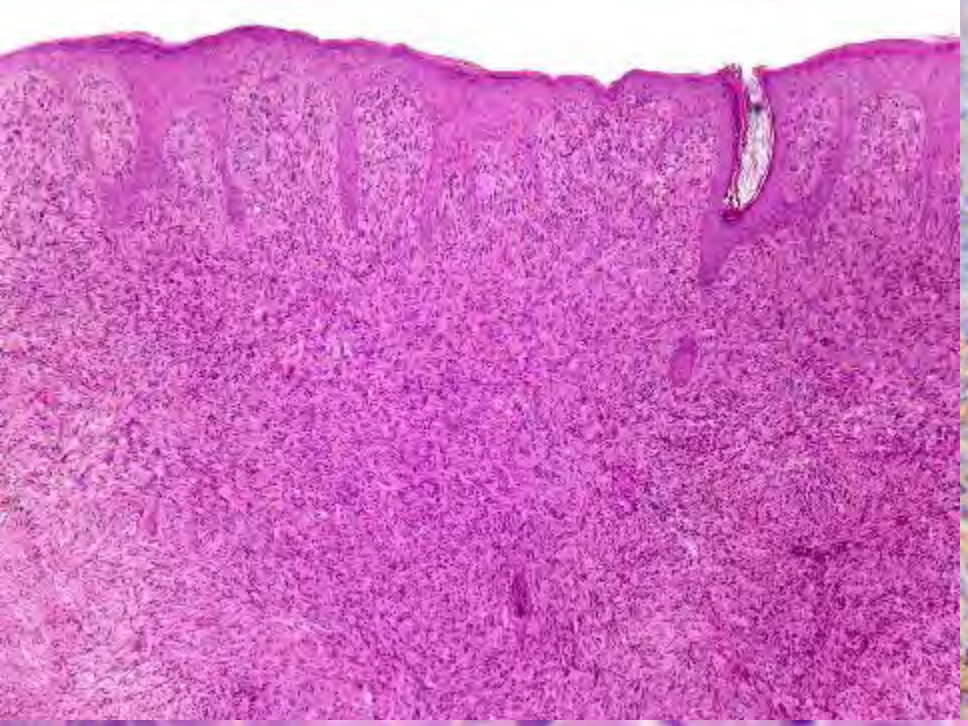
Normal pregnancy and labor; no remarkable familial history.

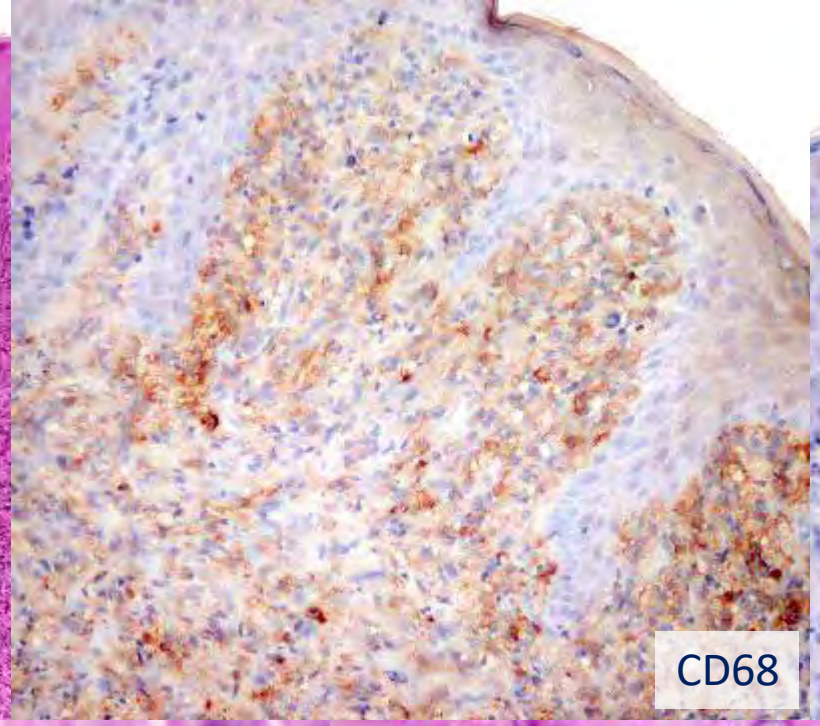
Three large, red-brownish nodules on the trunk and neck, present at birth.

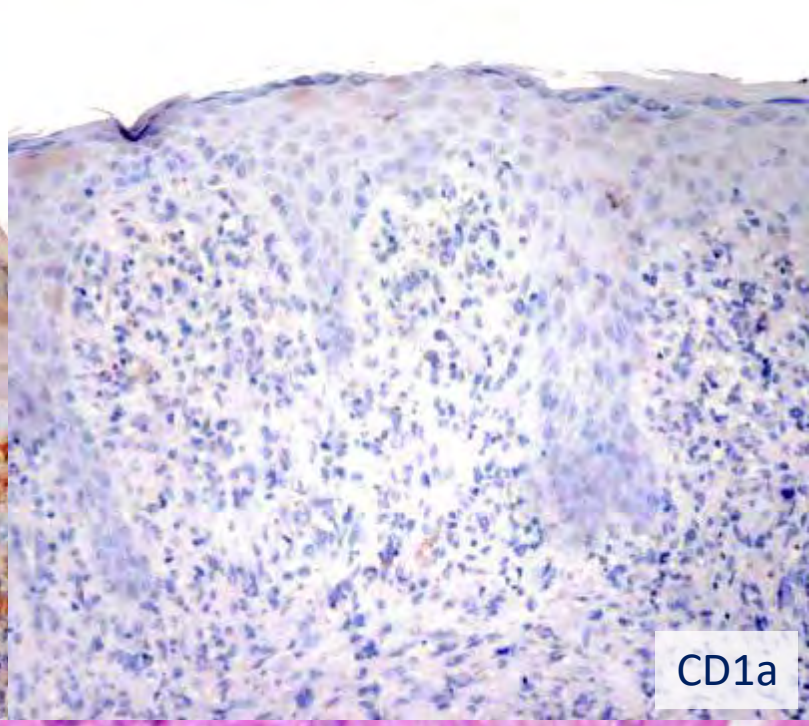
Anemia (Hgb 7,7 g/dl), severe thrombocytopenia (10.000/mm^3) and leukopenia (110/mm^3).

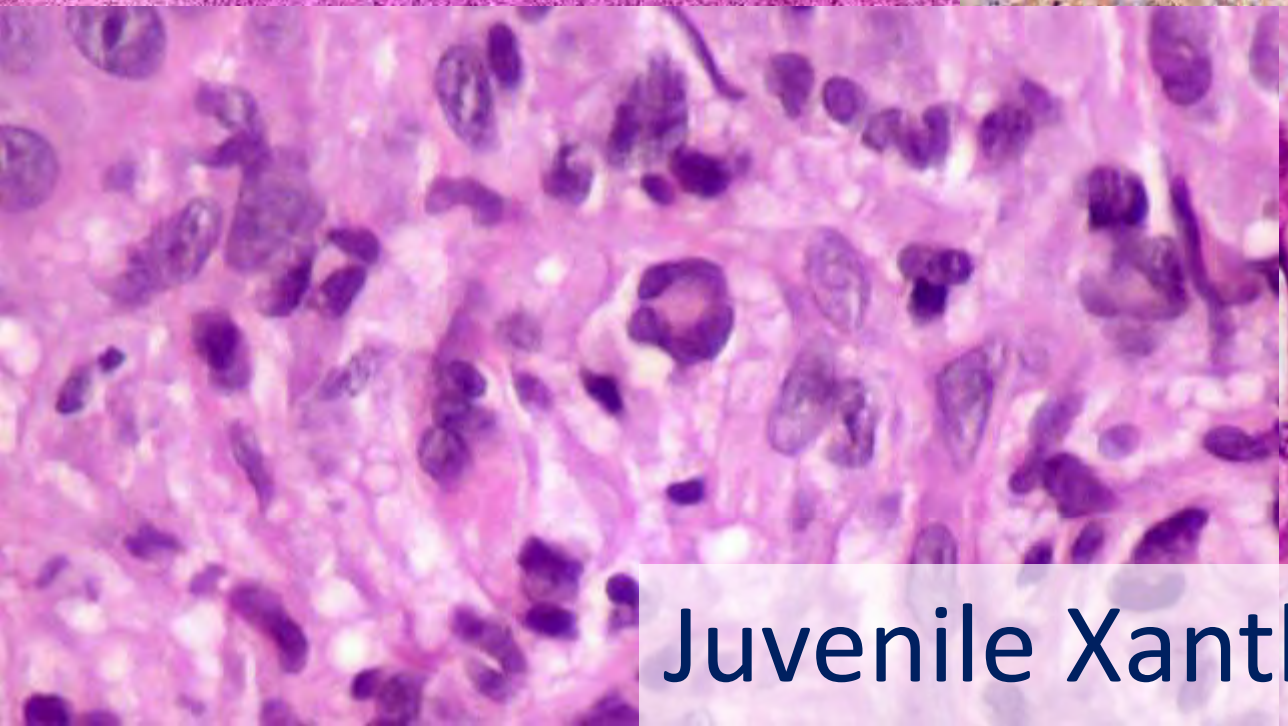
Serum chemistry: increased AST (500 U/l), ALT (809 U/l), and bilirubin (24.20 mg/dl).

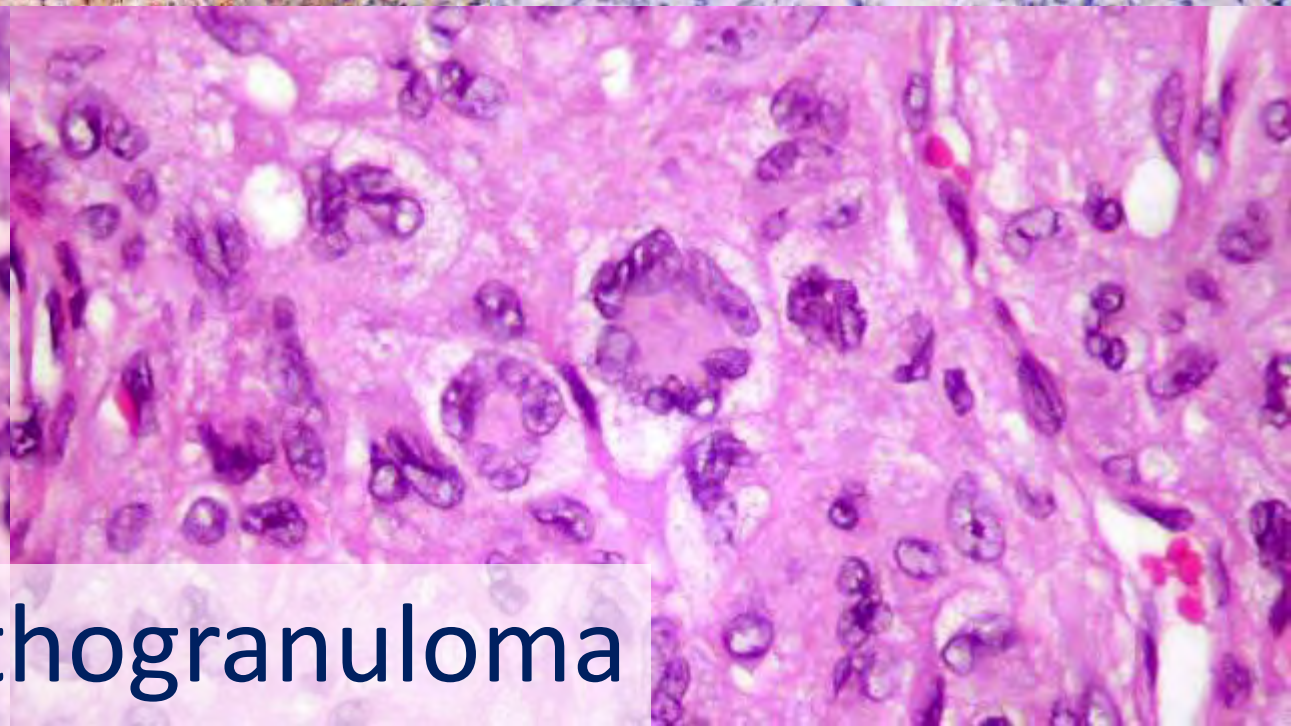
(Courtesy Dr. A. Torrelo, Madrid)



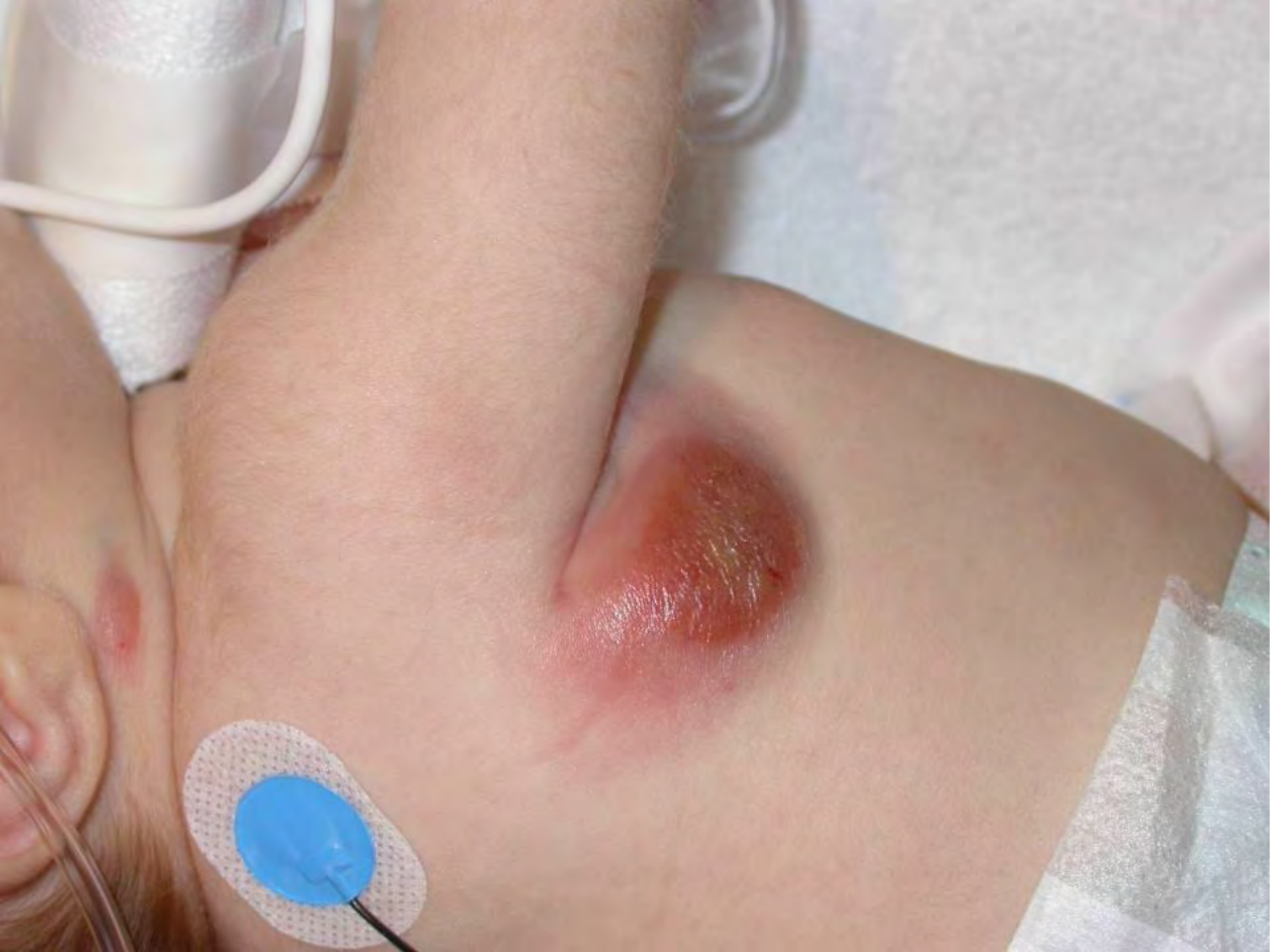








Juvenile Xanthogranuloma



Bone marrow biopsy: almost absent stromal tissue.

Liver biopsy: diffuse infiltration by XG.

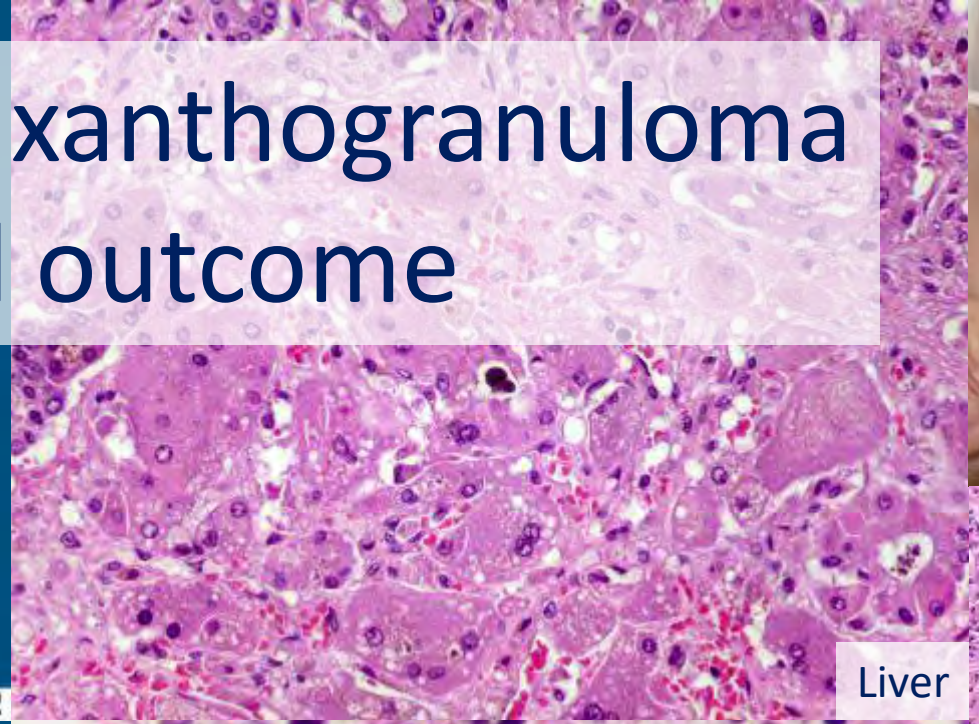
Rx survey, brain MR, cytogenetic studies, studies for leukemia translocations, and complete serological work-up: normal or negative.

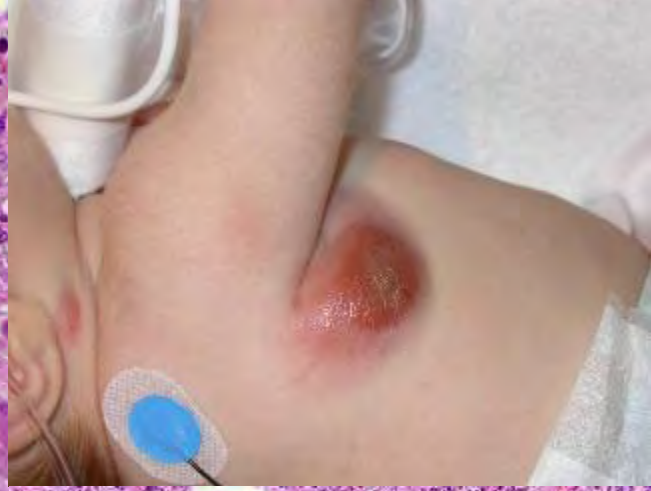
Therapy: prednisolone + vinblastine.

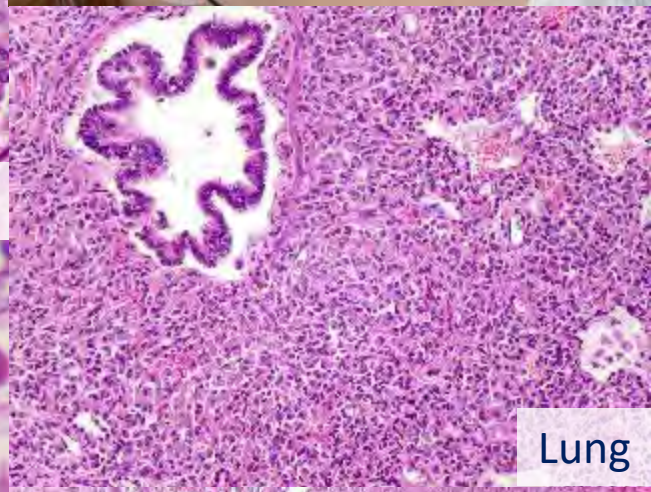
Progressive hepatic failure; cytarabine and methotrexate added.

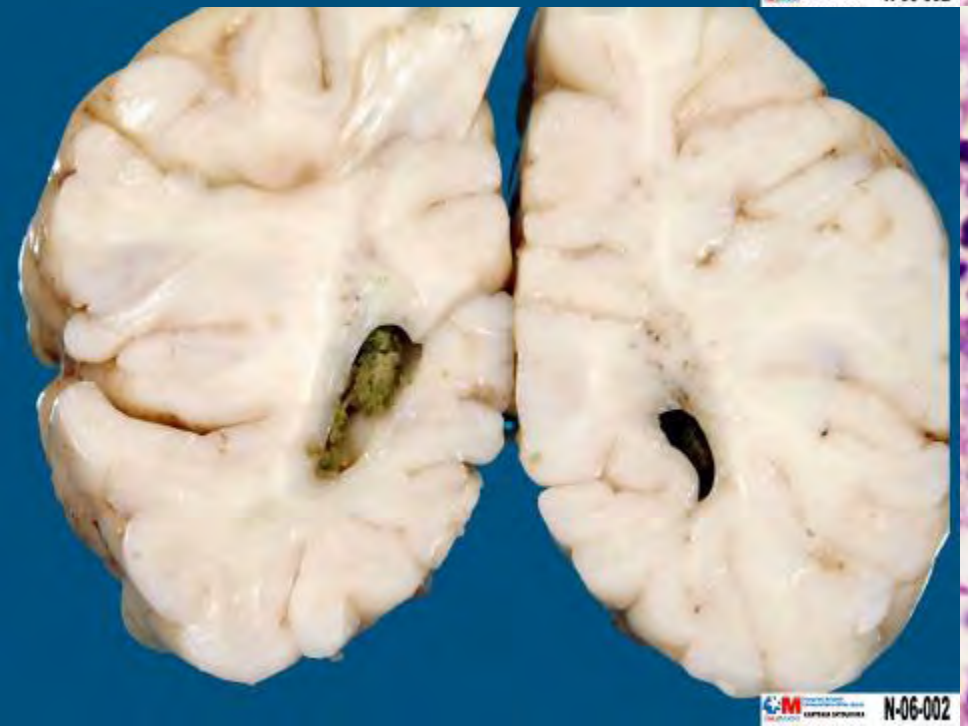
No response (skin, liver, bone marrow aplasia).

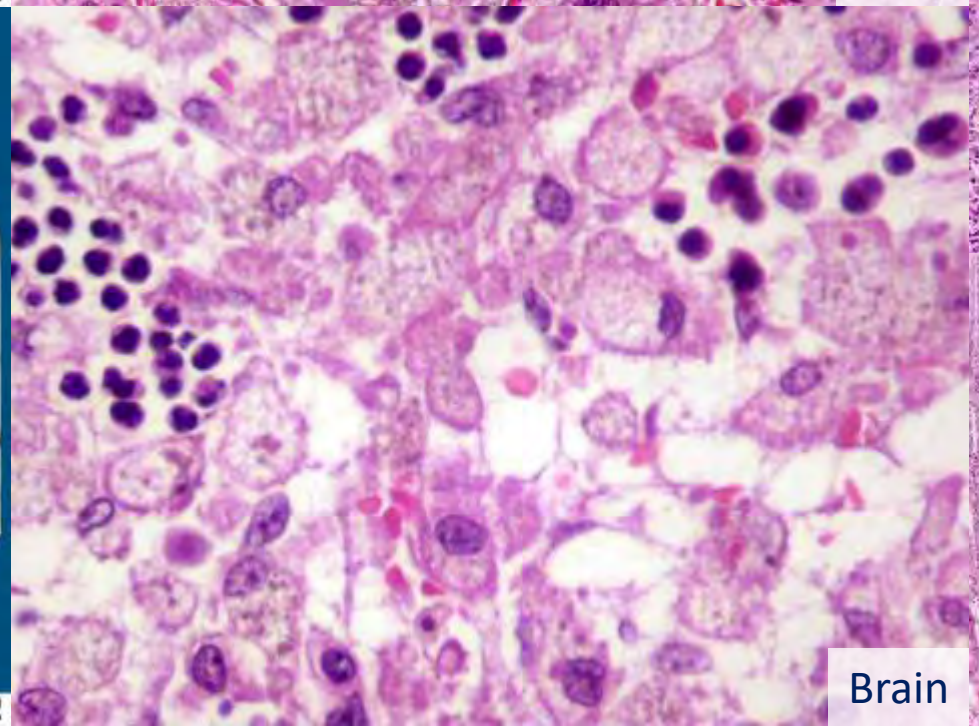
Systemic juvenile xanthogranuloma with fatal outcome

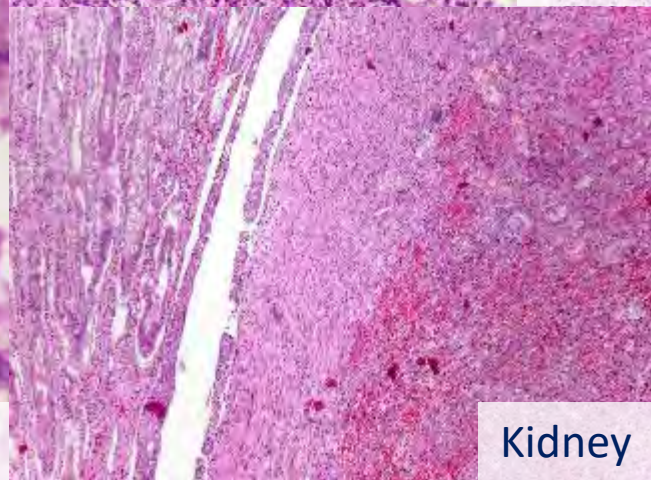












Pediatric Dermatology Vol. 26 No. 6 709–712, 2009

Systemic Juvenile Xanthogranuloma with Fatal Outcome

Daniel Azorín, M.D.,* Antonio Torrelo, M.D.,† Alvaro Lassaletta, M.D.,‡ Inmaculada de Prada, M.D.,* Isabel Colmenero, M.D.,* Trinidad Contra, M.D.,† and Imelda González-Mediero, M.D.*

*Departments of *Pathology, †Dermatology, and ‡Oncology, Hospital del Niño Jesus, Madrid, Spain*

Abstract: Juvenile xanthogranuloma is a benign and self-limited disease which usually appears in the skin of children. Visceral involvement has been rarely reported, as has fatal outcome in some affected individuals. We report a case of systemic juvenile xanthogranuloma in a female newborn with mainly skin, bone marrow, and liver involvement, leading to death at the age of 2 months.

Juvenile xanthogranuloma (JXG) is a common benign histiocytic disorder which usually appears in children as a solitary cutaneous lesion, but sometimes may involve internal organs. We report a female newborn who has hyperbilirubinemia and pancytopenia from the first 48 hours of life along with large skin lesions as the initial presentation of systemic JXG. Subsequently, she developed hepatic failure and eventually died at 2 months of age.

CASE REPORT

A Caucasian newborn female was referred to our institution for evaluation of pancytopenia and skin lesions which were present at birth. She was the second child of healthy parents, weighing 2,800 g at full-term delivery after an uneventful pregnancy. Both her blood group and her mother's were A positive. A previous 10 day treatment with gammaglobulin and corticosteroids had not improved her hematologic status.

On admission, the baby had three large yellowish brown skin nodules on her right axilla, neck, and back (Fig. 1). Slight hepatomegaly was seen, but the rest of the clinical examination was otherwise normal. A laboratory work-up disclosed severe anemia (7.7 g/dl), thrombocytopenia (10,000/mm^3), and leukopenia (1,700/mm^3). Serum chemistry was remarkable for increased AST (500 U/L), ALT (389 U/L), etc. bilirubin (24.20 mg/dL), the rest of the parameters including serum triglyceride, ferritin, and fibrinogen levels, were normal. An extensive serological work-up for neonatal disorders including TORCHES (Toxoplasma, Rubella, Cytomegalovirus, Herpes, Syphilis) was negative. A skin biopsy from the axillary lesion showed a dense cellular infiltrate extending from the dermis into the subcutaneous fat, composed of a mixed population of foamy macrophages, lymphocytes, and Touton giant cells (Fig. 2). Immunohistochemistry showed reactivity for CD68 and factor XIIIa, whereas the proliferating cells were negative for CD1a and S100 protein. Bone marrow (BM) biopsies were performed, but we were not able to collect sufficient amount of tissue for a diagnosis. Ultrasonography, abdominal ultrasound, and brain magnetic resonance imaging were normal. Cytogenetic and molecular biology studies were negative. A liver biopsy was carried

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TABLE 1. *Cases of Systemic Juvenile Xanthogranuloma with Mortal Outcome*

Reference	Age	Sex	Sites of involvement	Outcome/follow-up
Freyer et al (1)	12 yrs	NA	Soft tissue, eye, oropharynx, CNS	DOD/8 yrs
Freyer et al (1)	7 mos	NA	Oropharynx, liver, CNS	DOD/NA
Oehner (2)	Birth	M	Liver, spleen, lungs	DOD/2 mos
Janssen and Harms (3)	Birth	F	Lung, heart, liver, spleen, kidney, intestine, bone marrow	DOD/34 days
Hu et al (8)	Birth	F	Liver, spleen, diaphragm, pancreas, lymph nodes	DOD/29 days
Present case	Birth	F	Liver, lungs, kidneys, bone marrow	DOD/78 days

NA, not available; F, female; M, male; CNS, central nervous system; DOD, died of disease.

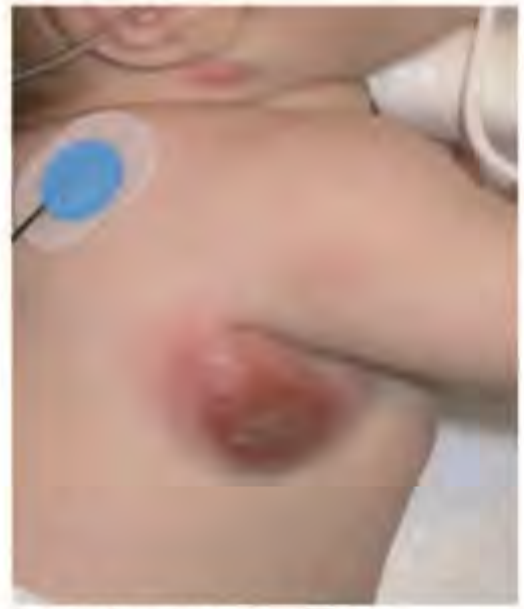

Figure 1. Skin nodules on the axilla and neck.

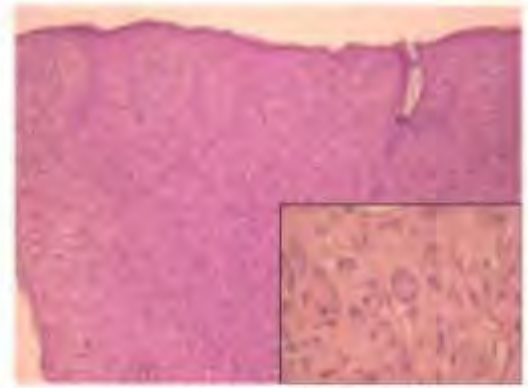

Figure 2. A histiocytic dermal infiltration. Inset foamy histiocytes and Touton giant cells within the infiltrate.

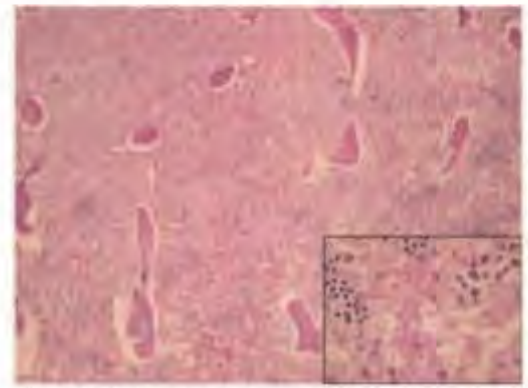

Figure 3. Bone marrow at autopsy showing massive infiltration by foamy histiocytes (see inset).

36 systemic cases
(2 deaths)

174 cases of JXG
(8 systemic, 3 deaths)

129 cases of JXG
(5 systemic, 1 death)


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https://doi.org/10.1007/s00277-024-05955-x

RESEARCH

Clinical features and outcomes of 17 children with systemic juvenile xanthogranuloma (sJXG) including five complicated with hemophagocytic lymphohistiocytosis (HLH)

Yunze Zhao · Tong Zou · Ang Wei · Honghao Ma · Hongyun Lian · Dong Wang · Zhigang Li · Tianyou Wang · Rui Zhang

Received: 16 January 2024 / Accepted: 16 August 2024 / Published online: 25 August 2024
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Abstract

Keywords Systemic juvenile xanthogranuloma · Hemophagocytic lymphohistiocytosis · Hepatosplenomegaly · Prognosis

Abbreviations

17 children, all with systemic involvement; 9 with skin lesions

1 patient died

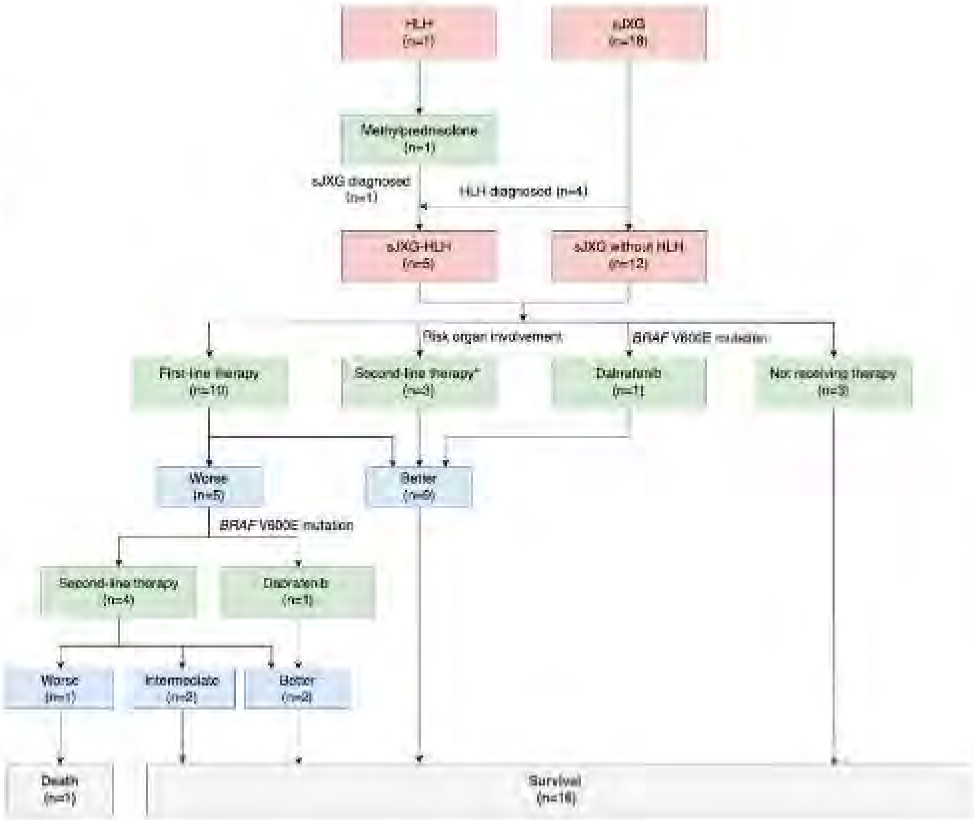
15 patients alive with disease (8 stable, 7 better)

Hemophagocytic lymphohistiocytosis: 5 cases

Juvenile myelomonocytic leukemia: 1 case

Histiocytic sarcoma: 1 case

Fig. 1 Treatment strategy and response of 17 sJXG patients, including five complicated with hemophagocytic lymphohistiocytosis. *Patient 1 was initially treated with second-line therapy and then underwent liver transplantation for liver failure. This part was not shown in the figure



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REVIEW

Pediatric Blood & Cancer aspho WILEY

Systemic juvenile xanthogranuloma: A systematic review

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Abstract

Objective: To perform a systematic review to investigate the available literature regarding systemic juvenile xanthogranuloma (SJXG) and report the population characteristics, clinical manifestation, therapy and outcome.

Review methods: A search of PubMed, Embase, and Cochrane Library for all articles published between 1981 and 2022 was performed with variations and combinations of the following search terms: extracutaneous, visceral, systemic, and juvenile xanthogranuloma (JXG). Data extracted included demographics, organ involvement, treatment, outcome and permanent sequelae.

Results: A total of 100 articles encompassing 157 patients met the inclusion criteria. The median onset age was 9 months, with a male predominance (61%). The distribution of major involved organs varied by age, and younger onset age was associated with more organ involvement. The most commonly involved site was the central nervous system (CNS) (40.9%), followed by the liver (31.4%), the lung (18.9%), and the eye (18.2%). At the termination of follow-up, 93 patients (58.5%) were alive with no disease, 56 (35.2%) were alive with disease and 10 (6.3%) were dead of disease. There was a significant difference in outcome between patients with and without spleen involvement ($p = .0003$), and patients with spleen involvement suffered a higher risk of death. Permanent sequelae mainly comprised CNS symptoms and ocular manifestations.

Conclusions: SJXG can involve varying numbers and combinations of extracutaneous sites. There is no standard therapy for SJXG and clinicians should choose individualized therapy modalities.

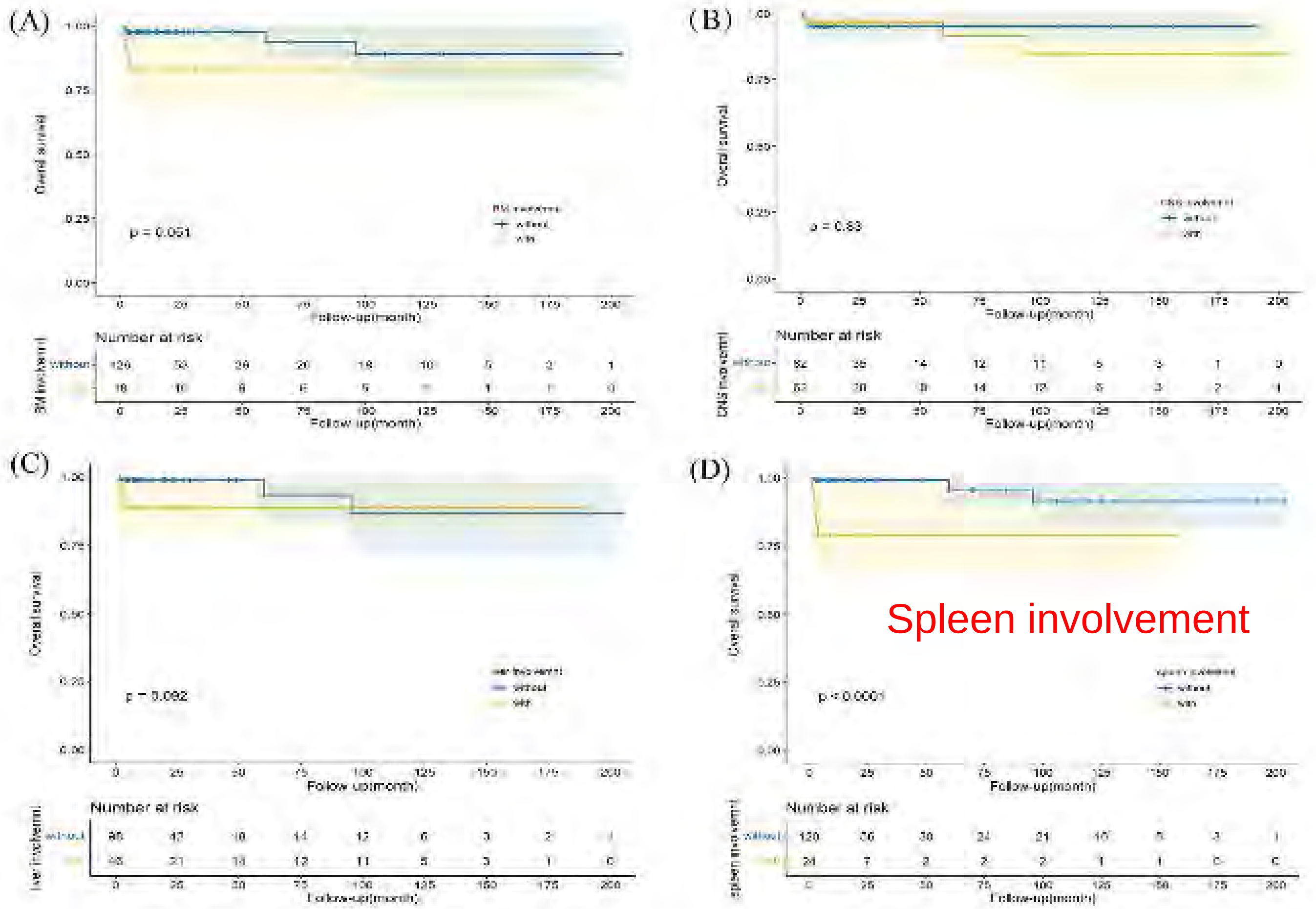
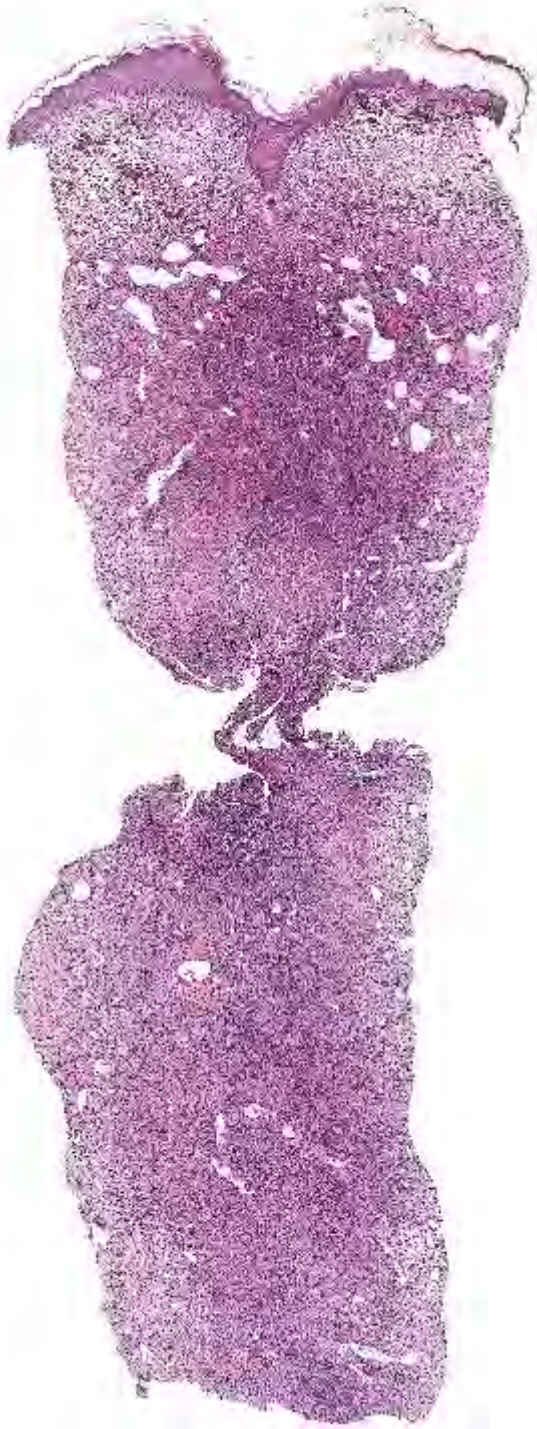
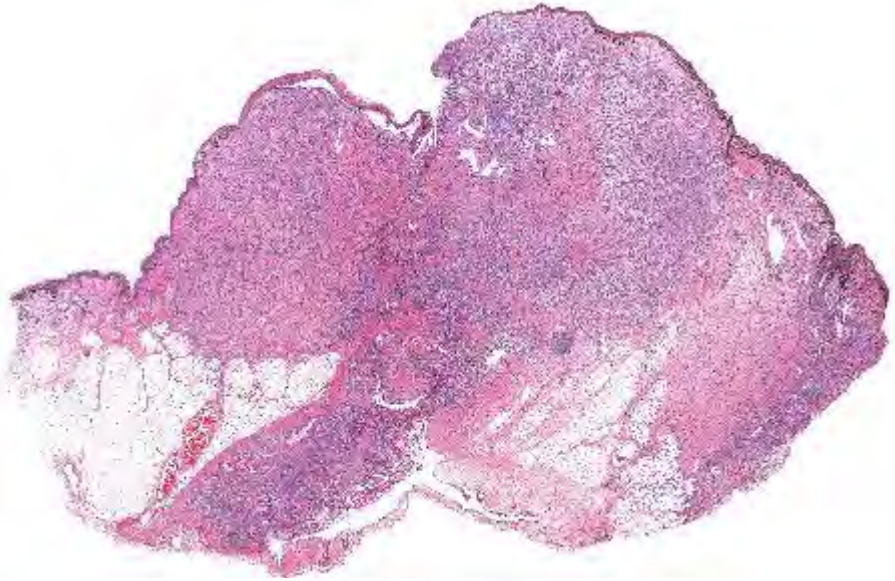
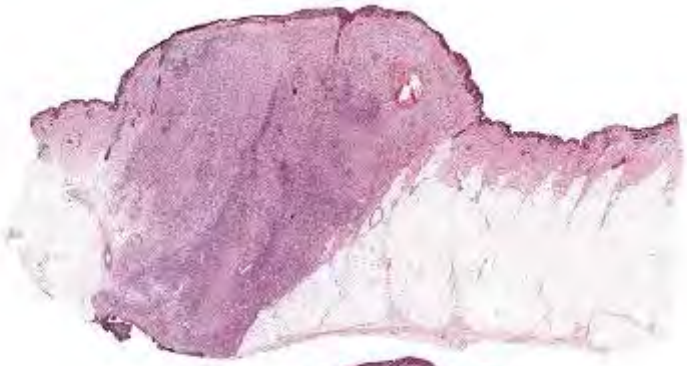
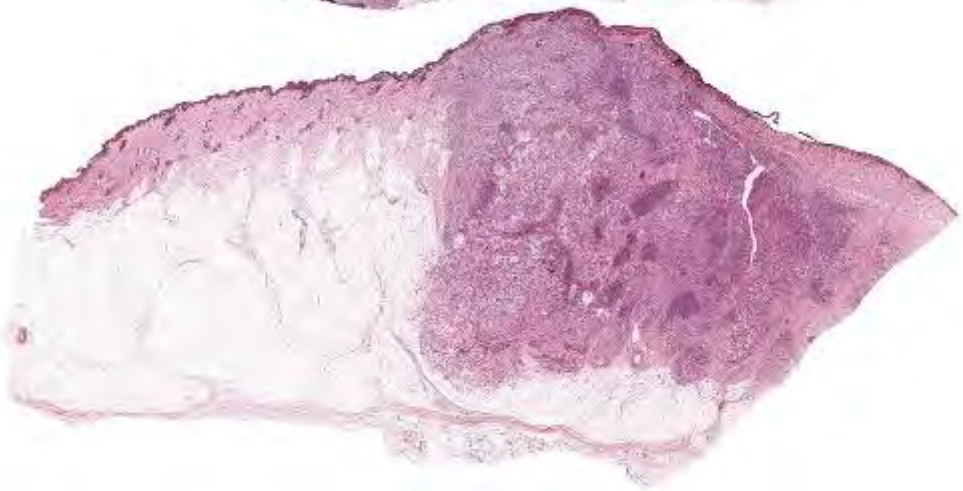


FIGURE 3 Kaplan–Meier survival curves regarding different visceral involvements. (A–C) There is no significant difference between BM/CNS/liver involvements and OS. (D) There is a significant correlation between spleen involvement and OS ($p < .0001$). Median survival is not reached.



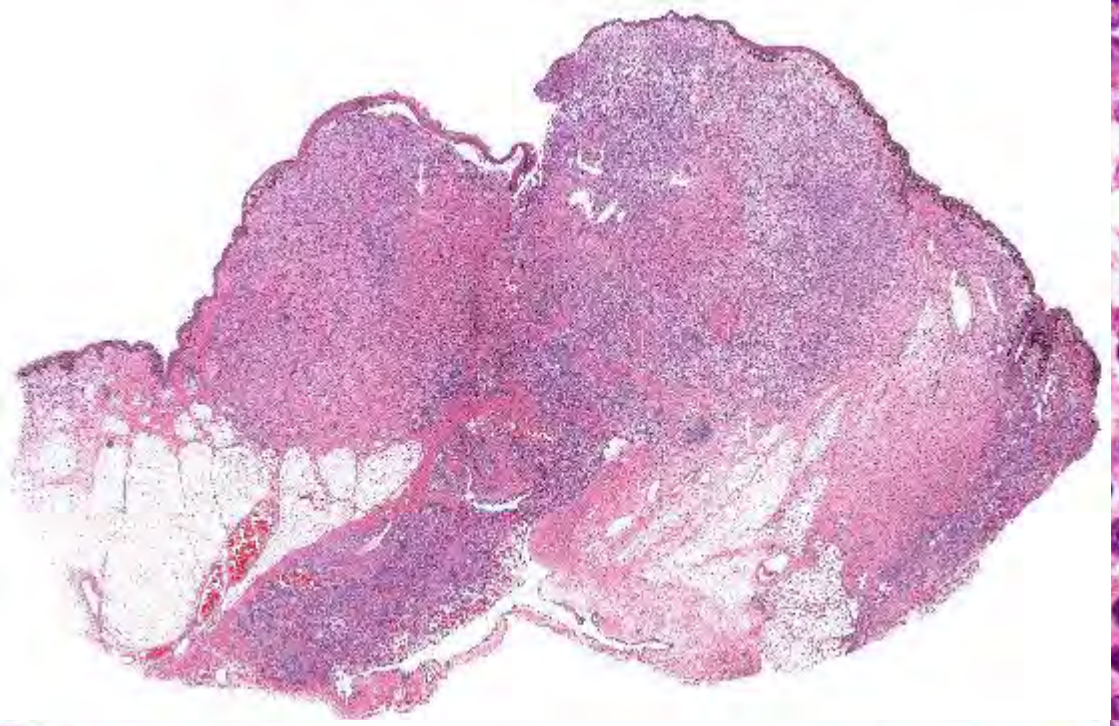


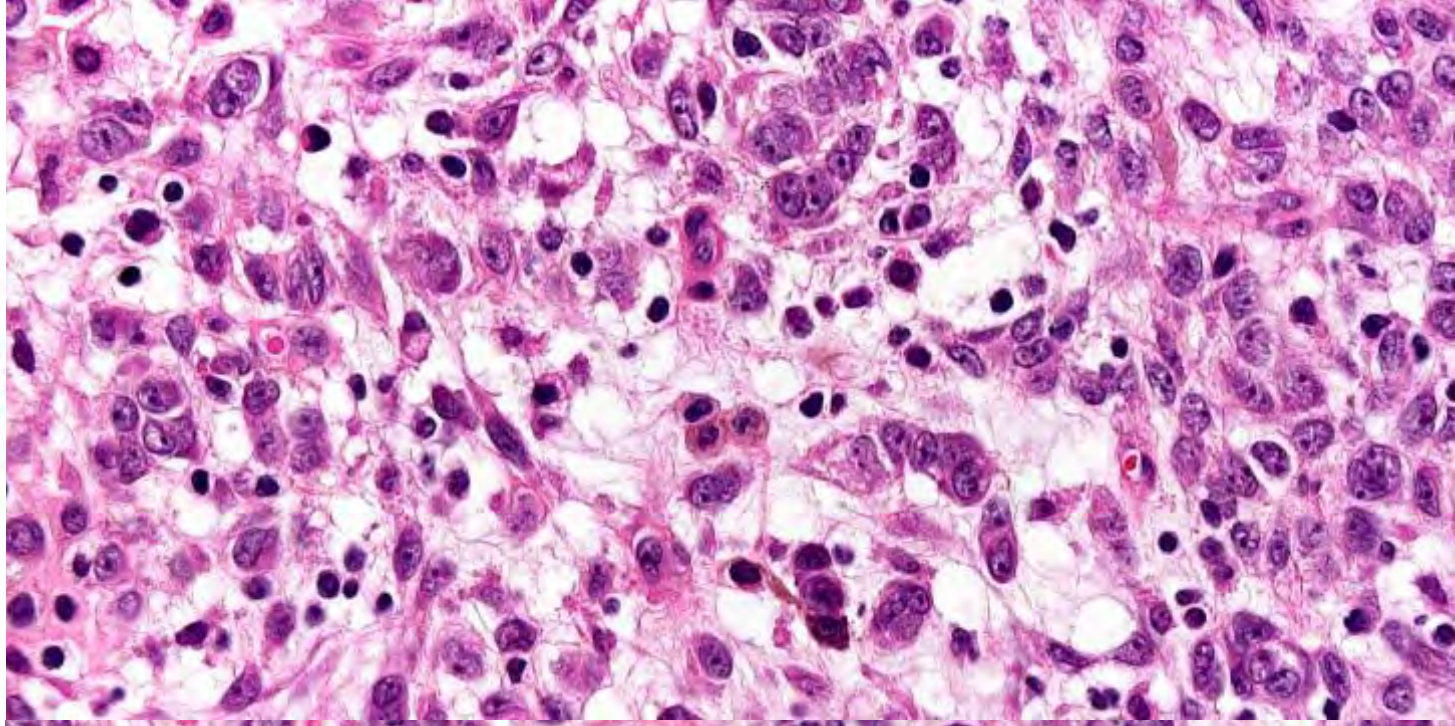


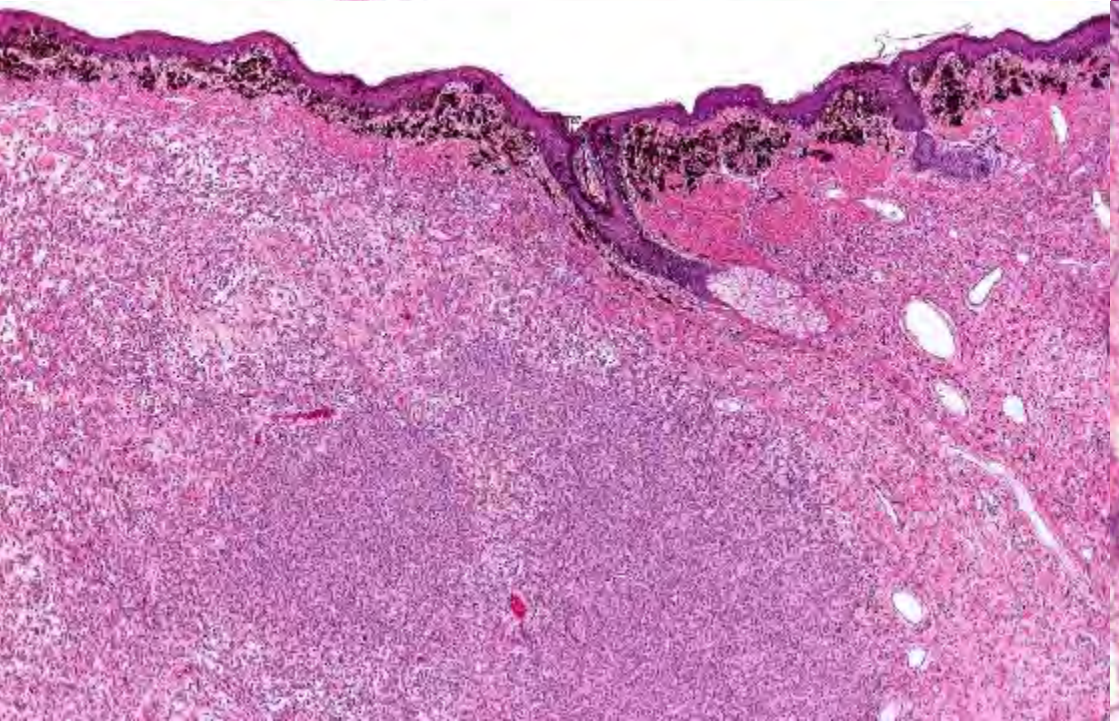


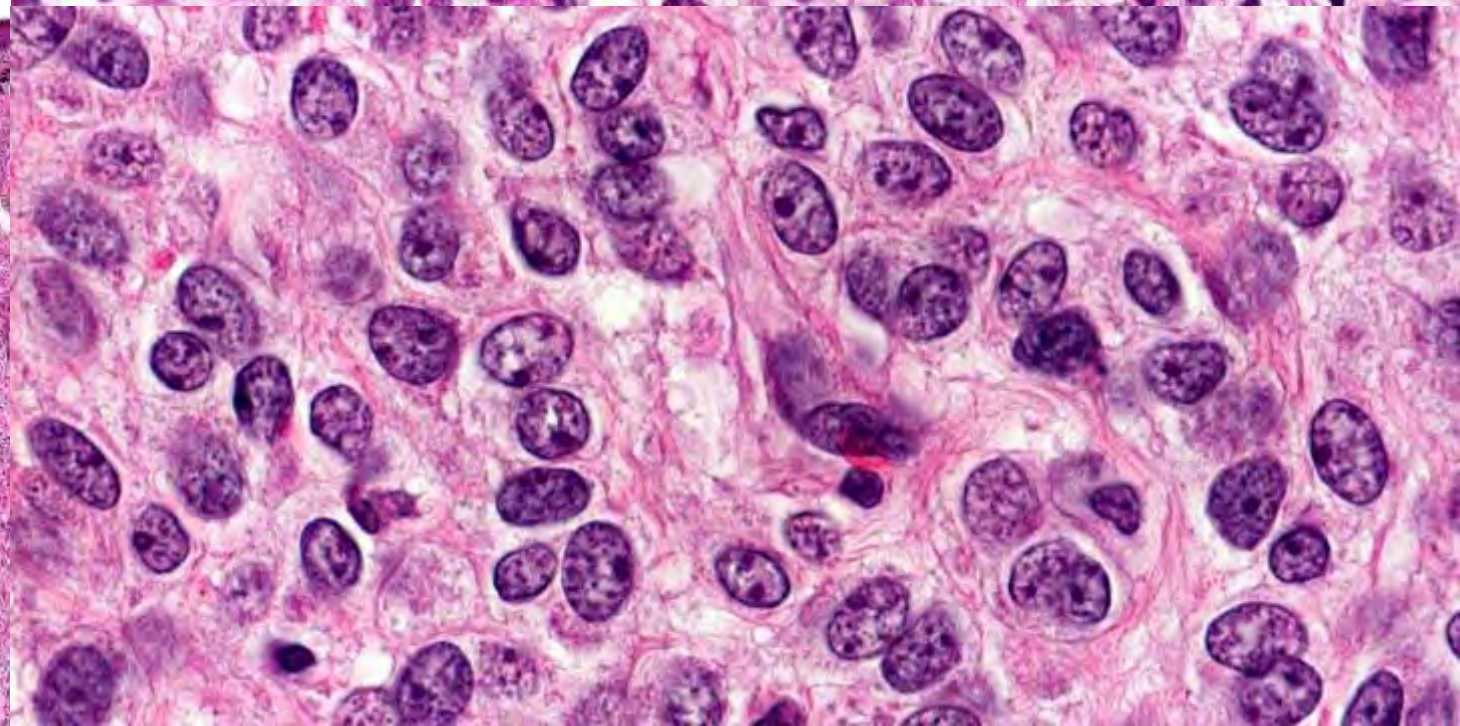
Male newborn.

Courtesy Dr. Boldrini (Napoli) and Dr. Ferrara (Benevento)

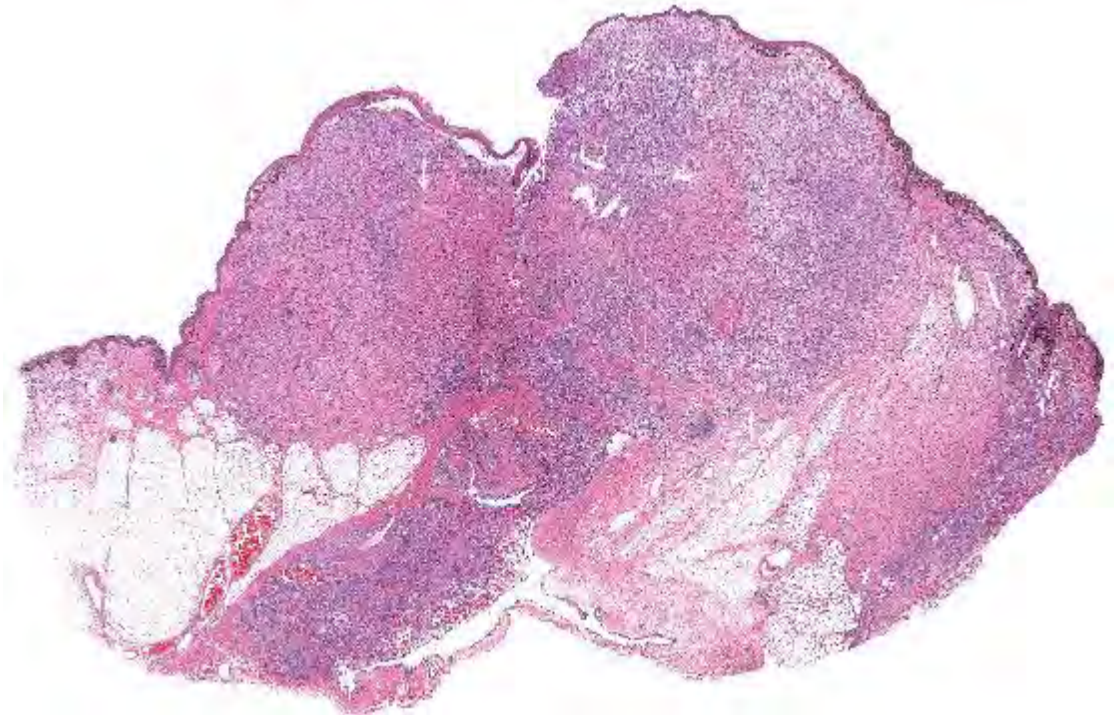


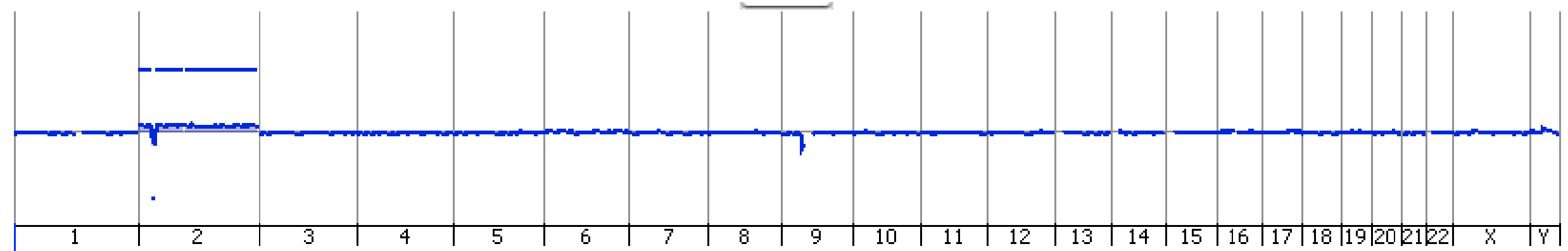


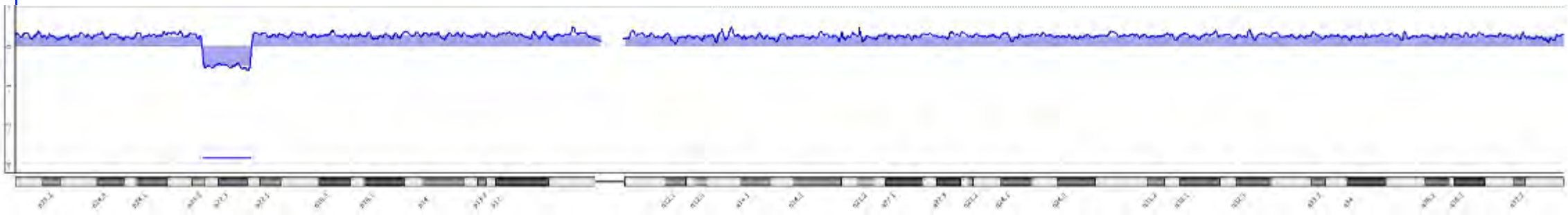




Lesion excised partially; patient alive and well 7 years later



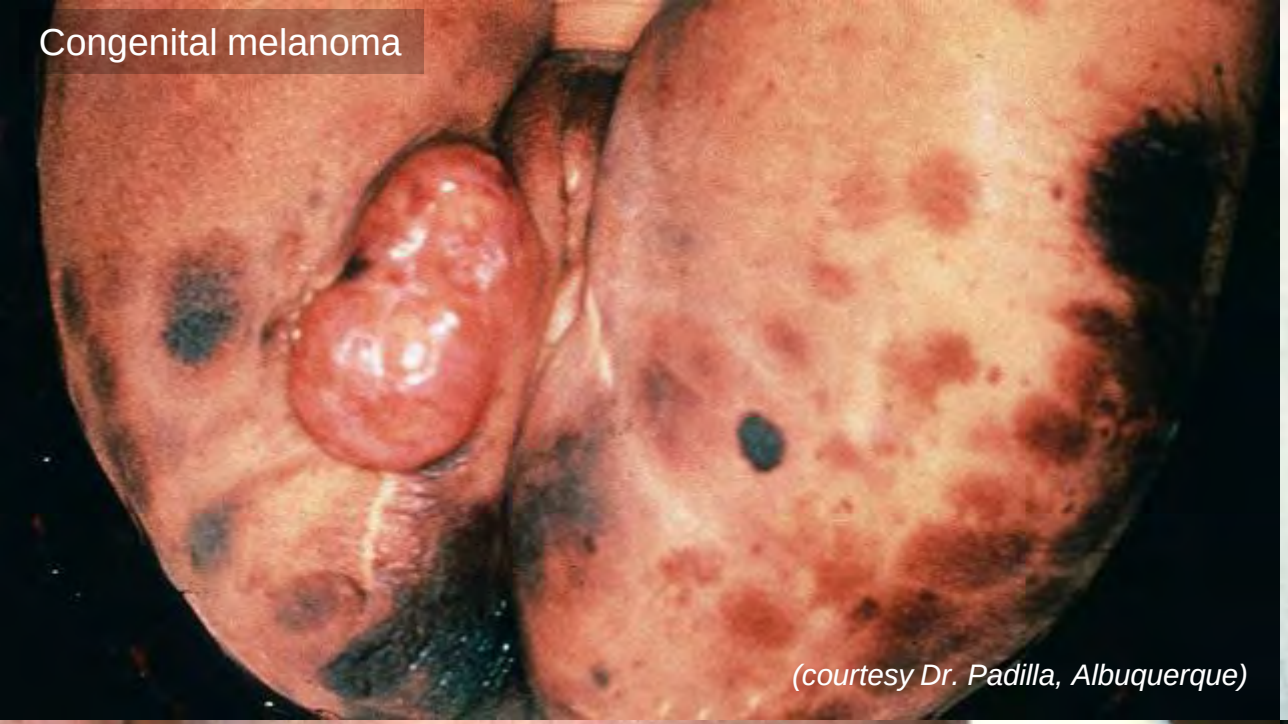


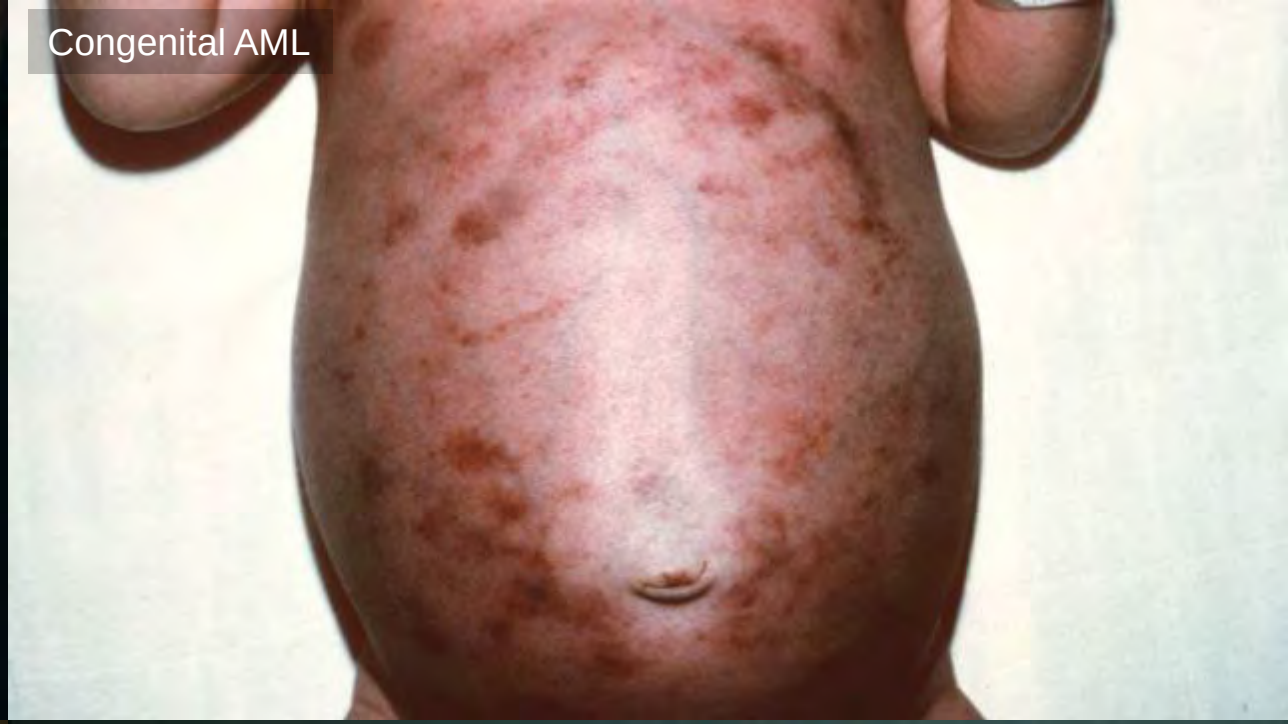


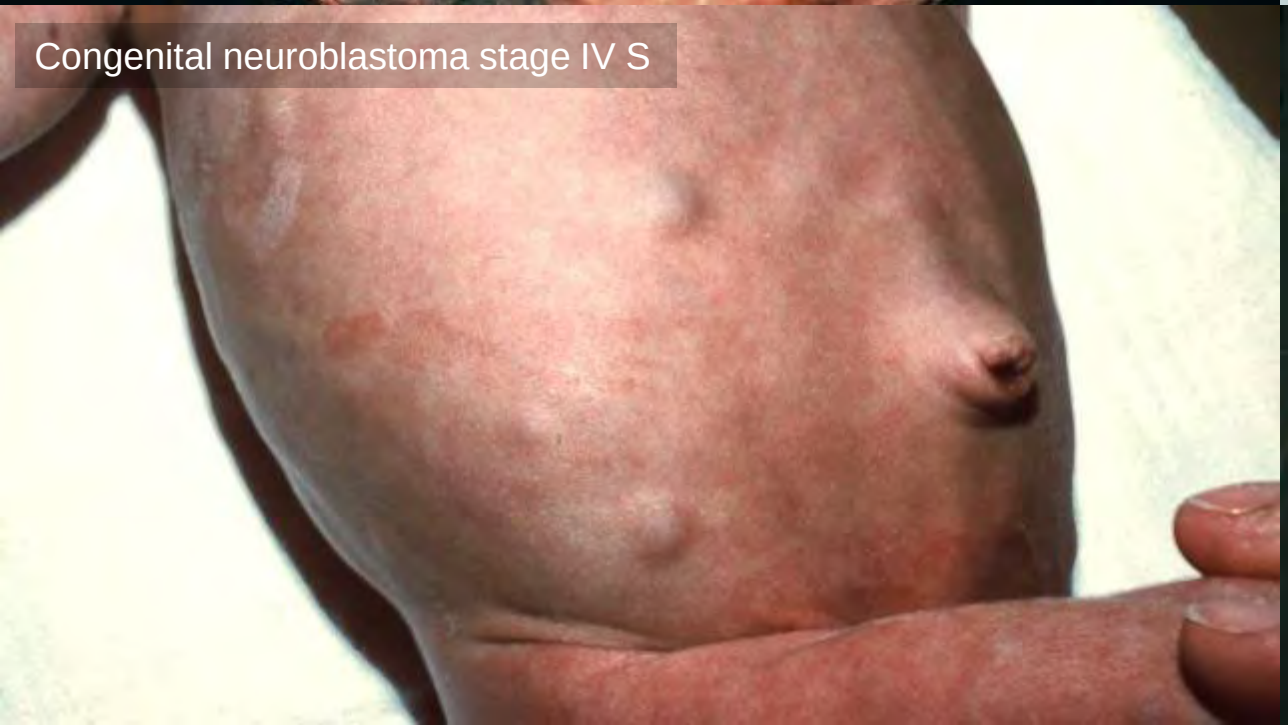
Chromosome 2 in detail

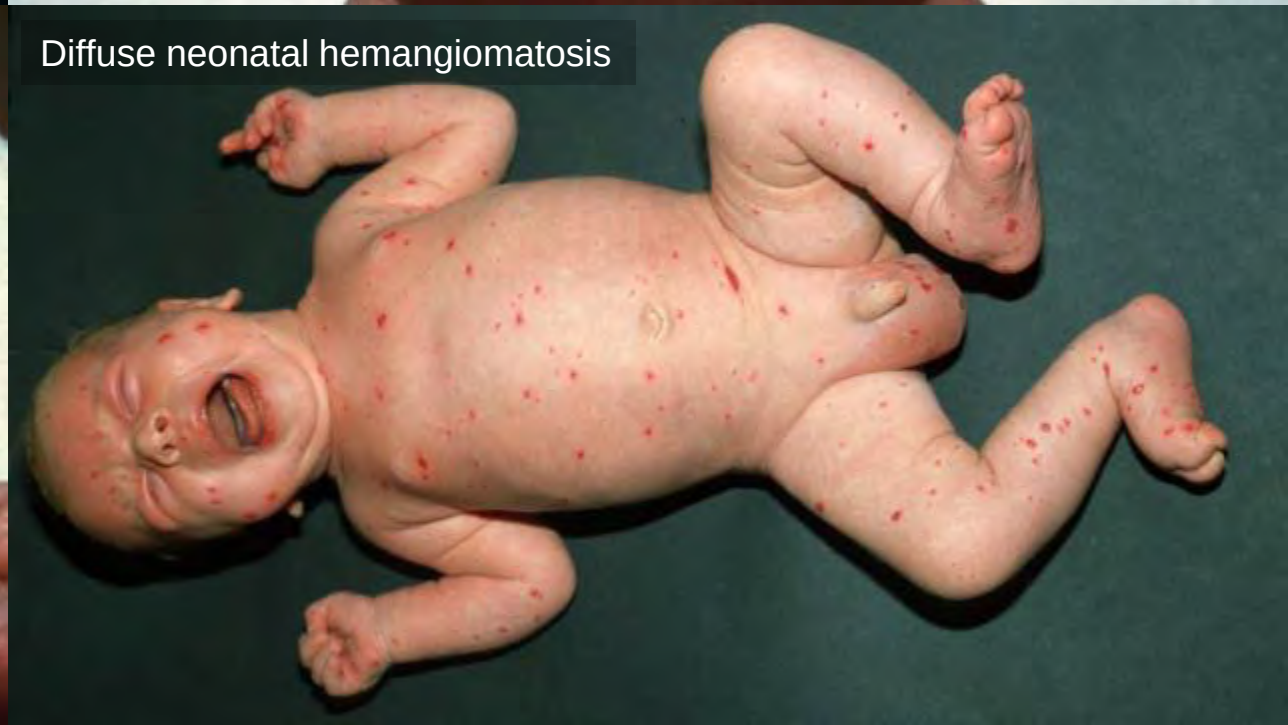
Cutaneous neonatal tumors

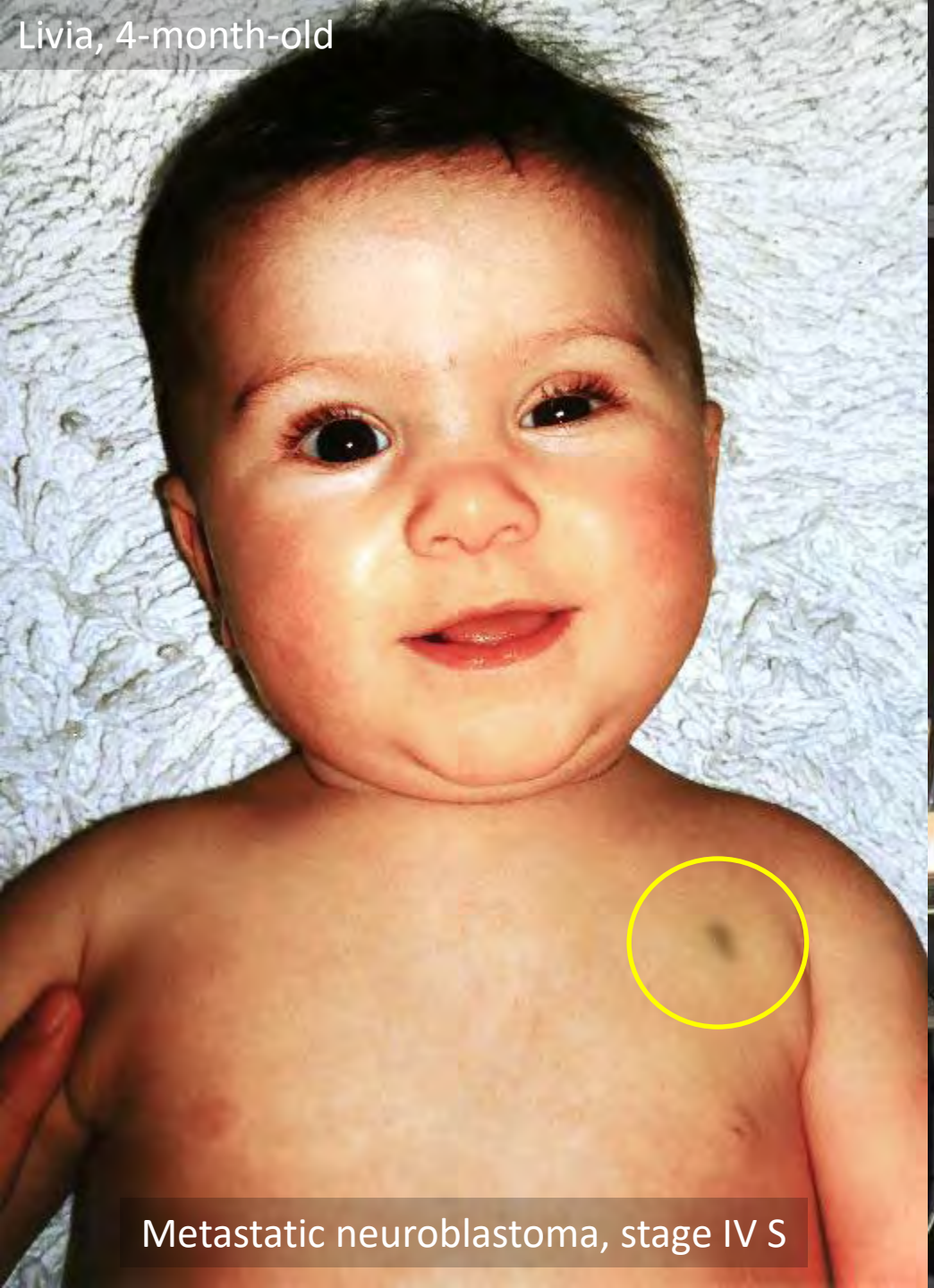
- Congenital myelogenous leukemia
- Metastatic congenital neuroblastoma (stage IV S)
- Congenital Langerhans cell histiocytosis (incl. Hashimoto-Pritzker)
- Blue rubber bleb nevus syndrome
- Diffuse neonatal hemangiomatosis
- Congenital xanthogranuloma
- Giant congenital melanocytic nevus (with or w/o proliferating nodule[s])
- Congenital melanoma
- Others


Congenital melanoma
(courtesy Dr. Padilla, Albuquerque)

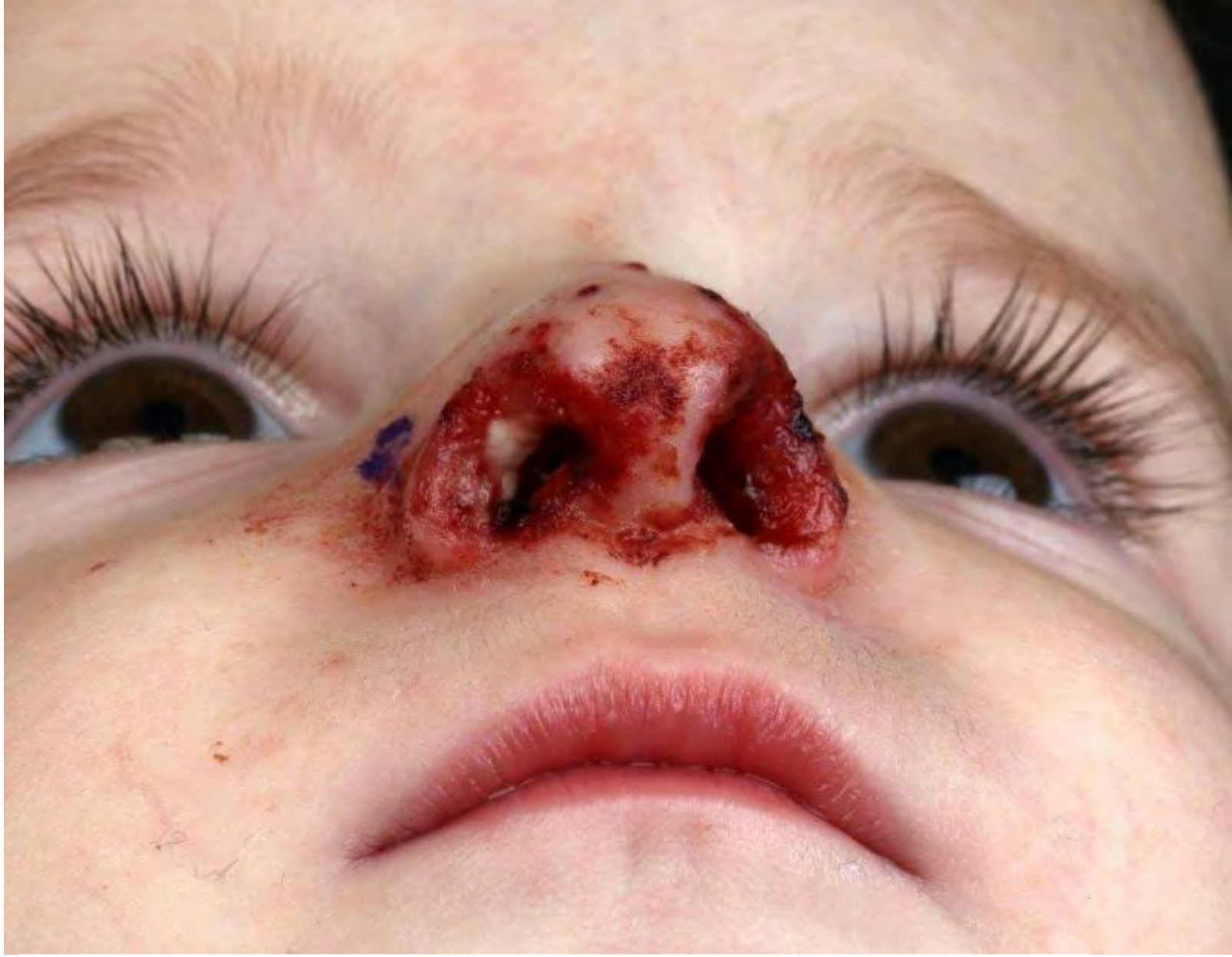

Congenital AML


Congenital neuroblastoma stage IV S


Diffuse neonatal hemangiomatosis

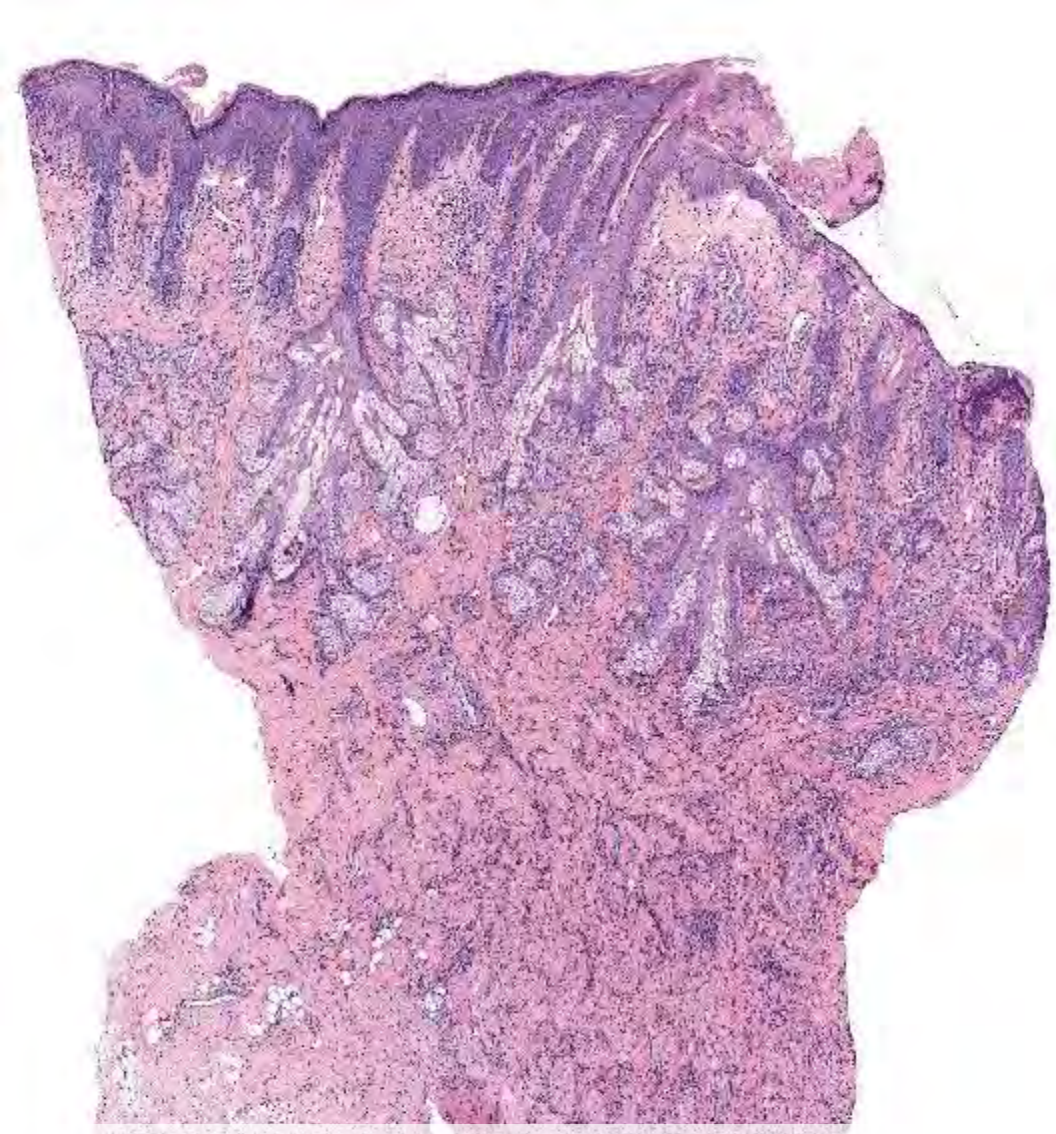

Livia, 4-month-old
Metastatic neuroblastoma, stage IV S

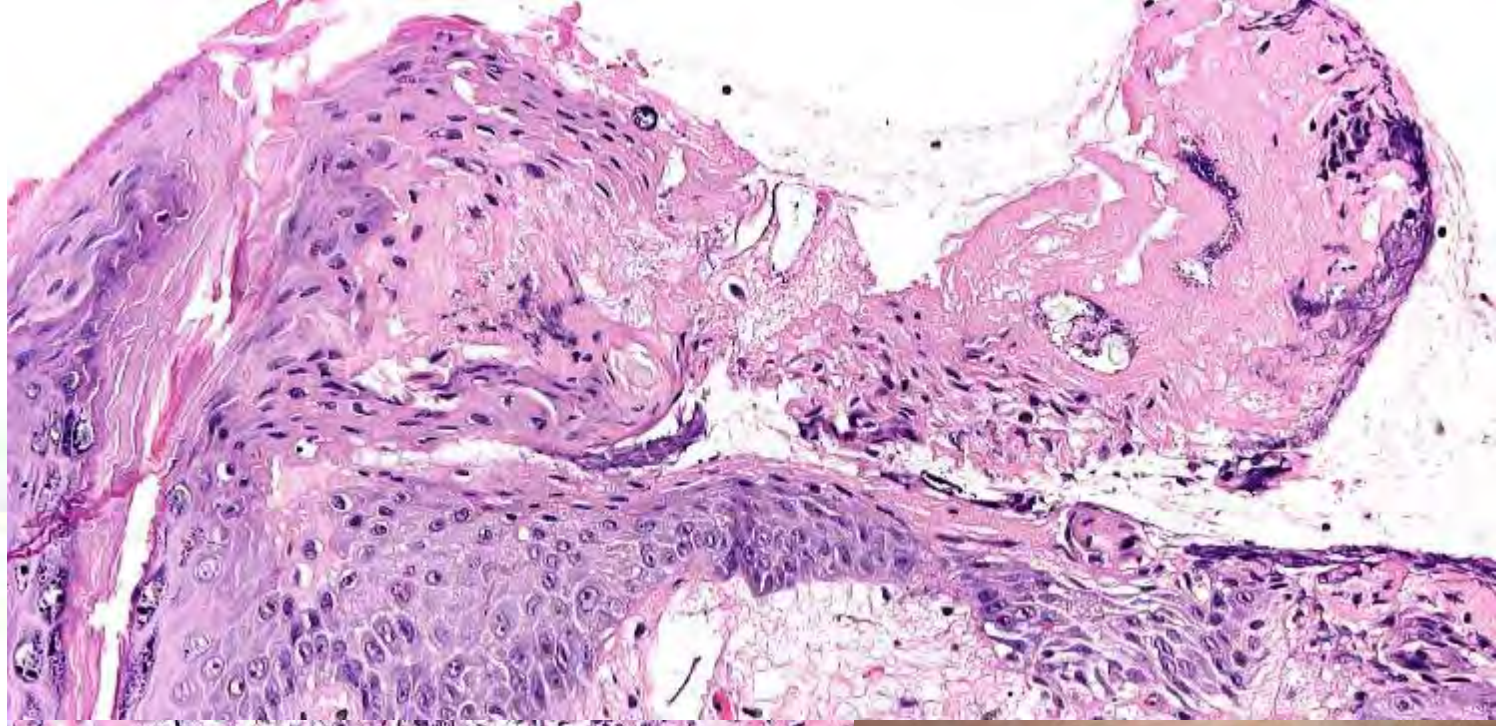

Livia, 25-year-old, Summer Academy of Dermatopathology, July 2025

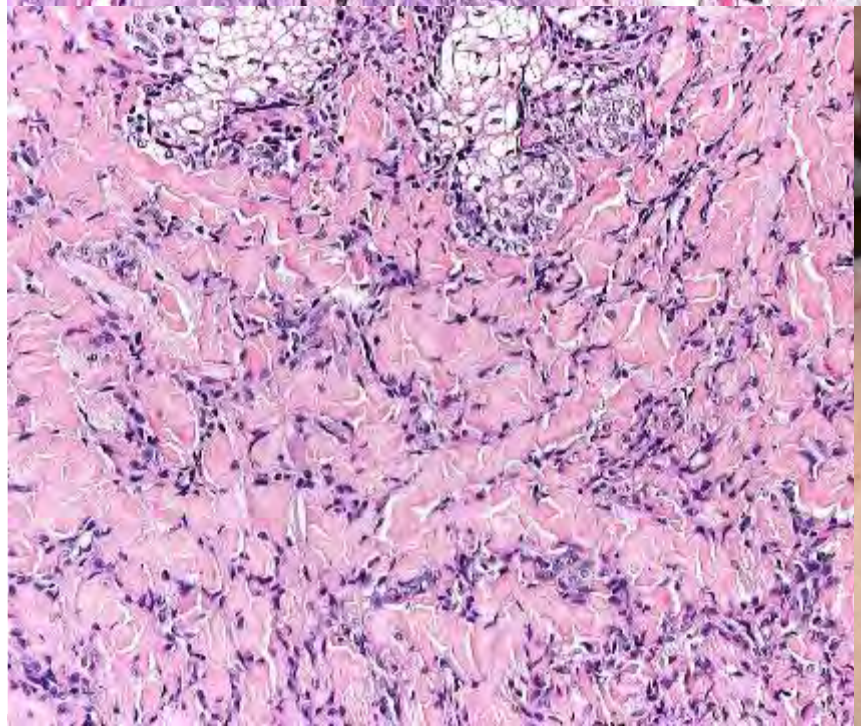


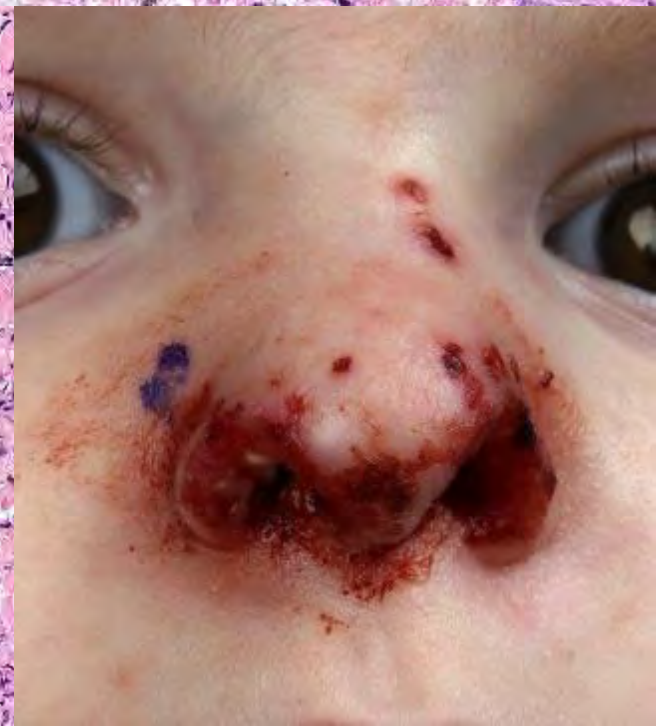
M, 1

Erosive lesions on the nose, not responding to local treatment.









Mid-facial toddler excoriation syndrome

Mid-facial toddler excoriation syndrome

- Autosomal recessive; Almost all cases have a homozygous GCC repeat expansion in the *PRDM12* gene, resulting in pain insensitivity (the *PRDM12* gene plays a crucial role in pain perception and the development of pain-sensing nerves)
- Onset between 3 and 10 months of age; subsides by the age of 5 – 10
- Restricted to the face; no abnormal pain and itch perception on other body sites

British Journal of Dermatology
Paediatric Dermatology

Midfacial toddler excoriation syndrome (MiTES): case series, diagnostic criteria and evidence for a pathogenic mechanism

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Linked Article: [illegible] Br J Dermatol 2024; 191:[illegible]

Abstract

Background [illegible]

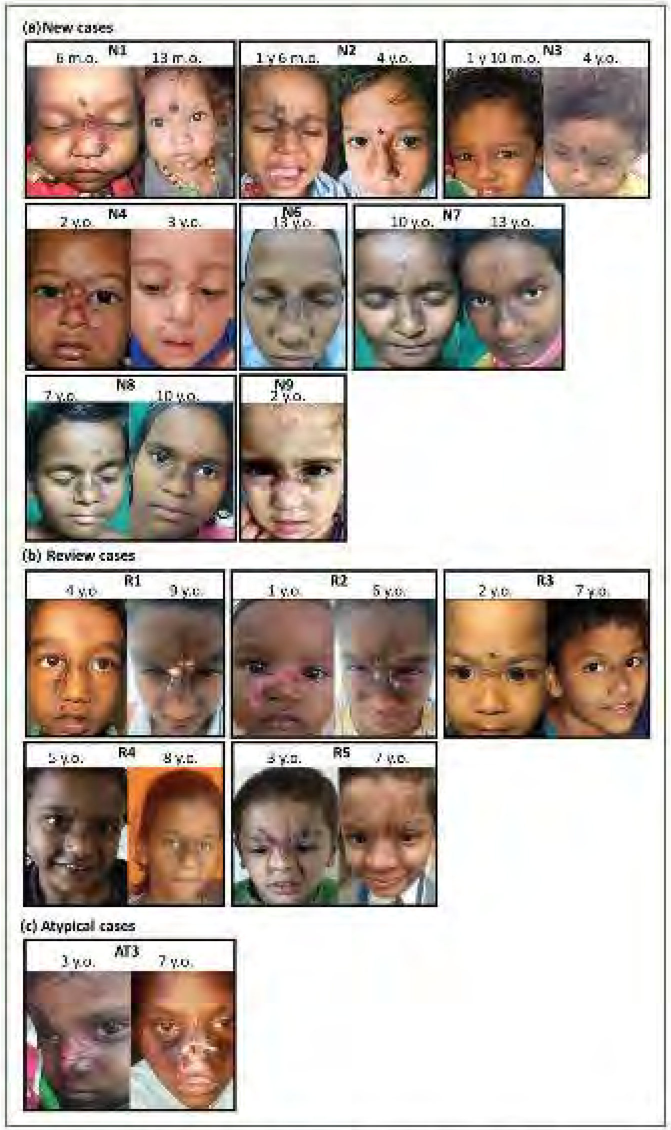
Objectives [illegible]

Methods [illegible]

Results [illegible]

Conclusions [illegible]

Accepted: [illegible] April 2024



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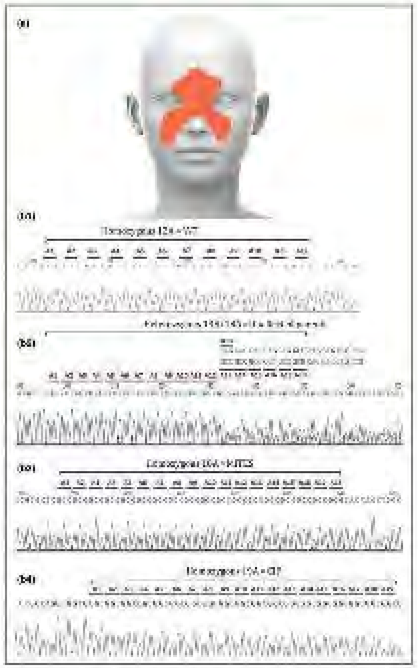

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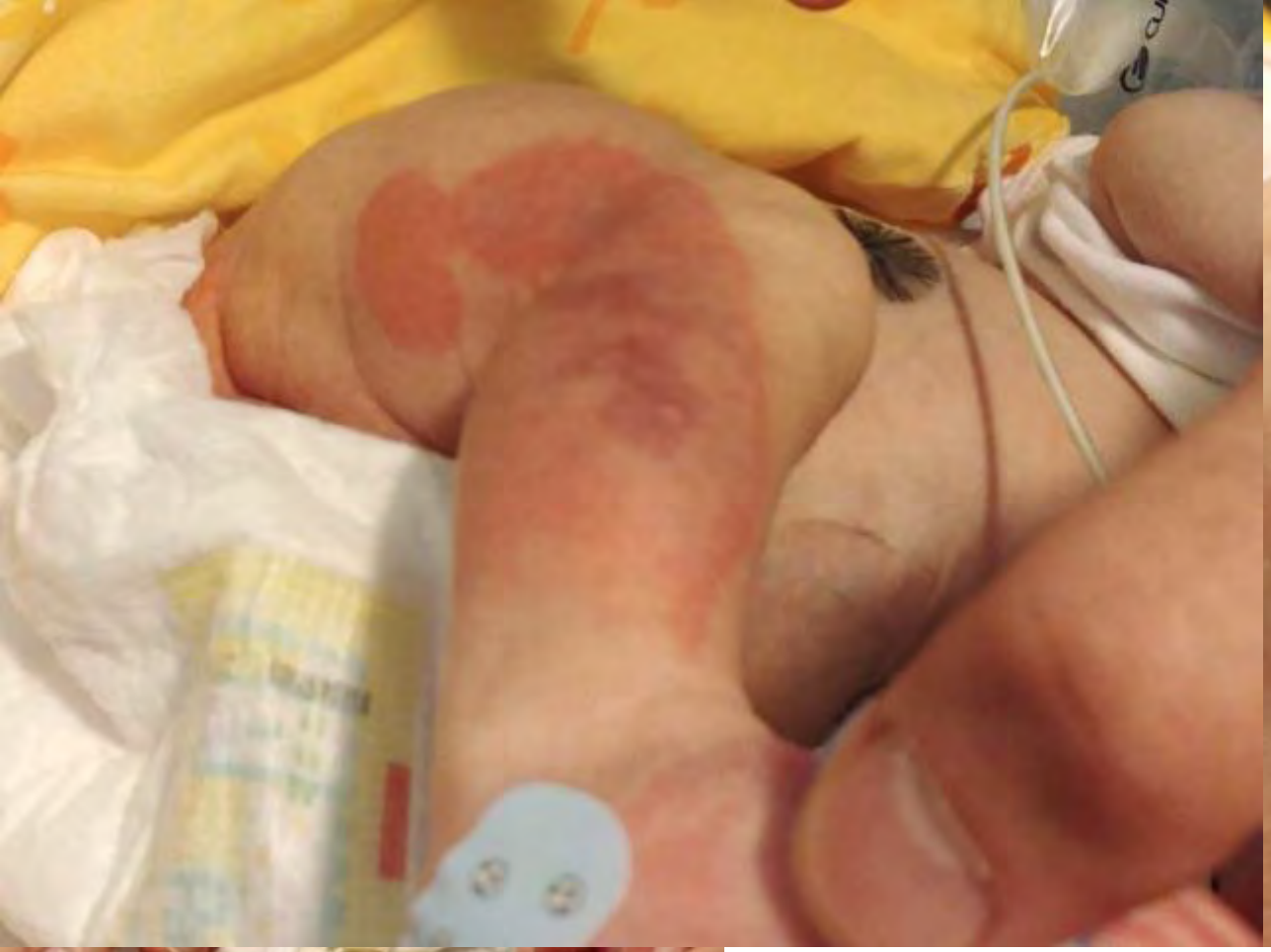
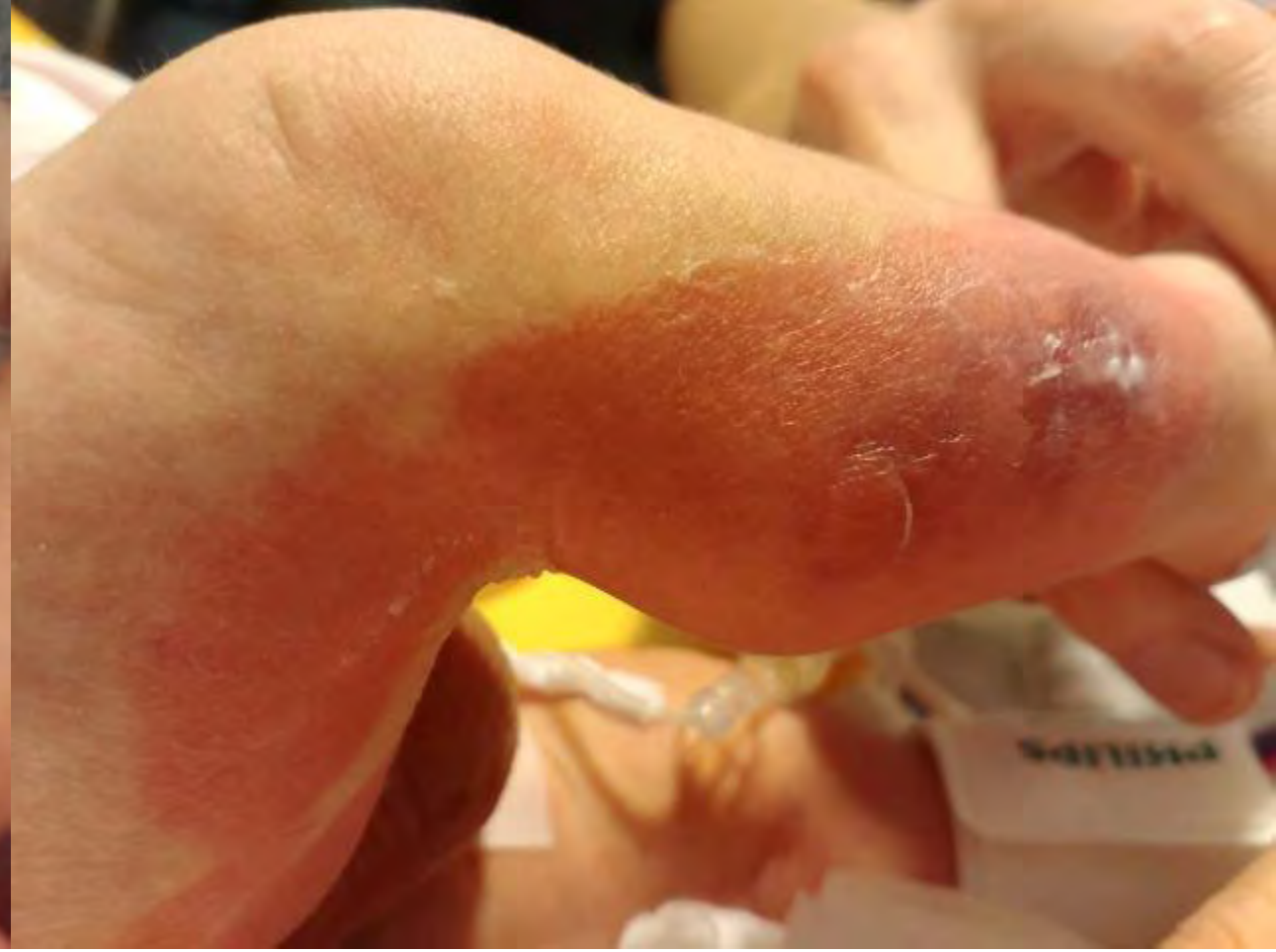
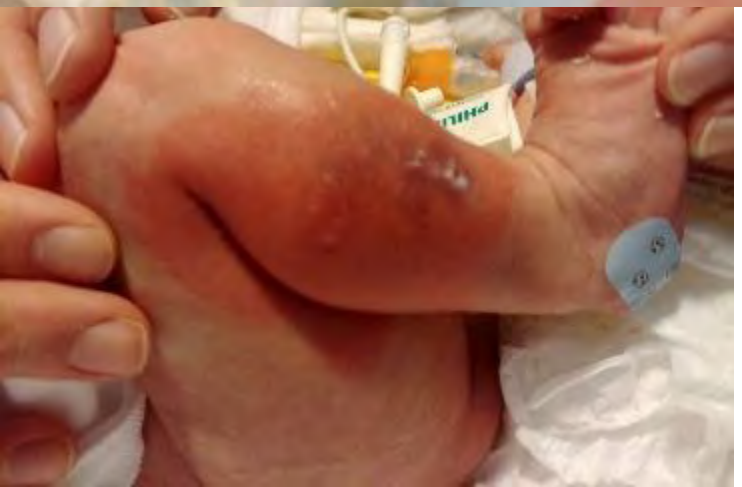






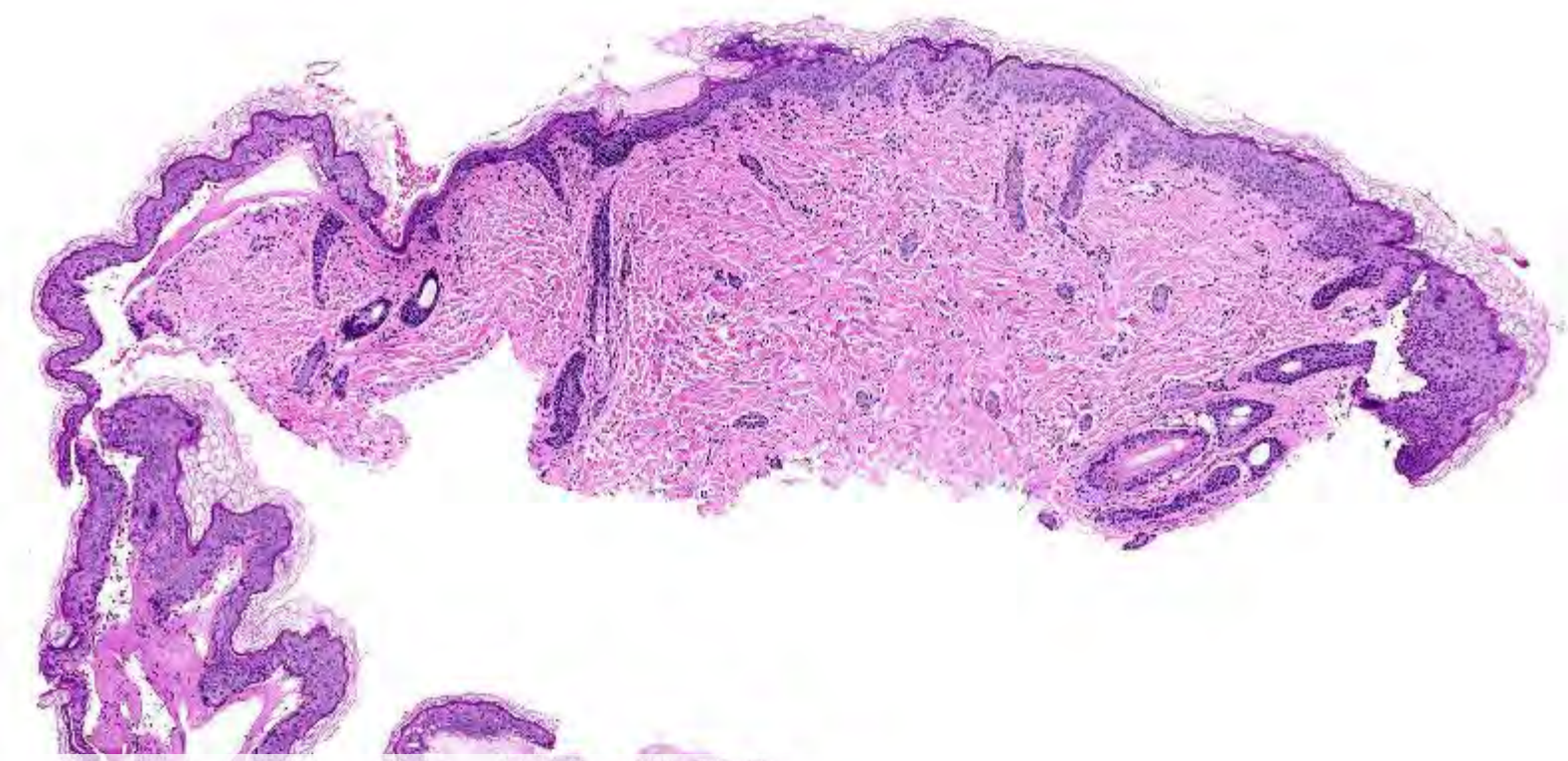
M, 27 days

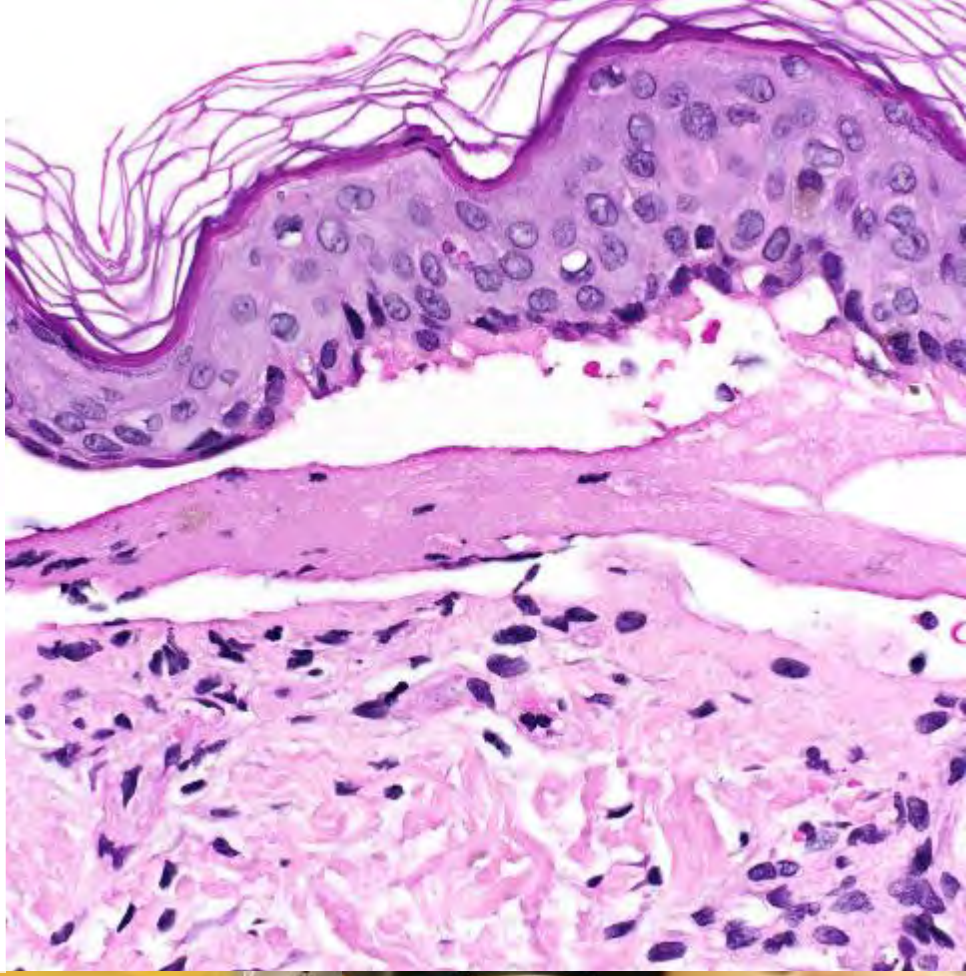
Premature birth (34th week). Omphalocele after caesarean section, reduced surgically at age 1d. Subsequent groin hernia operated 1 day before observation.

Partly bullous skin lesions on the right lower leg, arising soon after the reduction of the hernia.

A biopsy is taken.

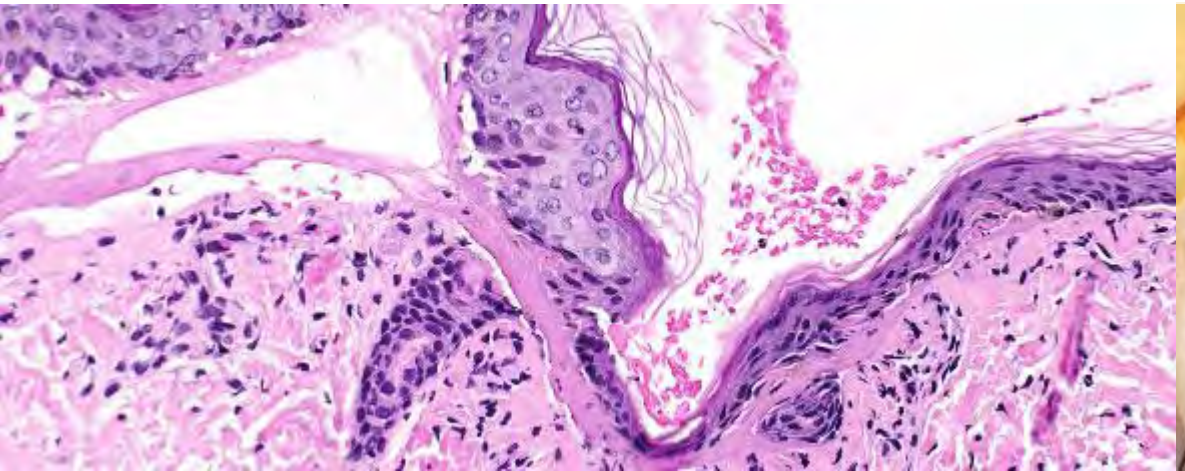
(Clinical pictures courtesy of Department of Pediatrics)

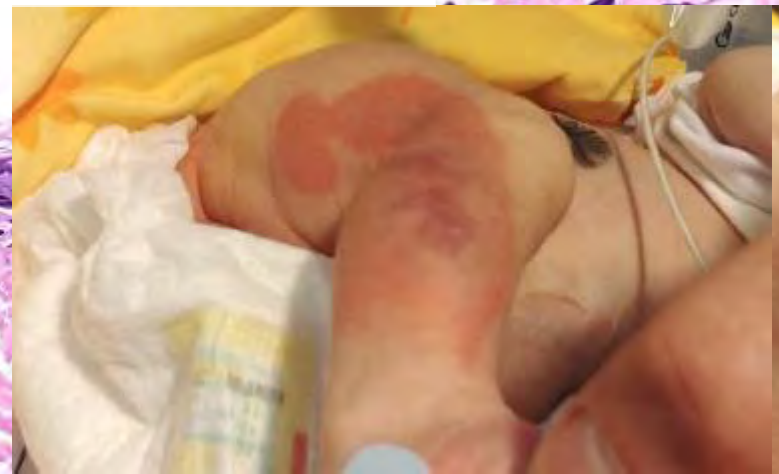


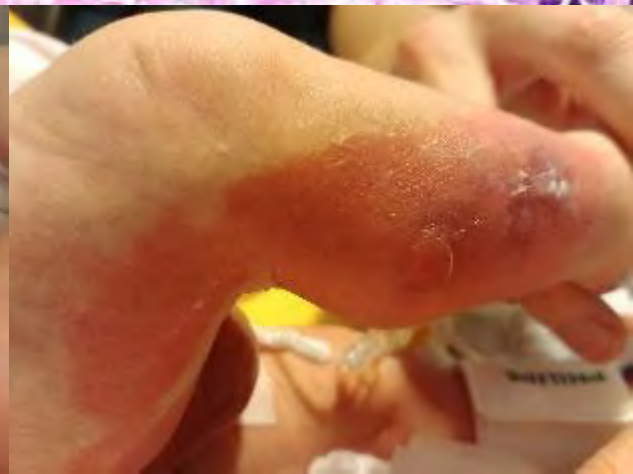


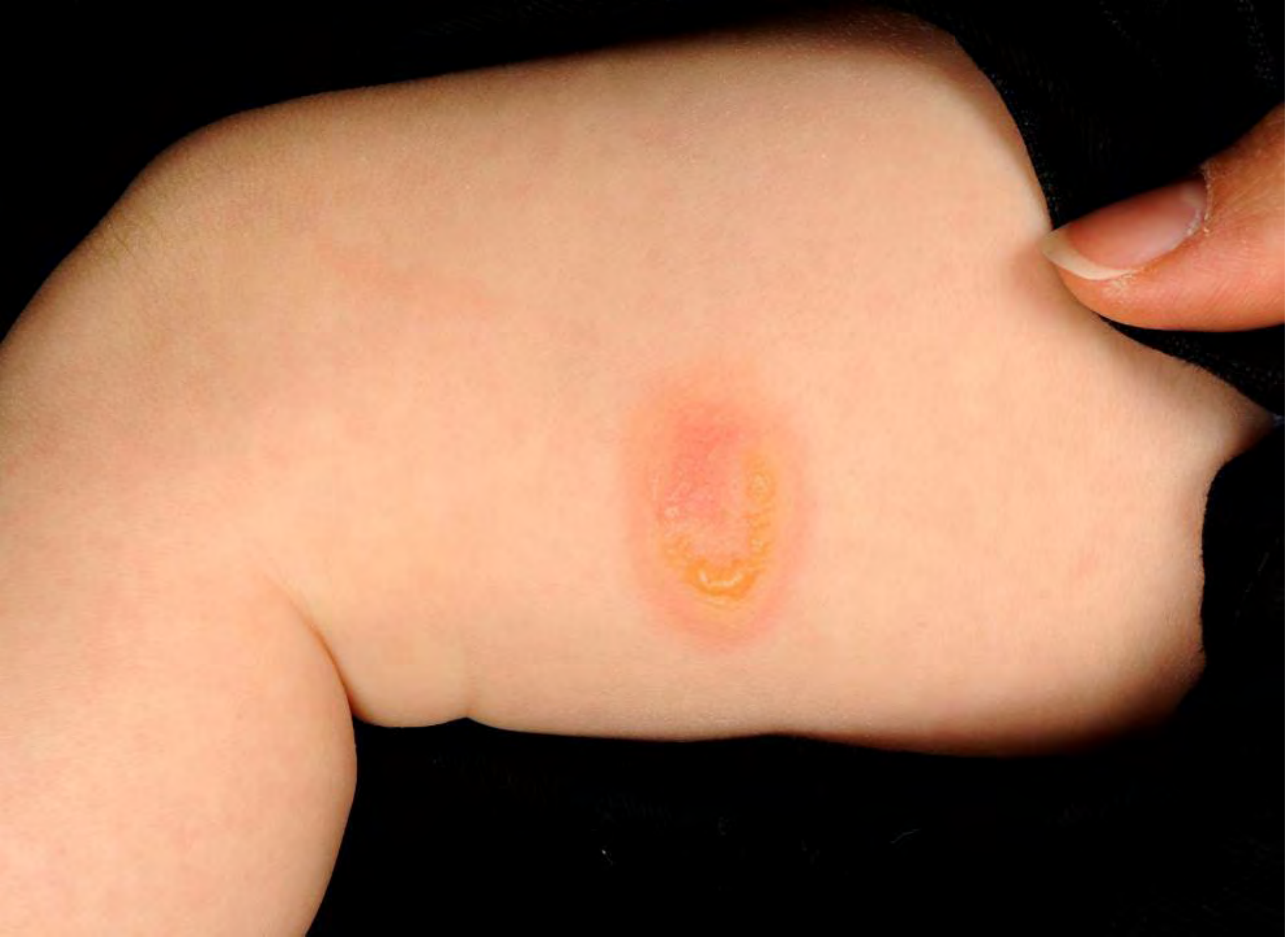
Mechanic artifact in premature skin

Complete resolution with symptomatic treatment; no further lesions







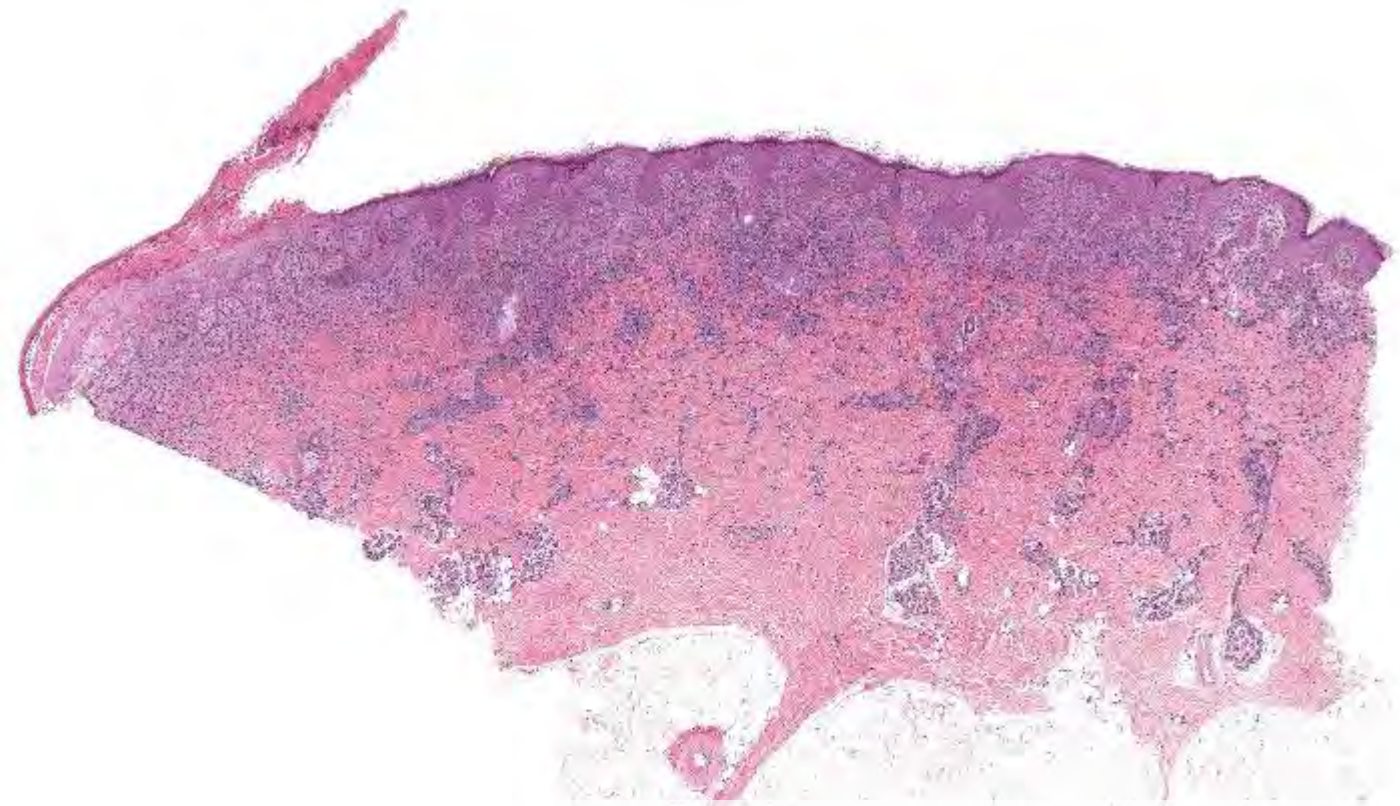


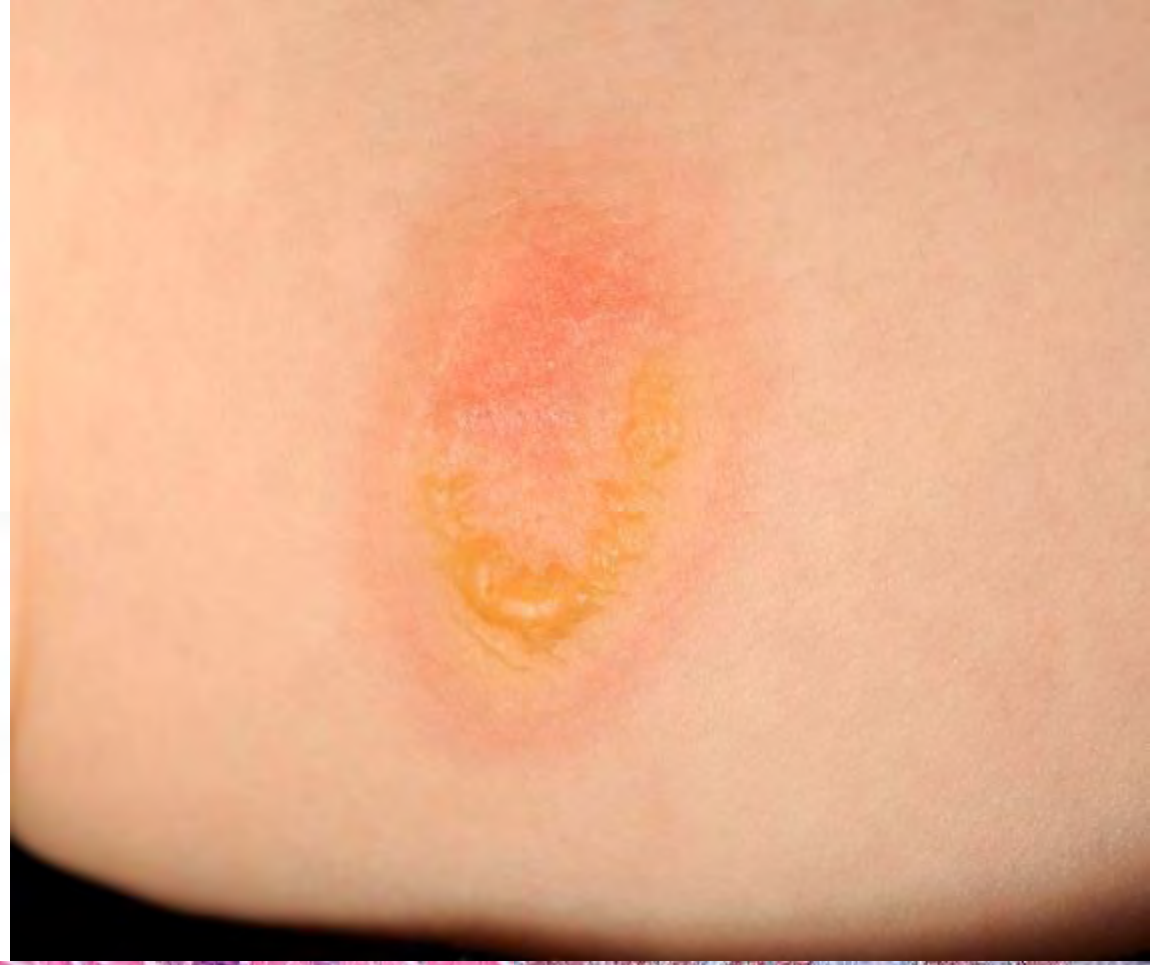
M, 4-month-old

Onset of a bulla on the thigh at the age of 2 months.

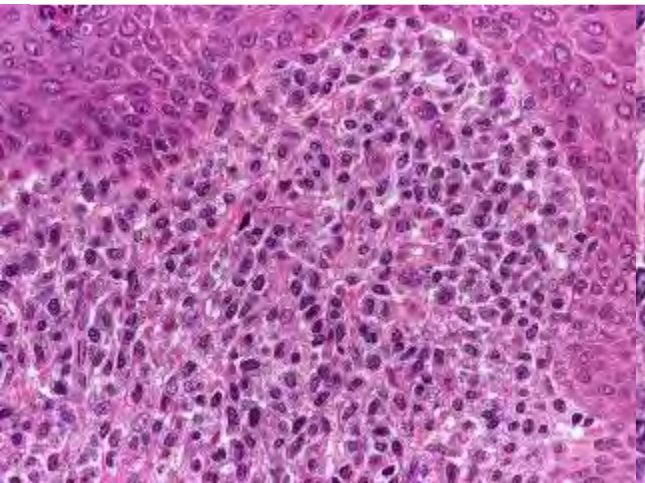
According to the mother recurrent bullous features; when the bulla disappears it leaves an erythematous plaque; at every recurrence short-term "redness of the entire body".

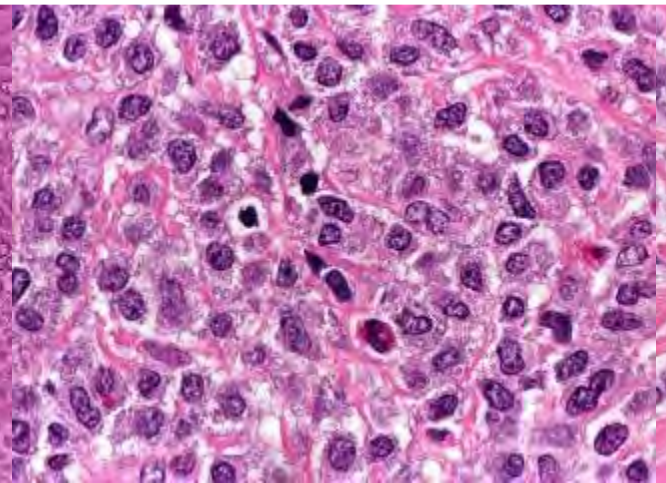
A biopsy is taken.

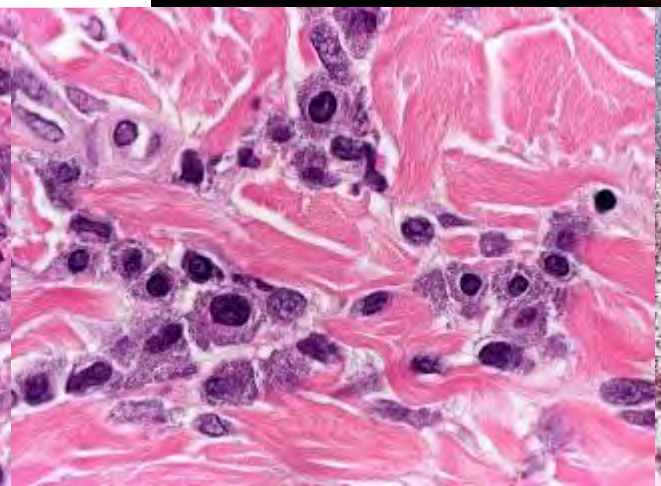


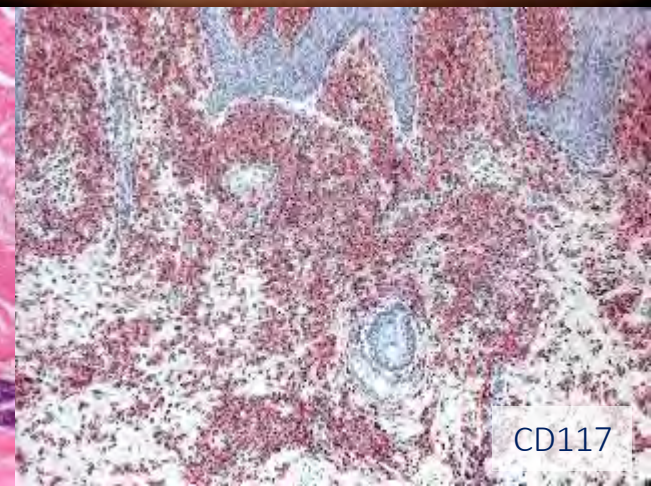


Mastocytoma (bullous)

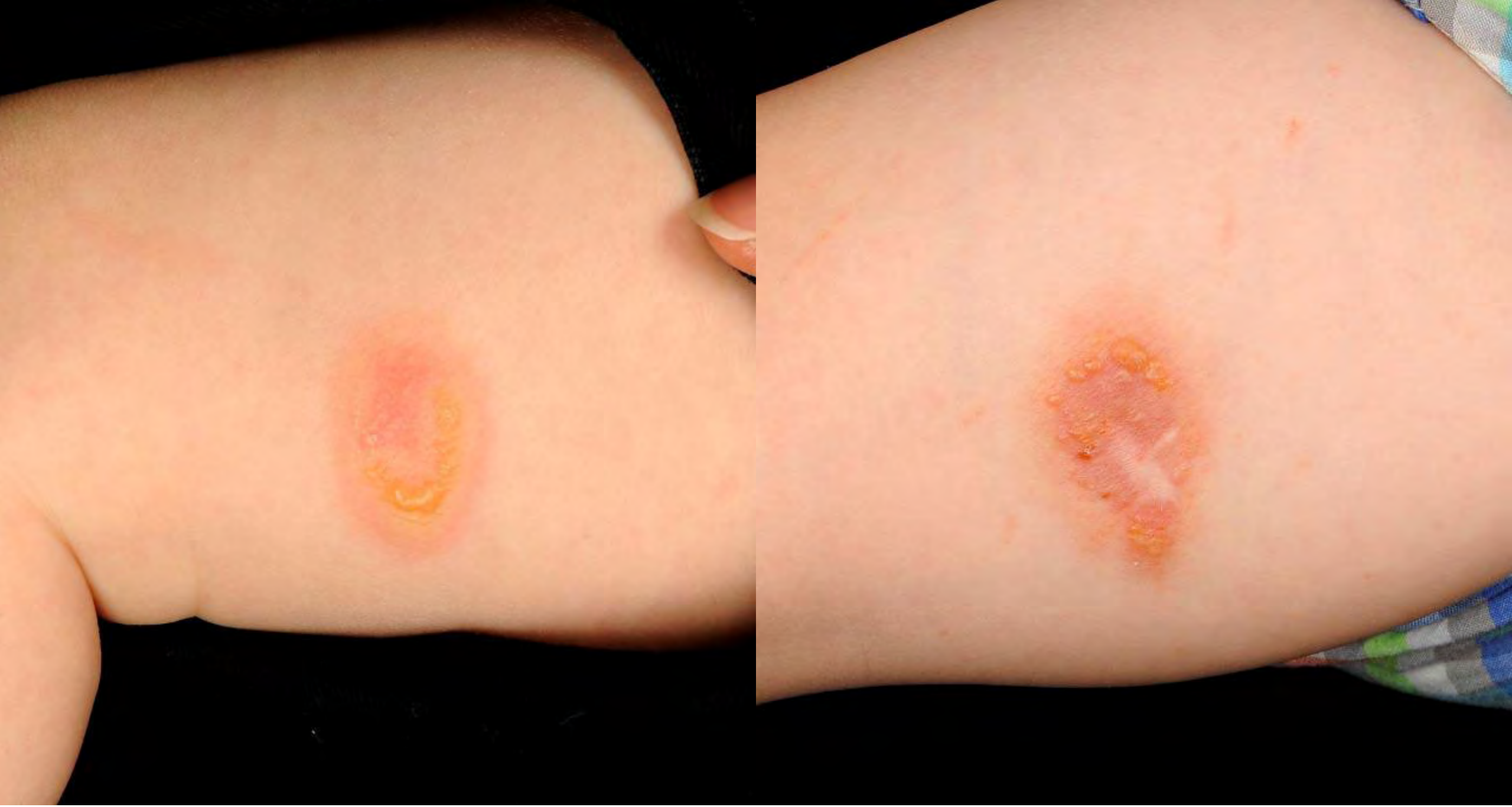






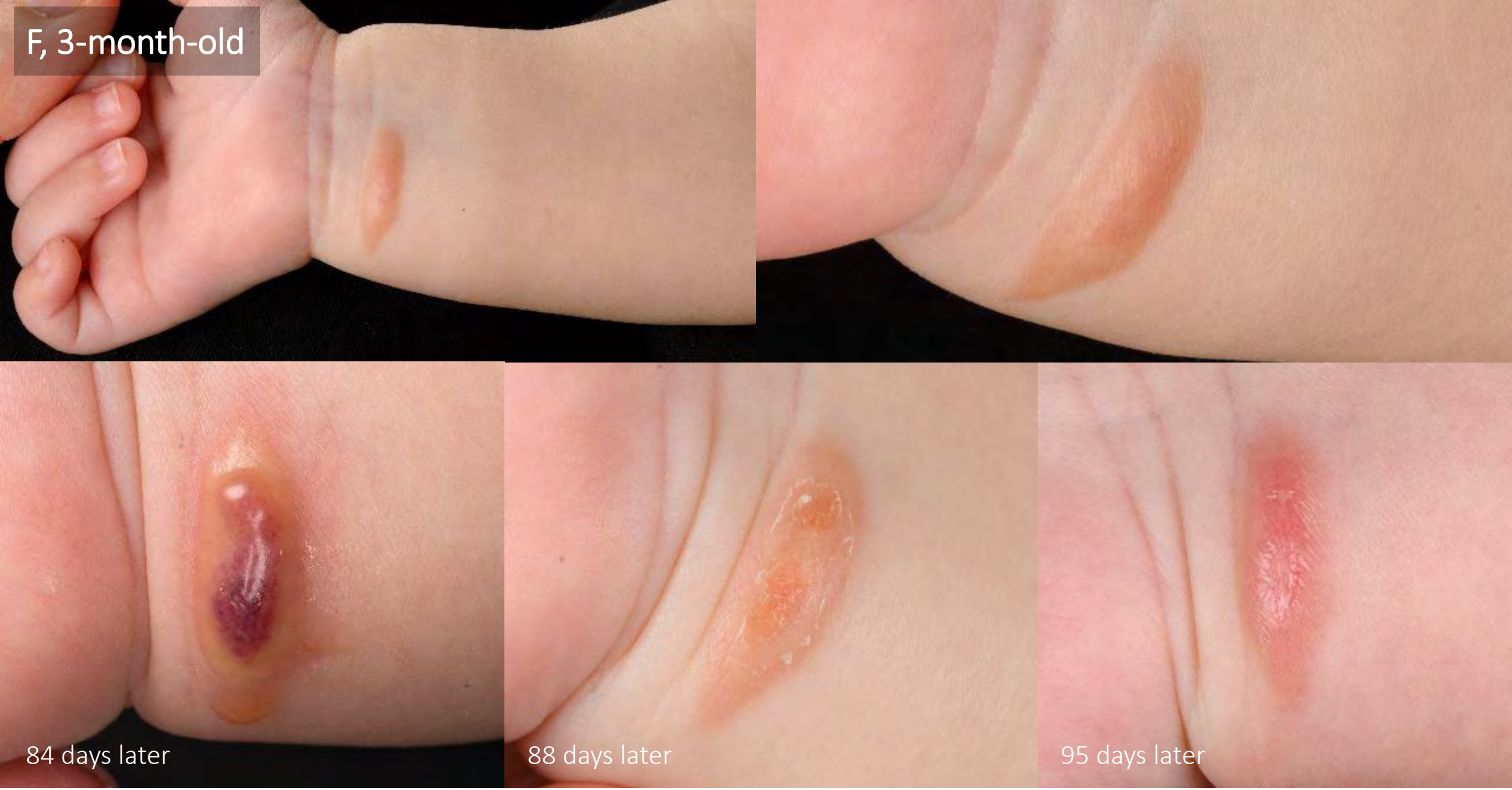


CD117



1st presentation

9 months later (complete resolution 13 more months later)



The dynamic of solitary (bullous) mastocytoma

WHO classification of tumours of haematopoietic and lymphoid tissues, 5th ed., 2024

Subtype	Clinical features
Maculopapular cutaneous mastocytosis (MPCM)	
Polymorphic MPCM	· Usually seen in children · Brown, yellow, or pale red papules, plaques, and/or nodules · Heterogeneity in number, shape, size, margination, and degree of confluence of the lesions
Monomorphic MPCM	· The most common subtype in adults; may be present from infancy or childhood · Small, round, pigmented macules and papules, ranging from a few scattered lesions to generalized skin involvement with confluent lesions
Diffuse cutaneous mastocytosis	· An extremely rare form of cutaneous mastocytosis occurring in infants · Generalized erythroderma, thickened skin, exaggerated folds, and episodic blistering often accompanied by severe systemic symptoms · Absence of individual skin lesions
Mastocytoma	· The most frequent type of mastocytosis in infants · Mastocytomas are usually solitary lesions, but as many as three lesions are accepted · Yellow to brown papules, nodules, or plaques, often with a leathery texture; less frequently, small and pigmented macules · Rubbing may cause wheals, blisters, and occasionally flushing and hypotension

Essential and desirable diagnostic criteria

Essential: cutaneous lesions with clinical features typical of mastocytosis; absence of clinical signs of systemic mastocytosis; bone marrow evaluation (when indicated) not meeting the criteria for systemic mastocytosis; skin biopsy showing increased numbers of mast cells; mast cells immunoreactive for KIT (CD117) and/or tryptase.

Desirable: aberrant dermal mast cell immunophenotype (CD2+, CD25+, and/or CD30+); detection of *KIT* mutation in lesional skin.

Histopathology

Establishing diagnostic criteria for mastocytosis in skin biopsies

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Establishing diagnostic criteria for mastocytosis in skin biopsies

Aims: The diagnosis of mastocytosis in skin biopsies can be challenging – particularly in cases with very few mast cells. More diagnostic criteria are needed.

Methods and results: We analysed 105 skin biopsies from patients with mastocytosis and compared them with biopsies from inflammatory skin lesions and normal skin. Using CD117 immunostaining, we determined the mast cell distribution pattern, the percentage of mast cells in the inflammatory infiltrate, and the mast cell count per mm². We found that a sheet-like or subepidermal distribution of mast cells was specific for mastocytosis. The most significant feature was the percentage of mast cells and not the mast cell count. We found that a mast cell percentage above 40% was fully specific in both adults and children but lacked sensitivity, especially in adults. In children, all cases with a percentage below 40% harbored a number of mast cells above 90 per mm², allowing a straightforward diagnosis. In adults, the diagnosis was more challenging and cases with less than 40% of mast cells could be diagnosed on account of a number of mast cells above 40 per mm², with 88.5% sensitivity and 95.2% specificity. Additional signs might be useful in difficult cases. However, CD25 immunostaining was not useful.

Conclusions: We confirmed that the criteria currently applied in the bone marrow were not appropriate for the skin. Accordingly, we developed an algorithm for the diagnosis of mastocytosis in skin biopsies with a high level of interobserver reproducibility (mean kappa 0.81).

Keywords: Biopsy, CD117, diagnosis, mastocytosis, skin

Introduction

Mastocytosis is defined as a clonal, neoplastic proliferation of mast cells, which accumulate in one or more organs. The skin is one of the major sites involved. Skin involvement can be the sole manifestation of disease in cutaneous mastocytosis (CM), but can also be observed in systemic mastocytosis (SM). Indeed, SM is often revealed by skin lesions.[1,2]

Depending on the clinical presentation and progression, SM is subclassified into five variants: indolent SM (ISM), smoldering SM (SSM), SM with associated

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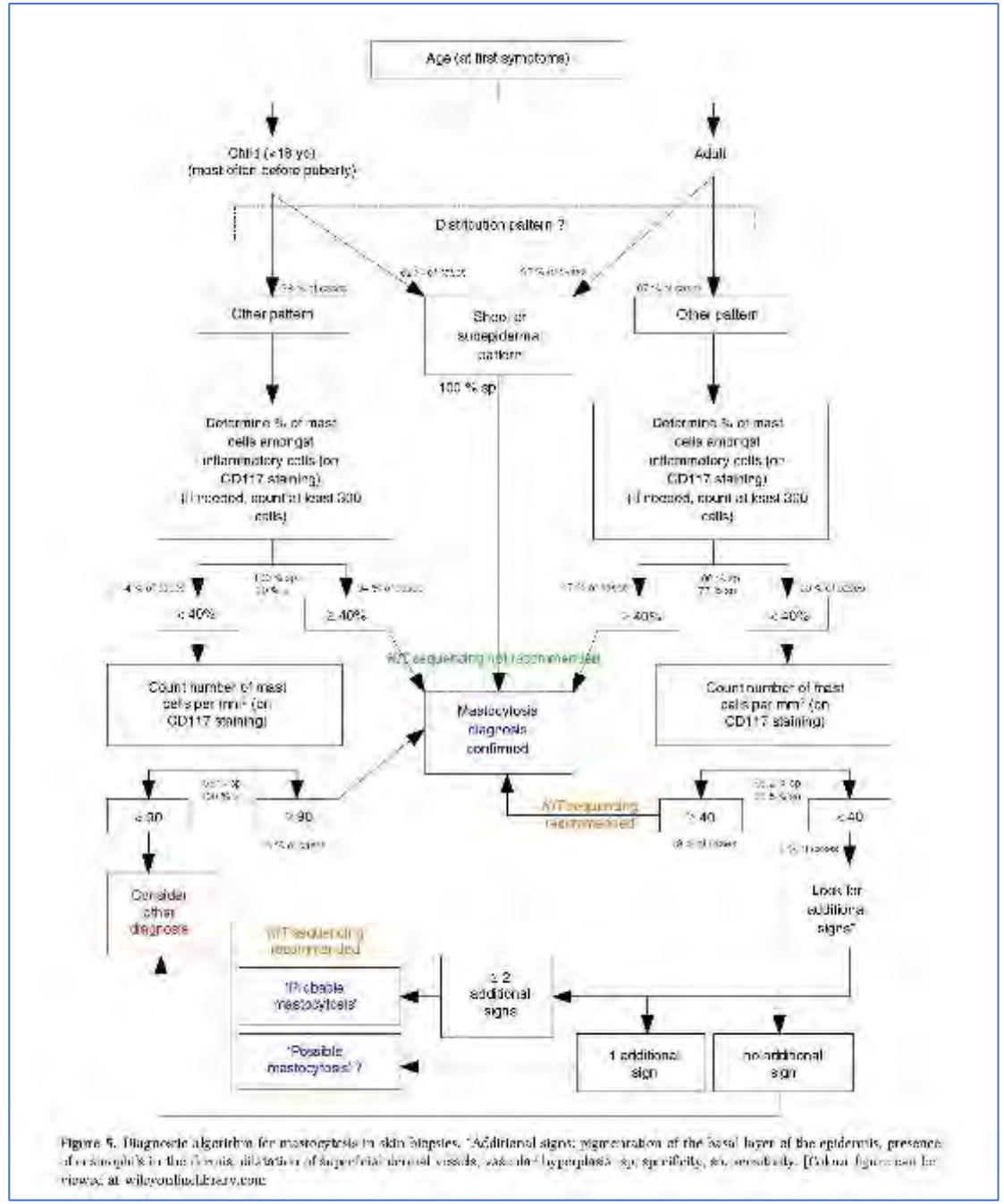
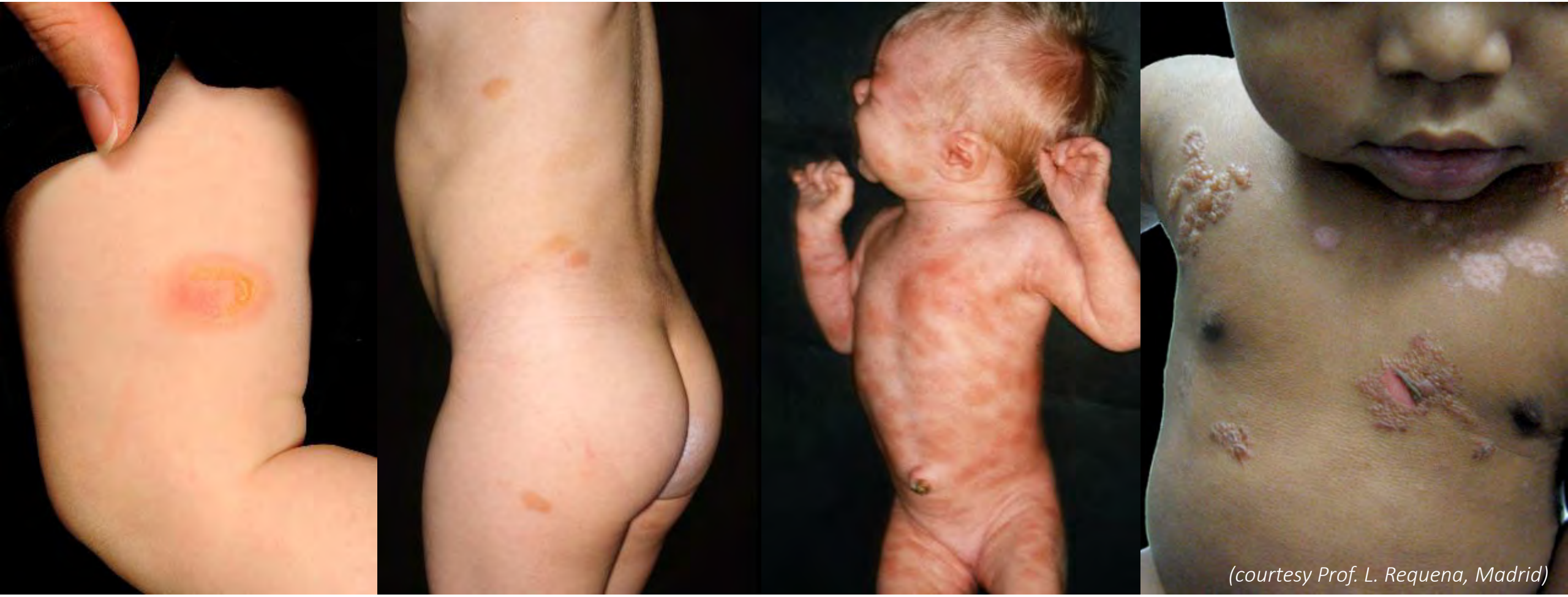


Figure 6. Diagnostic algorithm for mastocytosis in skin biopsies. *Additional signs: hypercellularity of the dermis, dilatation of superficial dermal vessels, vascular hyperplasia. Sp, specificity; se, sensitivity. [Colour figure can be viewed at wileyonlinelibrary.com]

Cutaneous mastocytoses - children



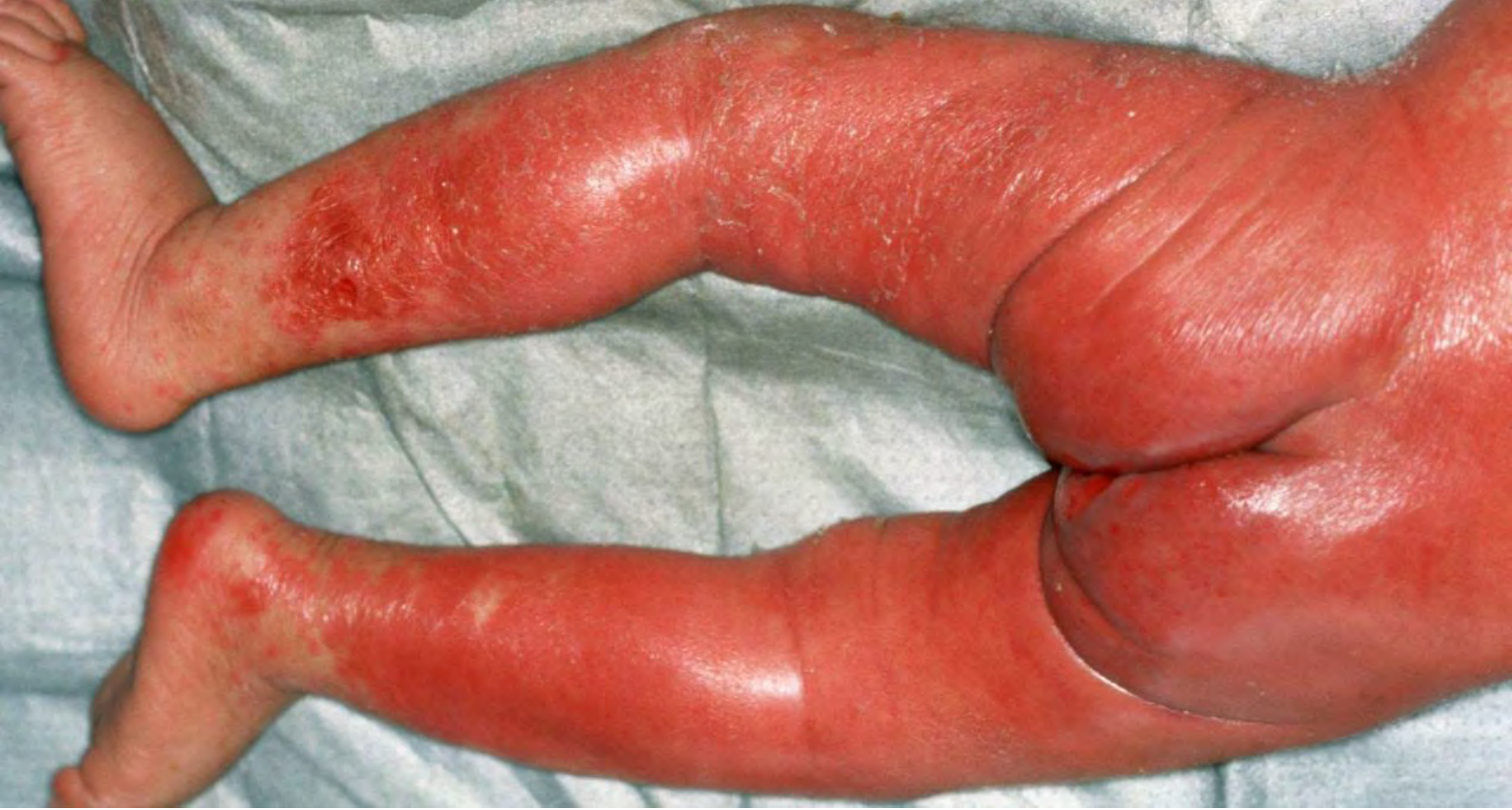
Solitary mastocytoma

Multiple mastocytomas

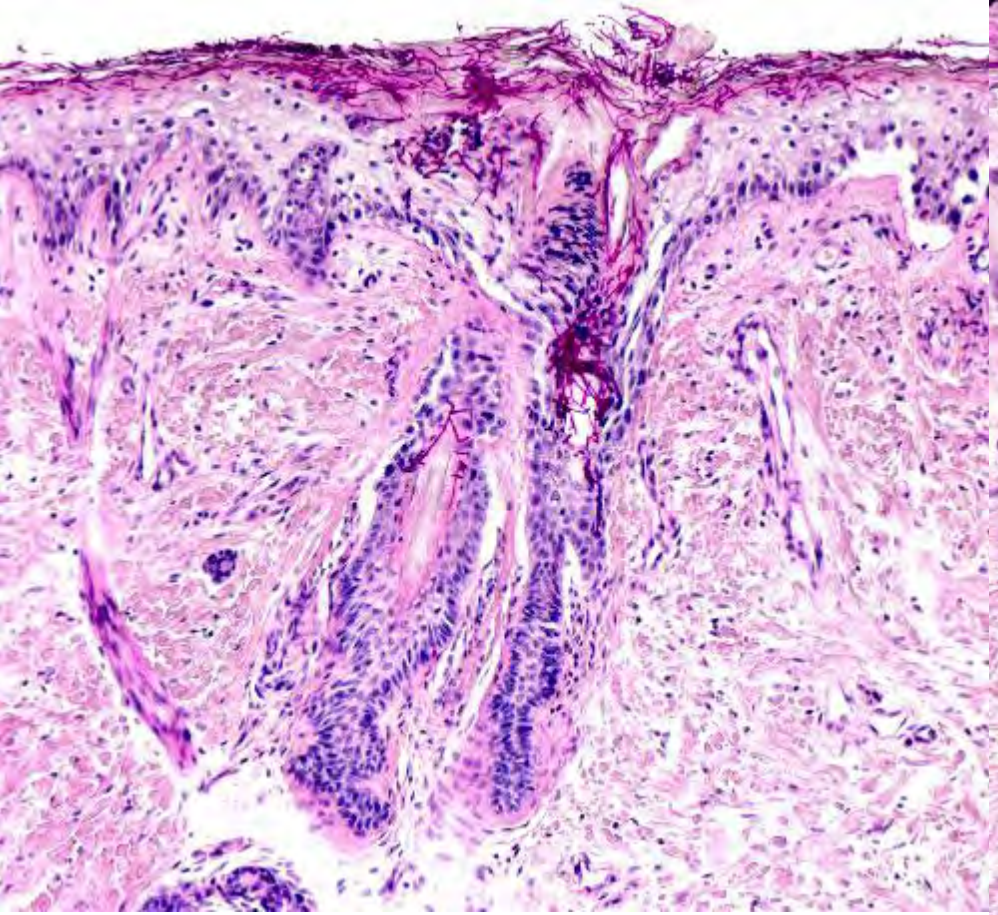
Urticaria pigmentosa

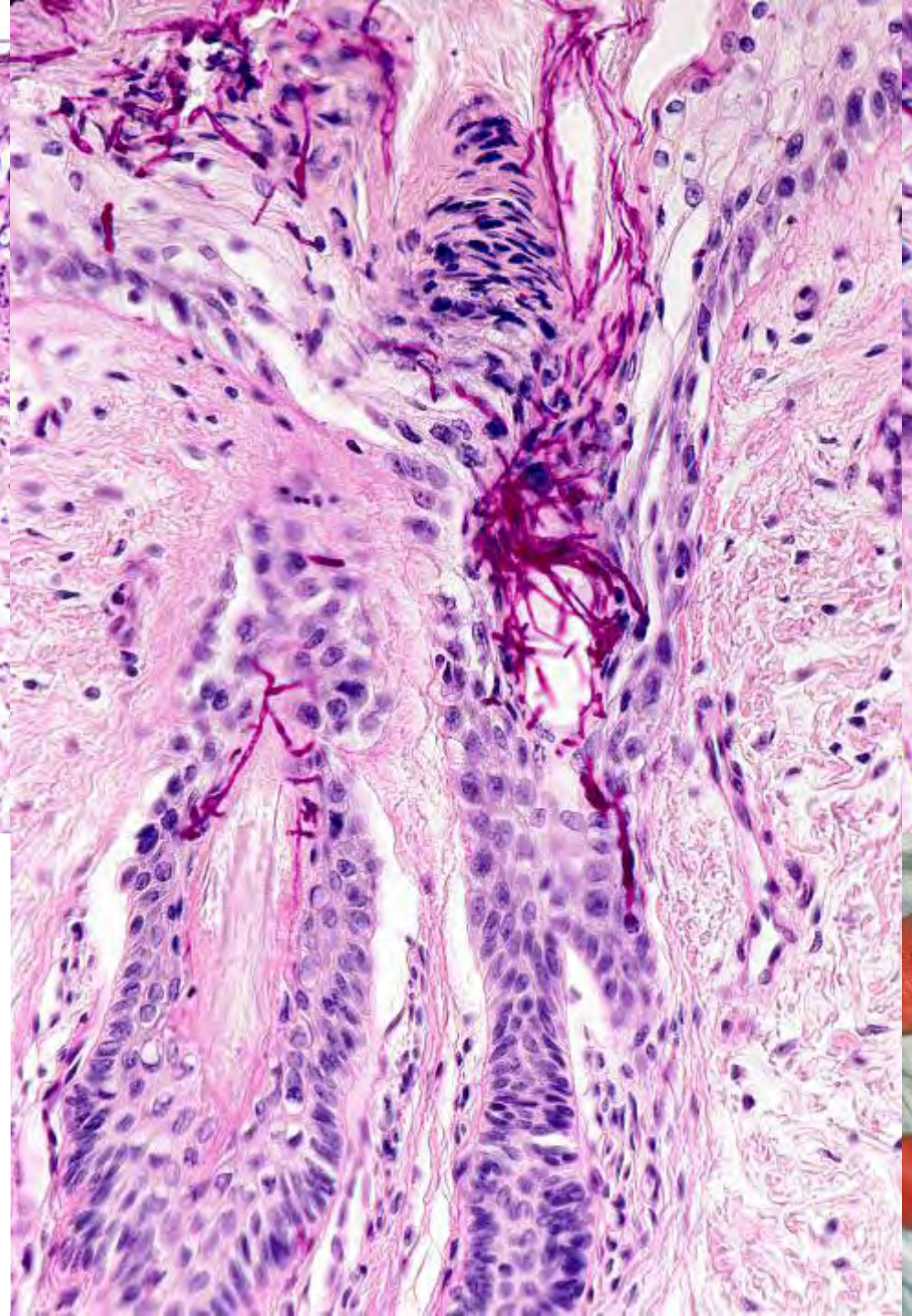
Diffuse ("erythrodermic") cutaneous mastocytosis

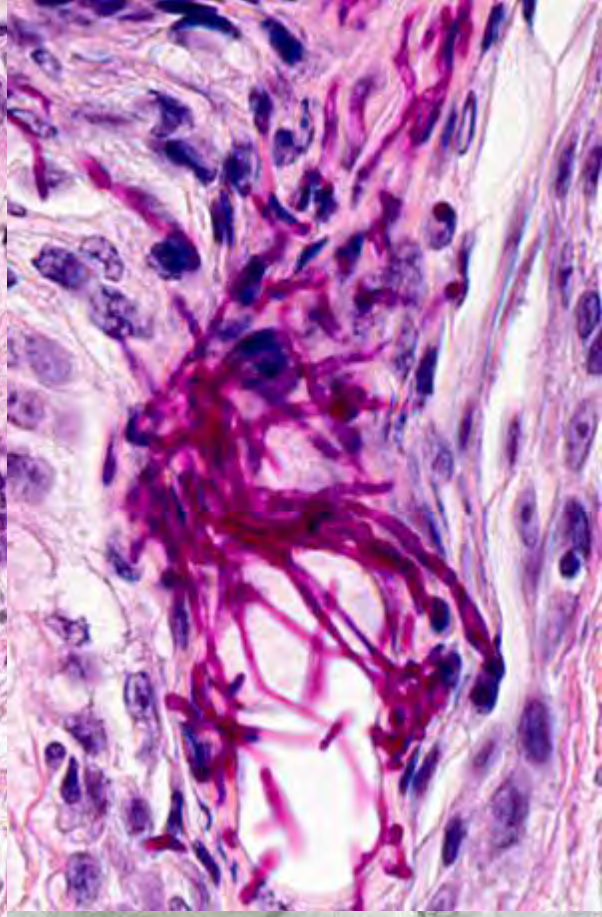
Range of presentations from solitary lesions to involvement of large part of the skin, sometimes with a "leathery" appearance. Bullous lesions may be present and/or develop upon friction. Lesions usually resolve by adolescence, in some patients persist (10-15% of cases).
Systemic involvement rare in children.



1-week-old female newborn with methylmalonic acidemia and progressive, partly pustular skin eruption since birth, becoming erythrodermic.

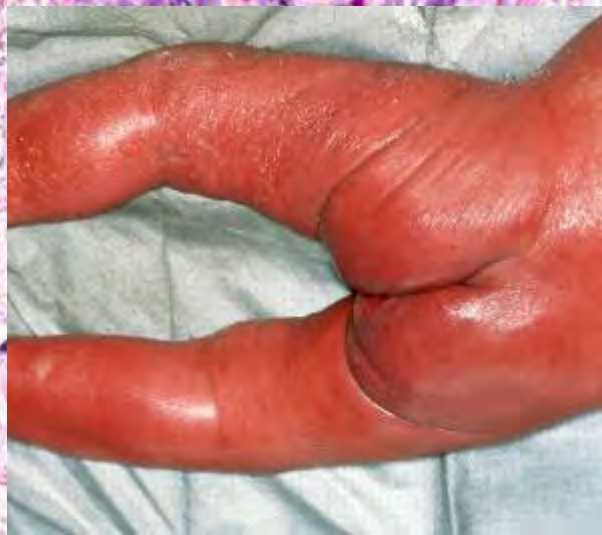






Congenital Candidiasis

Intrauterine infection acquired from the mother. The purely cutaneous form is a limited disease managed with topical antifungal creams; the systemic form (usually in pre-term newborns) may be life-threatening.



Widespread Erythroderma and Desquamation in a Neonate

B. D. Glassman, MD, J. J. Muglia, MD
New England Medical Center Hosptials, Boston, Mass

REPORT OF A CASE

A 1590-g girl was born at 32 weeks' gestation to a 21-year-old Hispanic (gravida 4, para 3) who had a history of intravenous drug abuse and hepatitis B infection and no prenatal care before delivery. Her pregnancy was complicated by vaginal yeast infections during gestation. Premature labor began 1 hour before delivery with rupture of the membranes and leakage of clear, amniotic fluid. A spontaneous vaginal delivery was performed, and the infant was born floppy with no respiratory effort. Apgar score was 6/8 at 1 and 5 minutes.

On initial presentation, a diffuse papular rash on an erythematous background was present on the chest, back, abdomen, buttocks, and face. No pustules were noted. The infant continued in respiratory distress and was intubated 4 hours after delivery. Intravenous ampicillin and gentamicin was begun. Initial laboratory tests showed the following values or results: leukocytes, 3.2×10^9/L, with 0.65 lymphocytes, 0.9 neutrophils, 0.5 band forms, 0.15 monocytes, and 0.6 eosinophils; human immunodeficiency virus, negative; and VDRL, nonreactive. No cultures were performed on the placenta or umbilical blood.

By age 3 days, the infant's rash progressed, producing diffuse erythema with scattered areas of sparing on the trunk and desquamative scale on the trunk and extremities with evidence of superficial erosion in some areas. (Figs 1 and 2).

A scraping was performed. Cultures were obtained from the eye, mouth, and nasopharynx and were consistent with the findings in Fig 3.

What is your diagnosis?

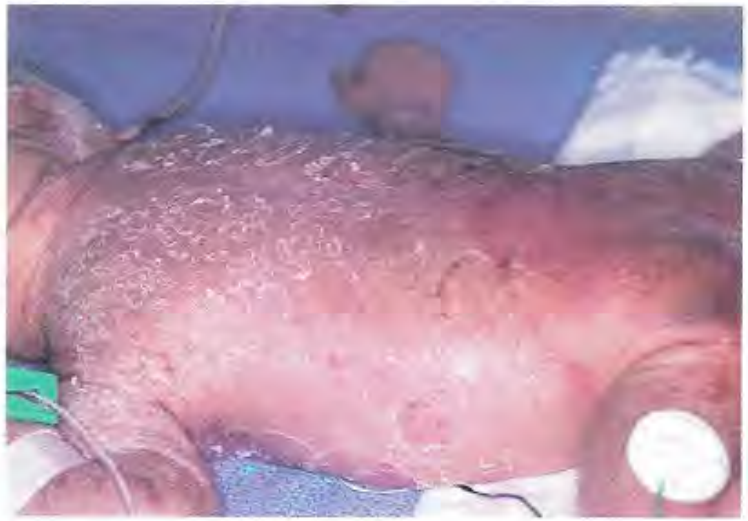


Figure 1.

Figure 2.

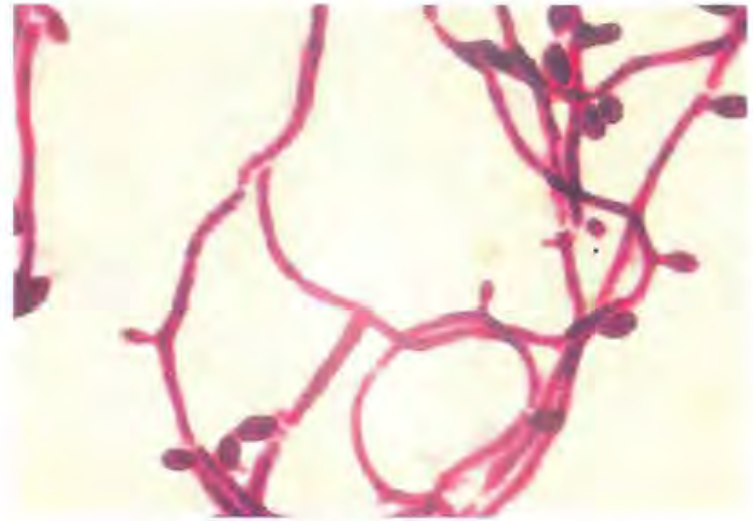
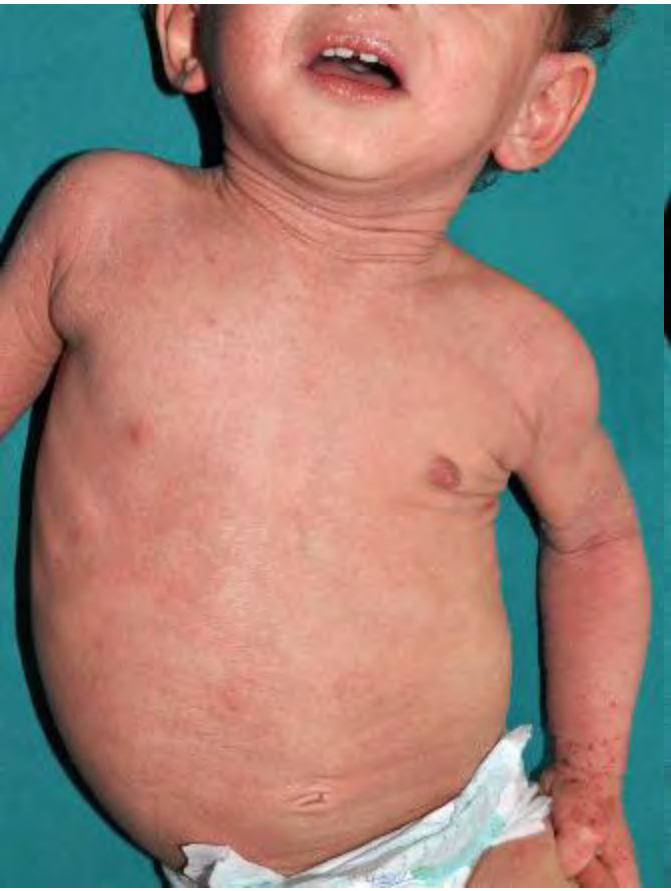


Figure 3.

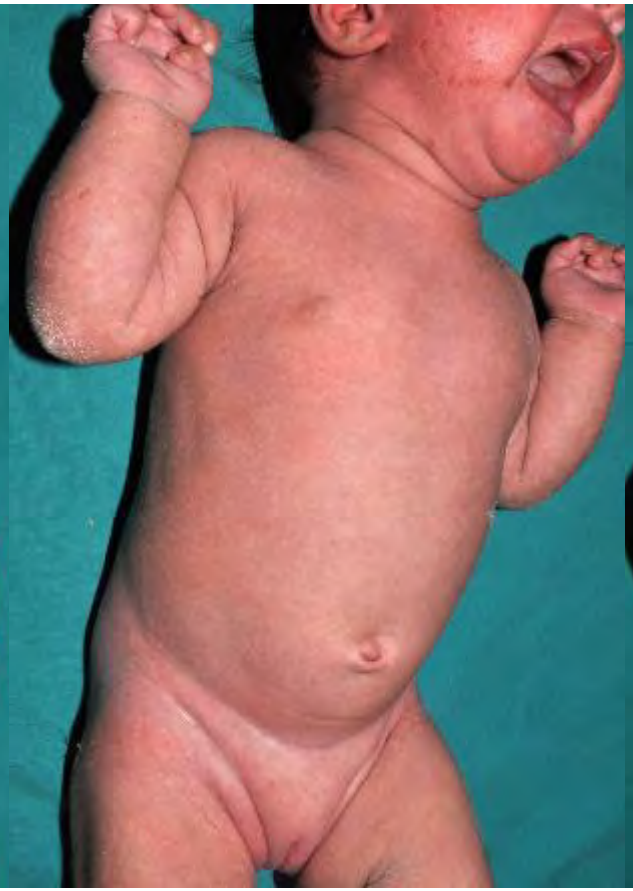
Neonatal erythroderma

- Congenital ichtyoses
- Atopic dermatitis
- Seborrheic dermatitis
- Neonatal acute generalized pustular psoriasis
- Diffuse cutaneous mastocytosis
- Staphylococcal scalded skin syndrome
- Congenital cutaneous candidiasis
- Congenital immunodeficiencies
- Malnutrition / Metabolic disorders
- Others

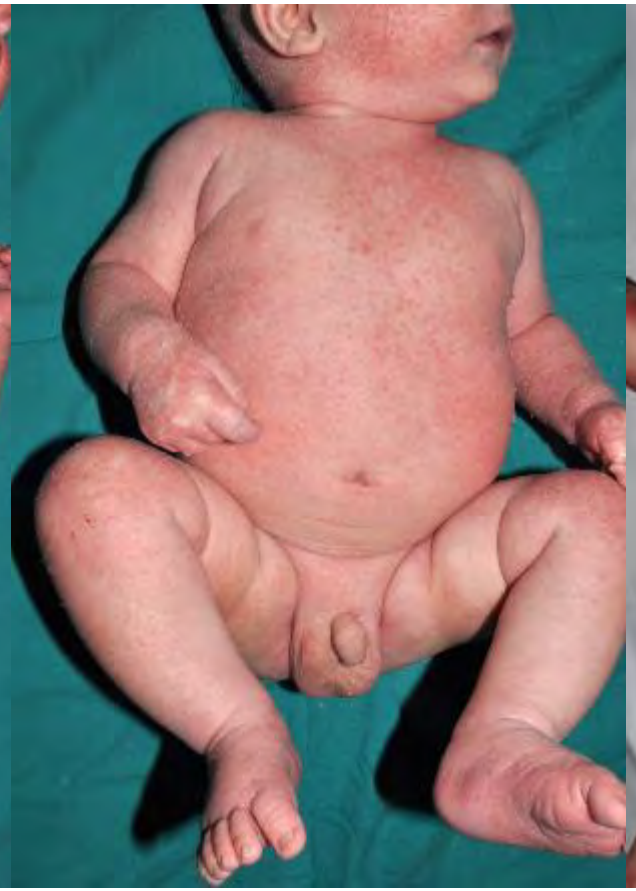
Neonatal erythroderma



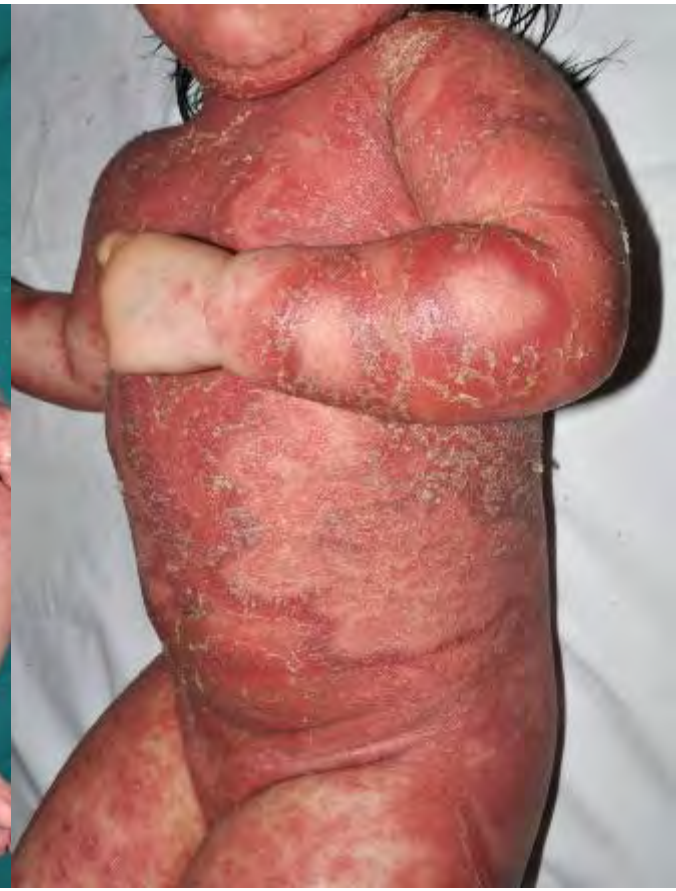
Atopic dermatitis



Epidermolytic ichthyosis

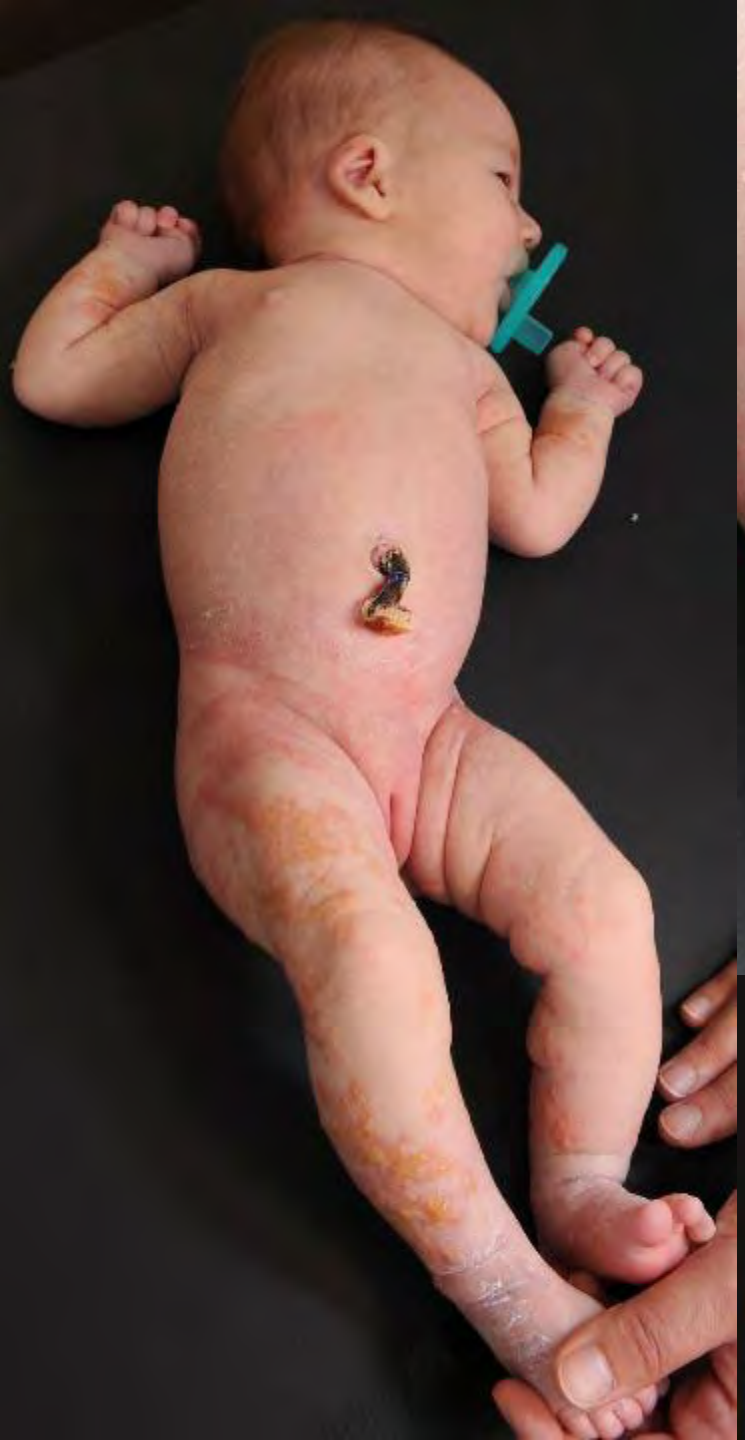


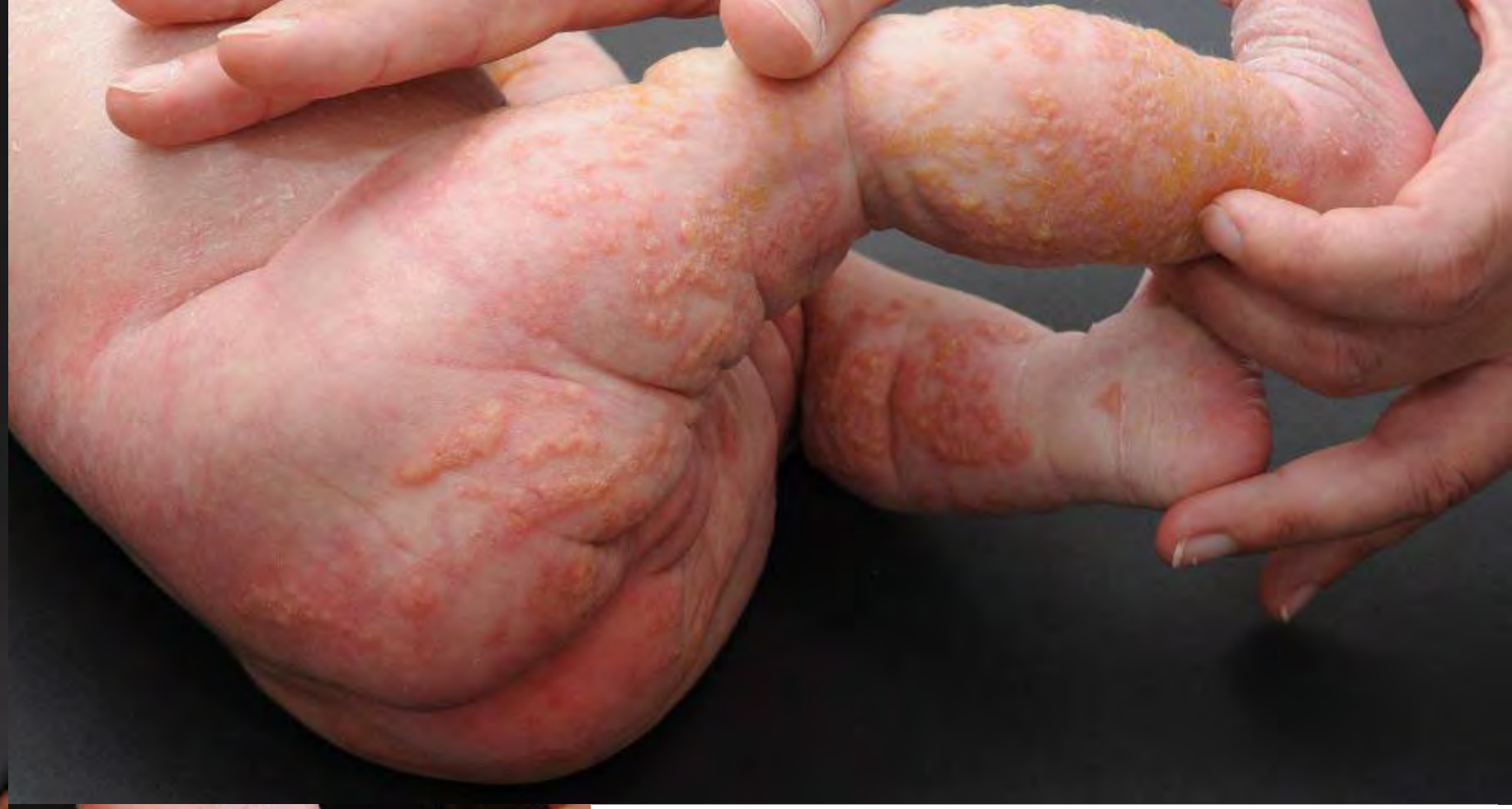
Congenital immunodeficiency

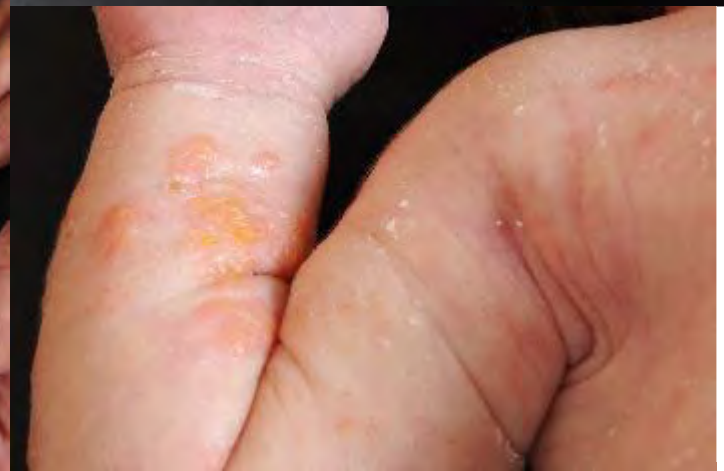


Pustular psoriasis

(Pictures courtesy Dr. A. Torrelo, Madrid)





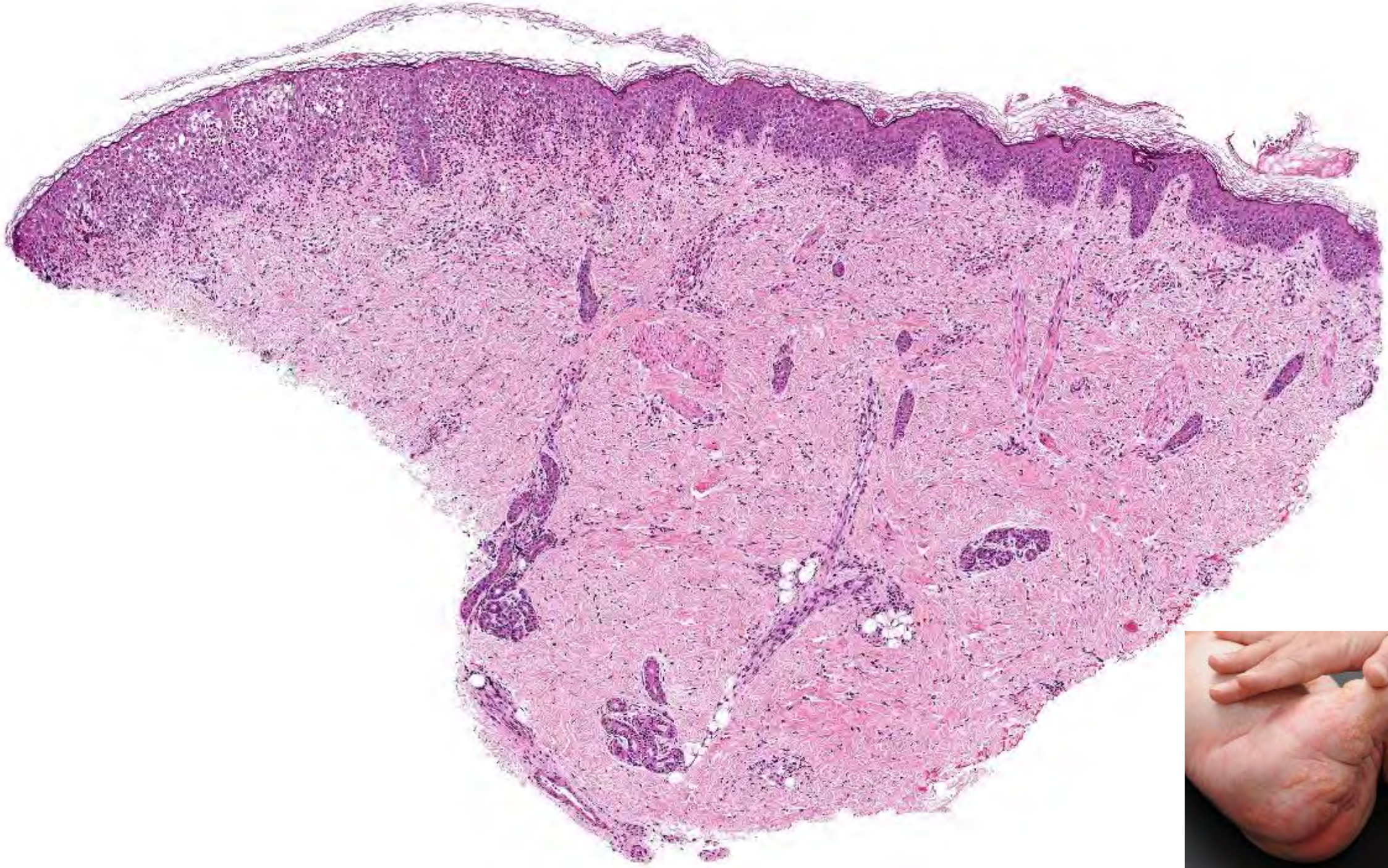


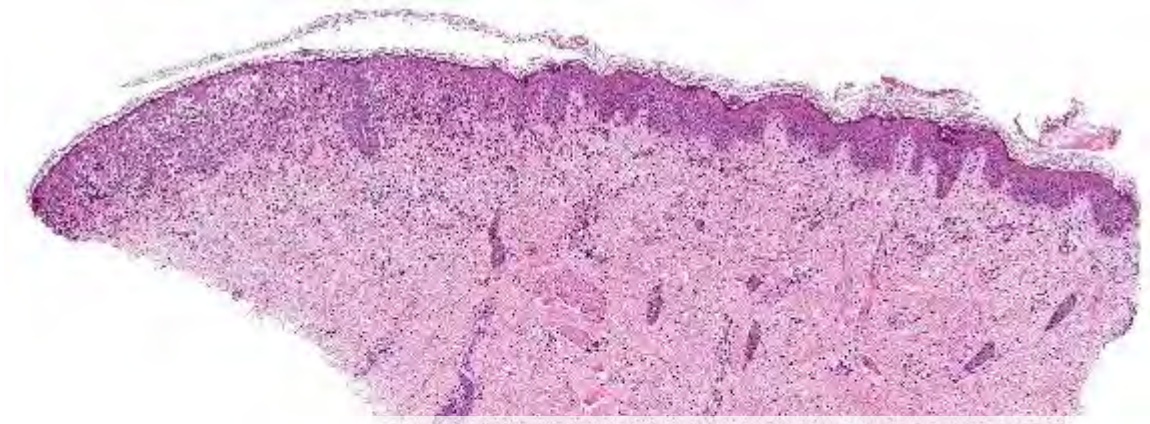
F, 11-day-old

Normal pregnancy and labor; no remarkable familial history.

Generalized, partly bullous lesions following in part the Blascko lines.

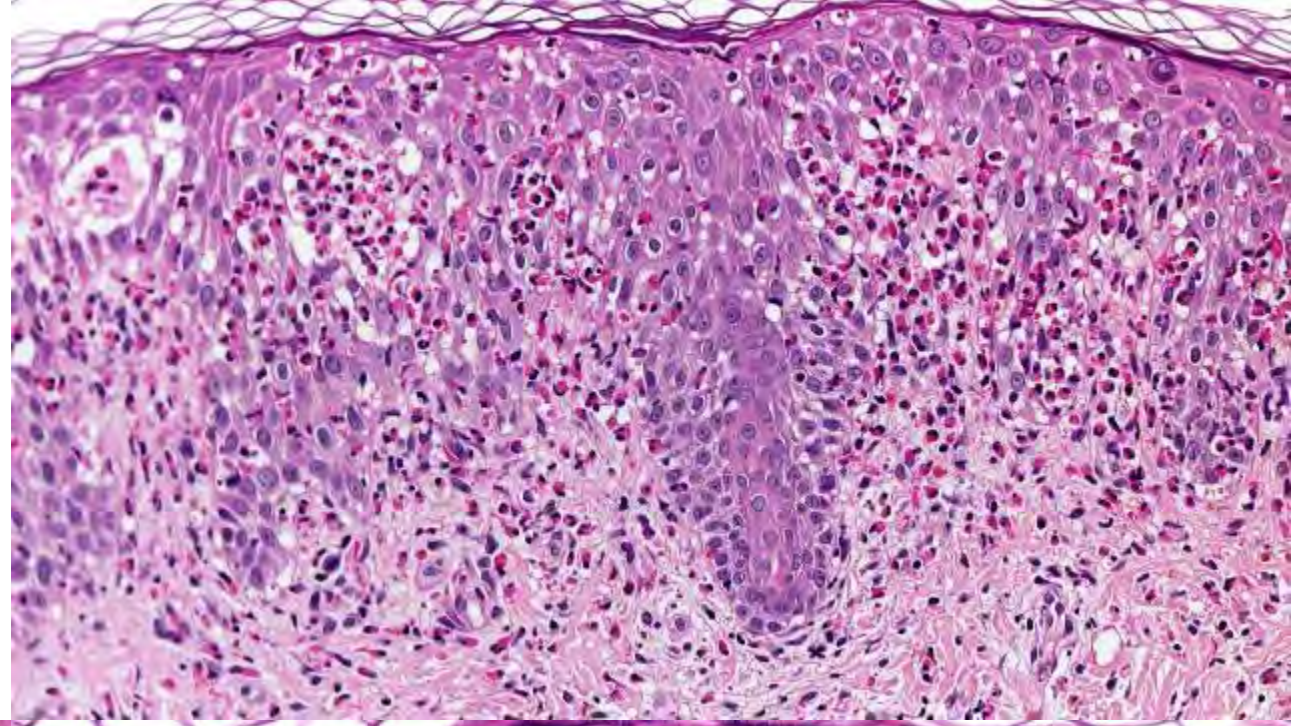
A biopsy is taken from the gluteal region.

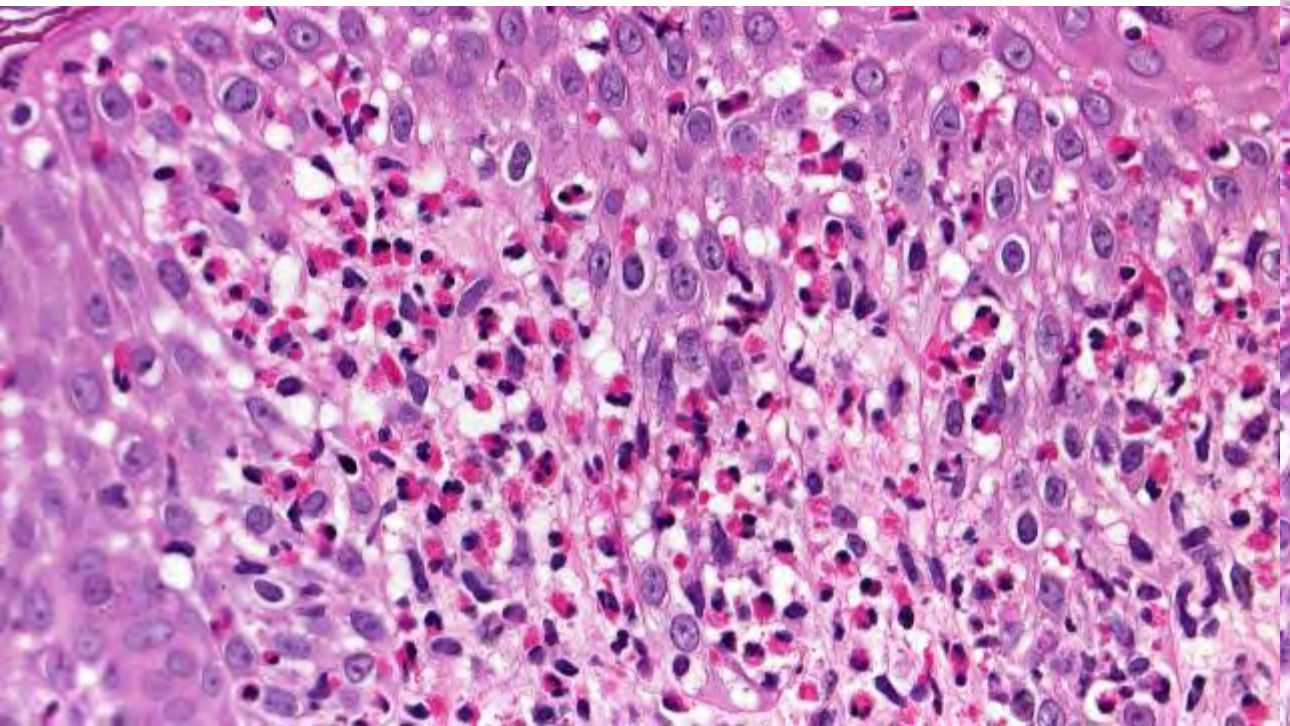


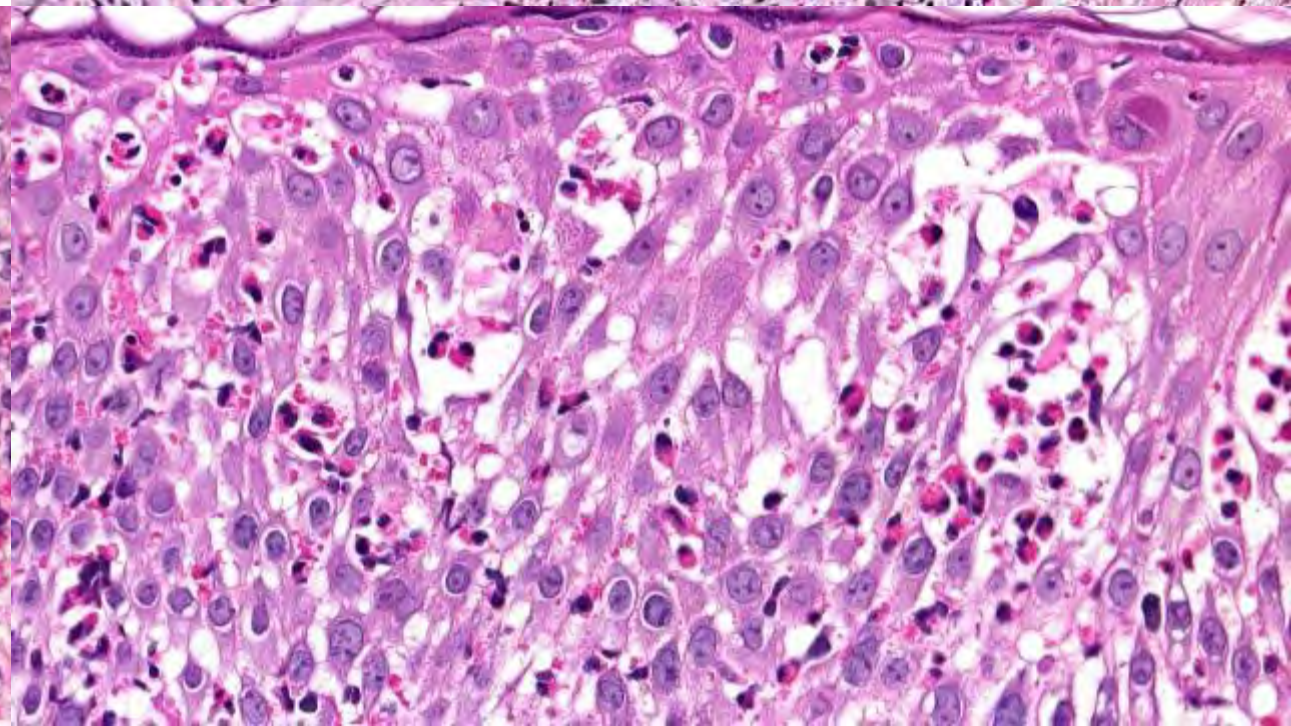


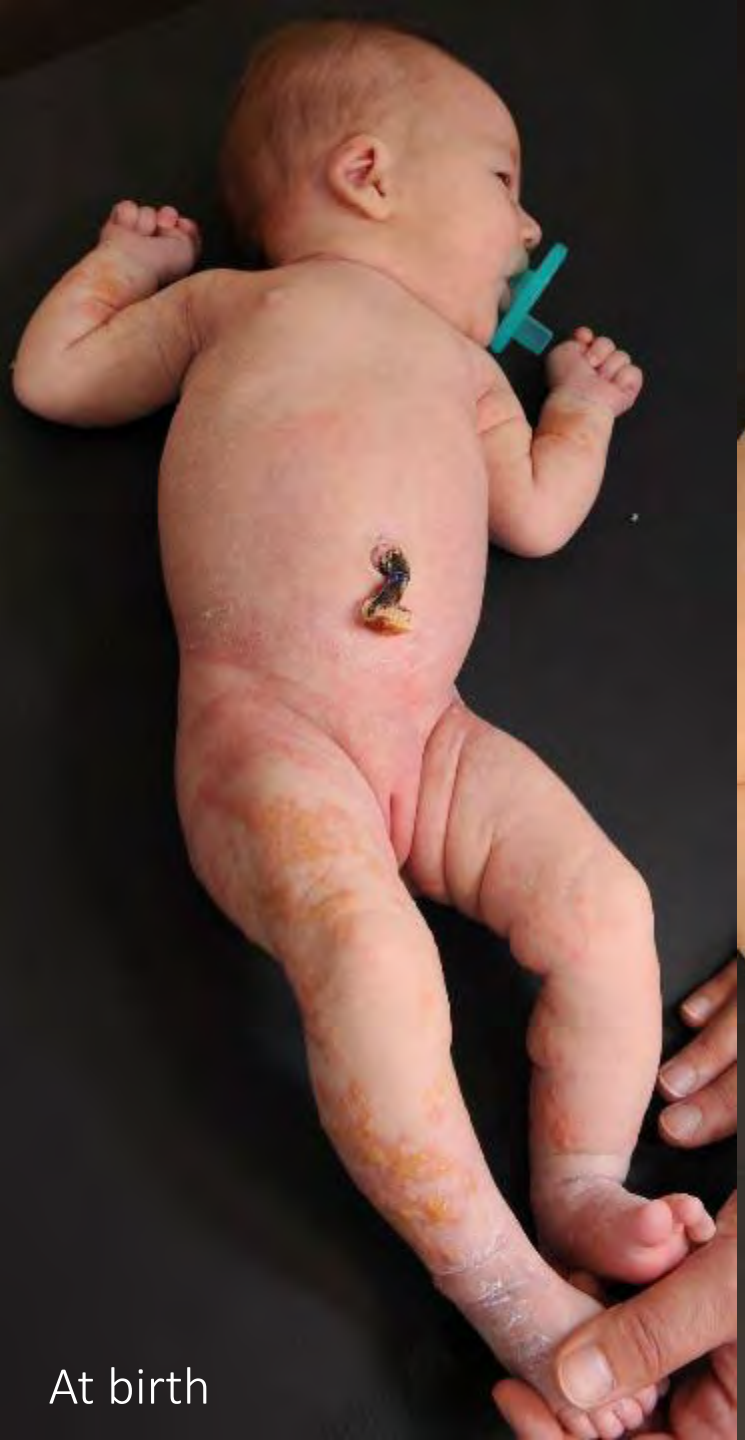
Incontinentia pigmenti

Stage I

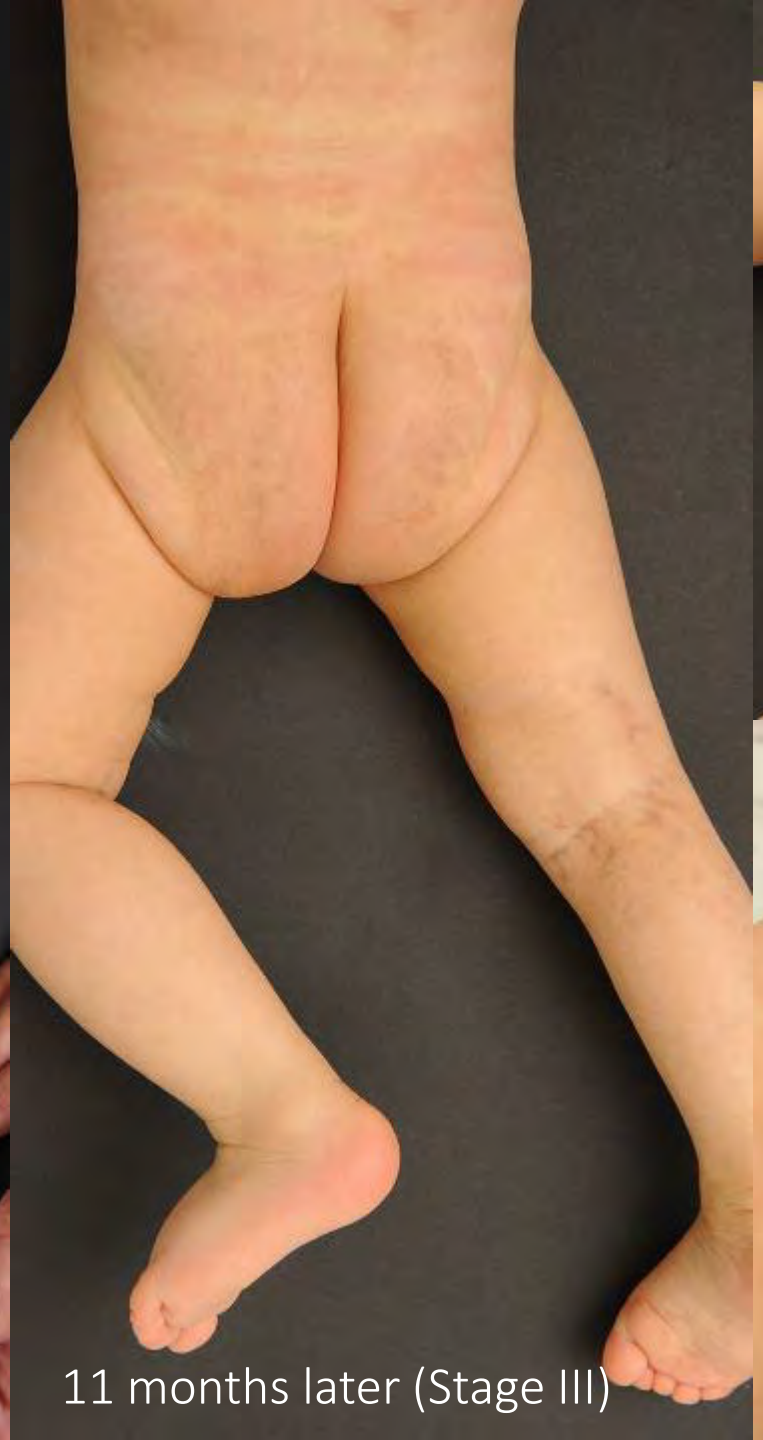




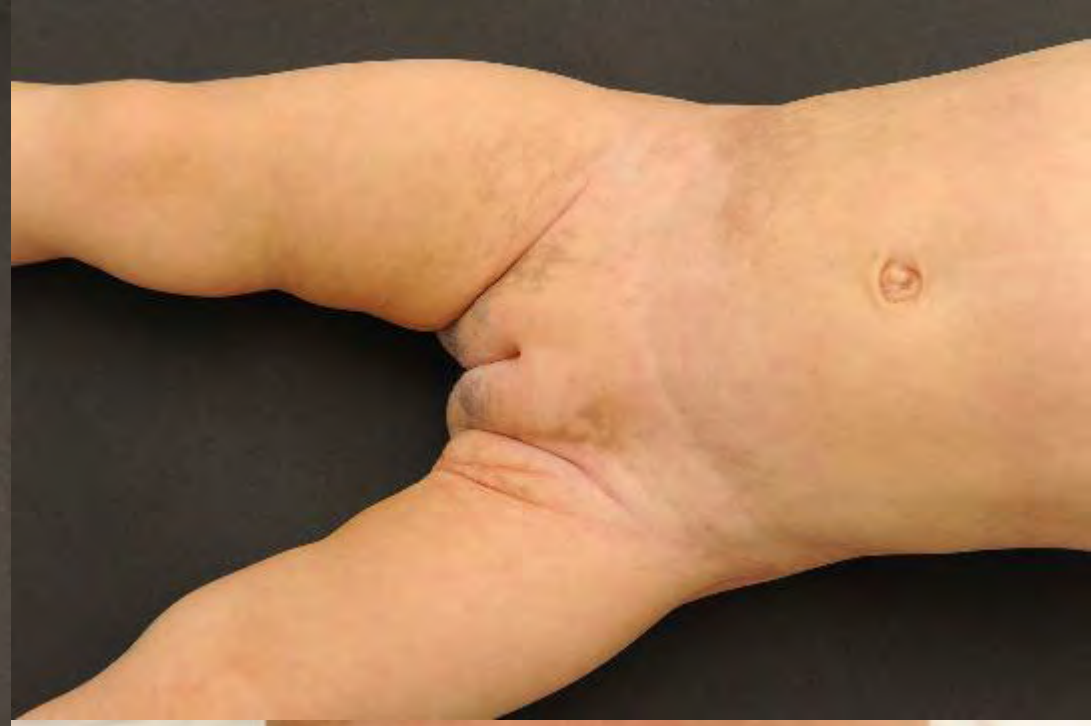


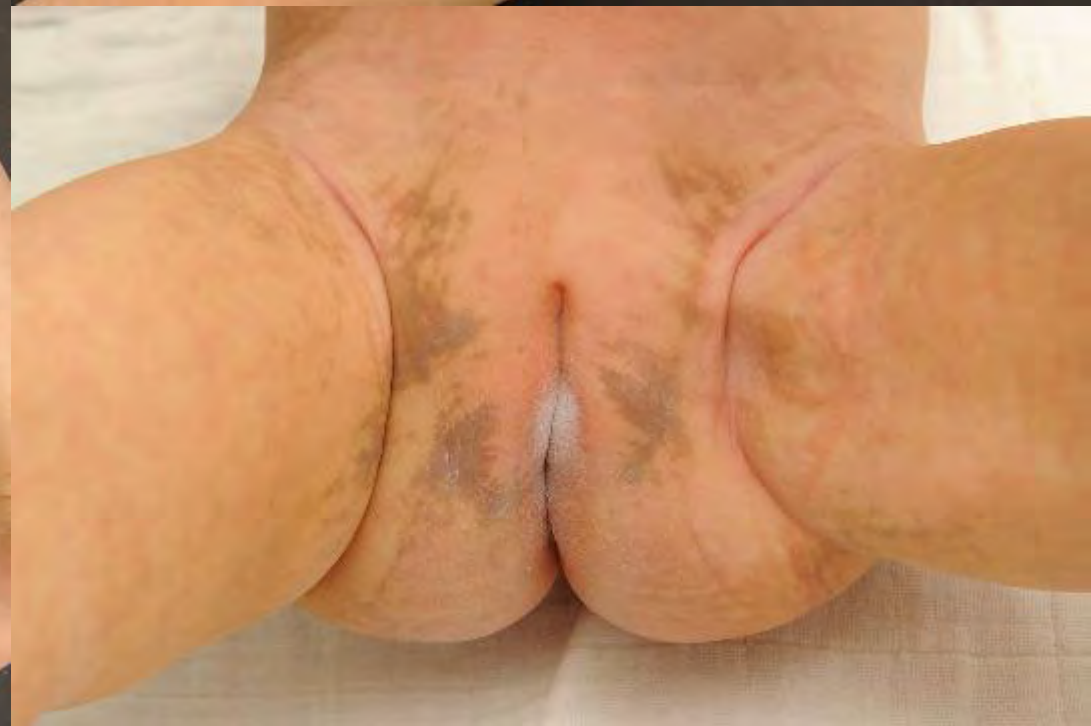


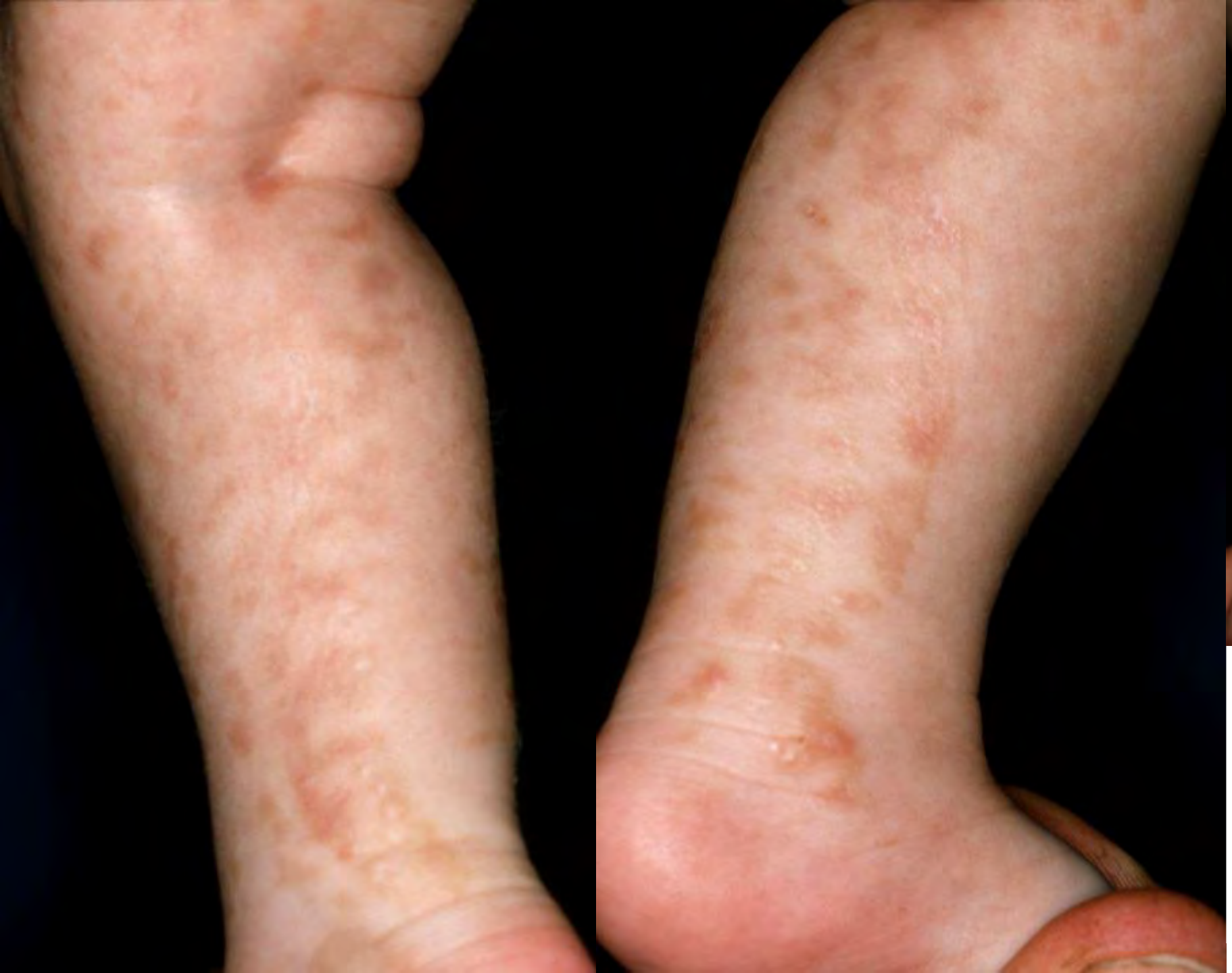
At birth

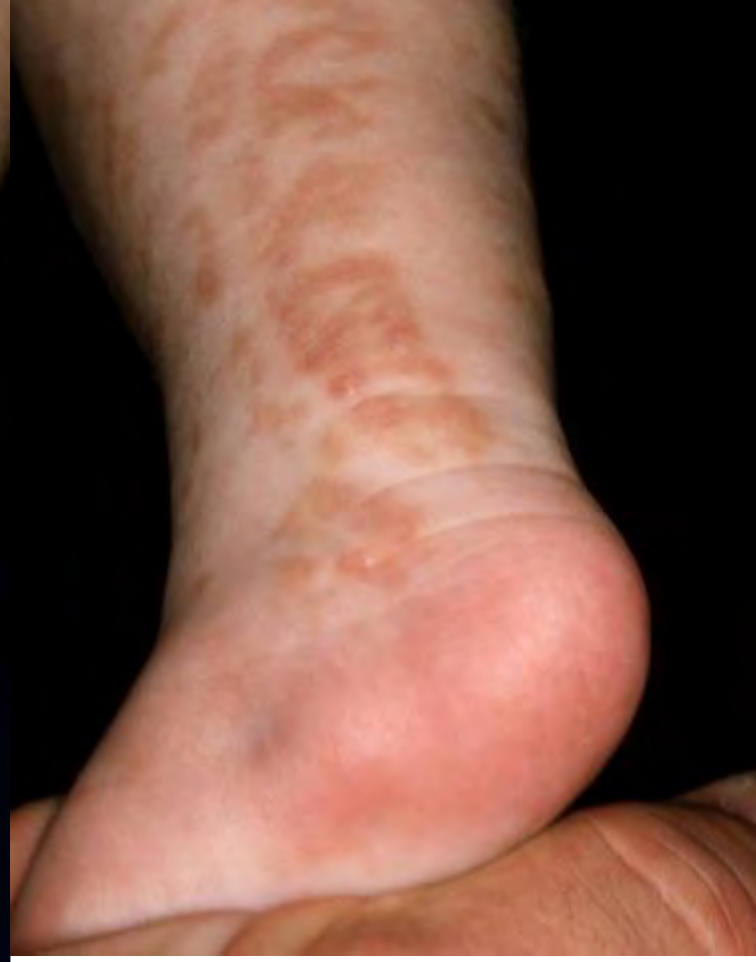


11 months later (Stage III)





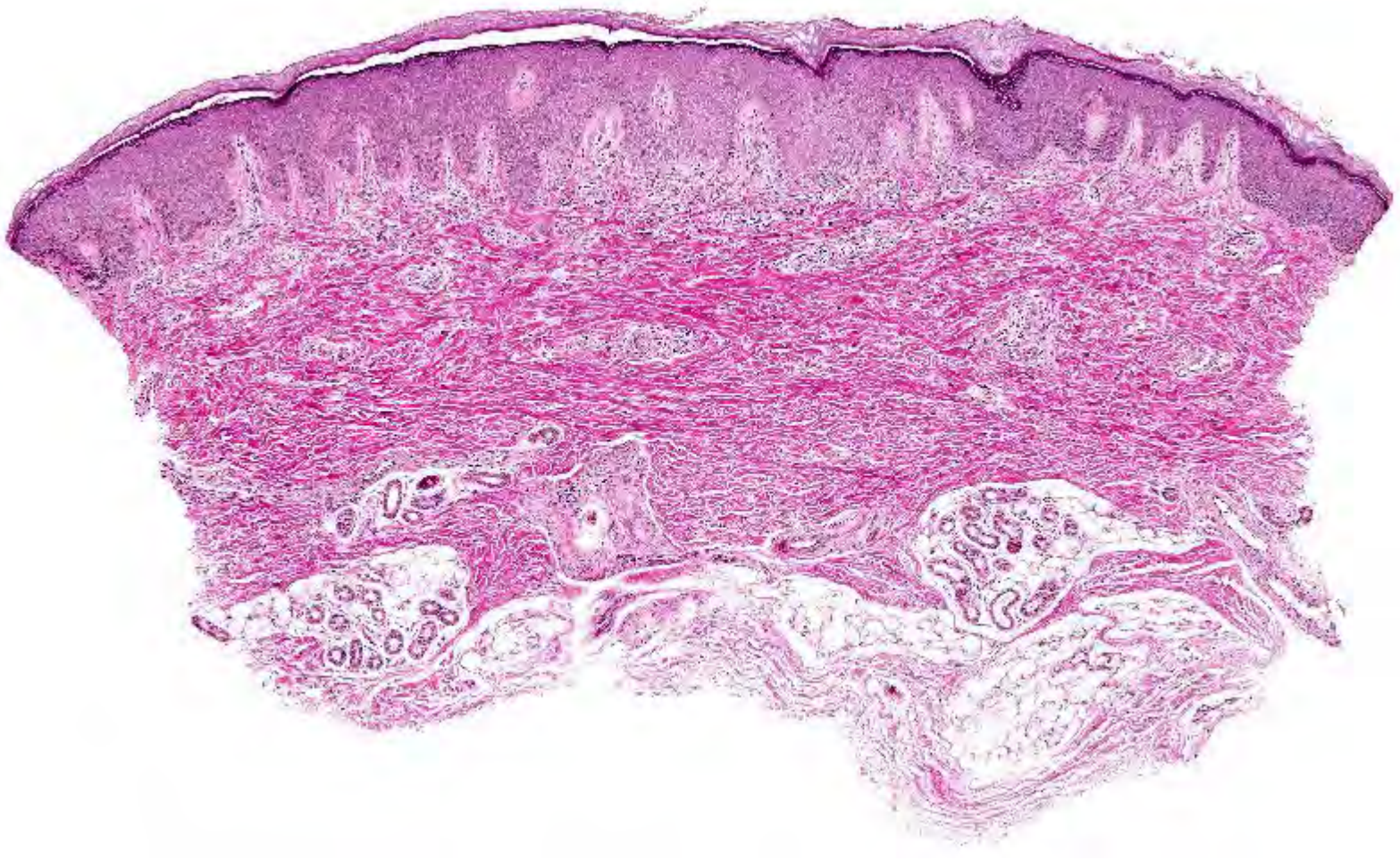


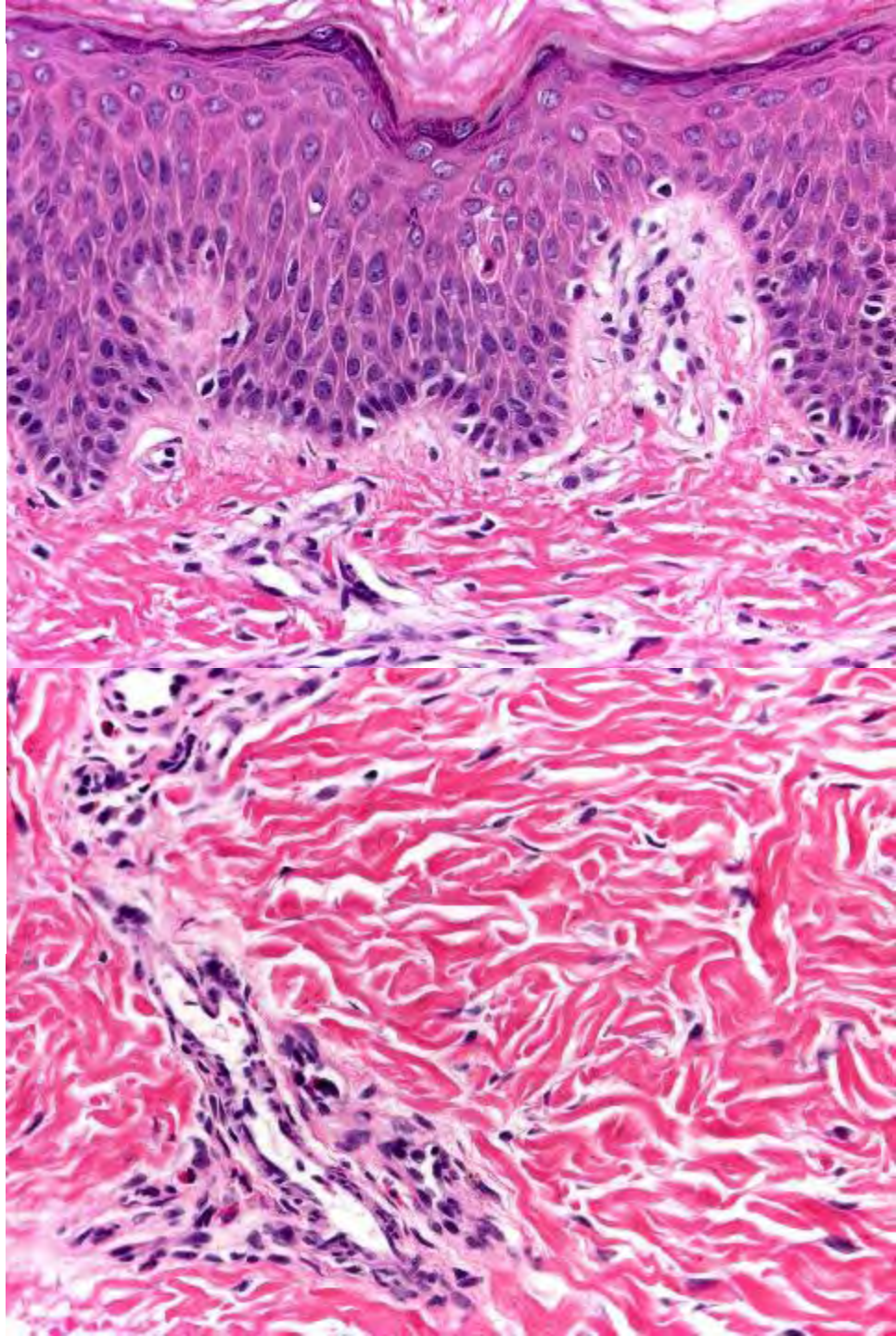


F, 6-week-old

Generalized, partly vesicular lesions with focal linear arrangement.

A biopsy is taken from the inner ankle.



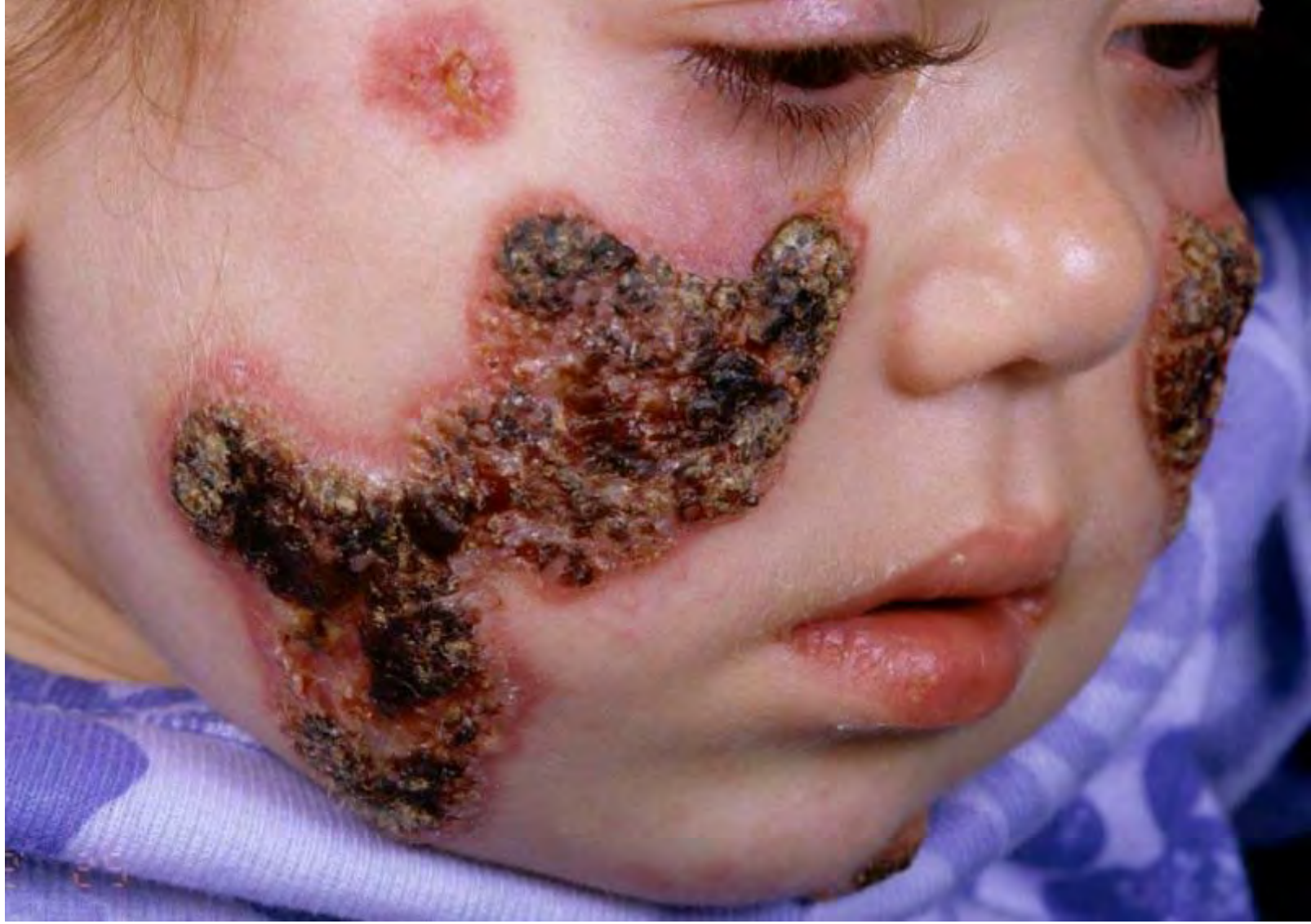


Incontinentia pigmenti

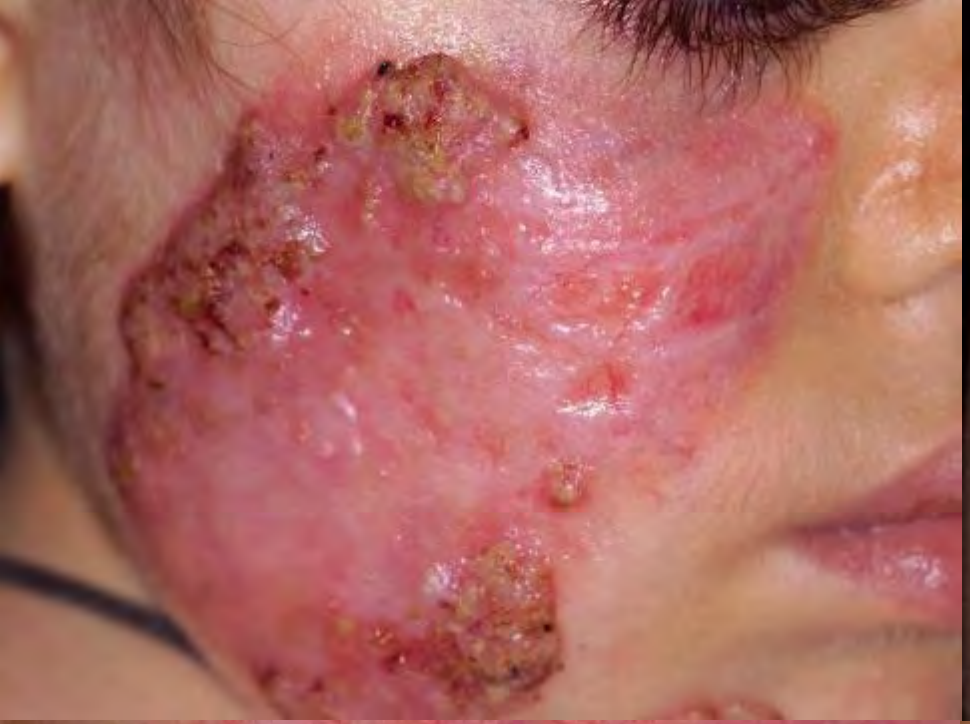
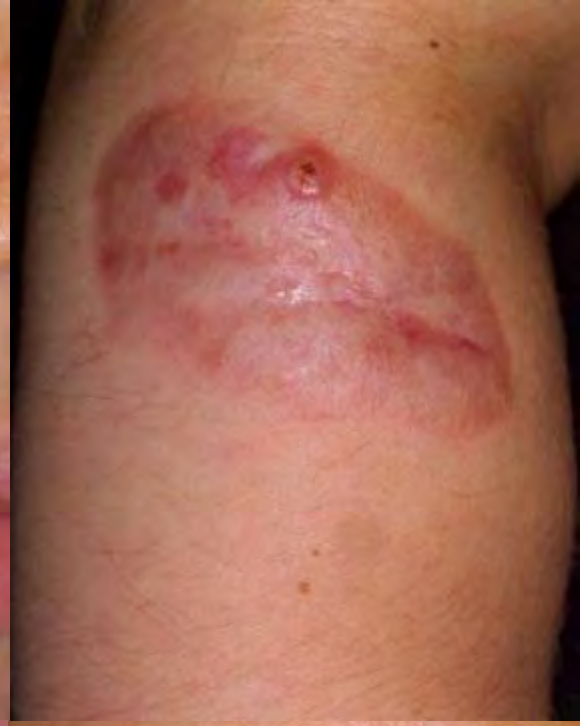
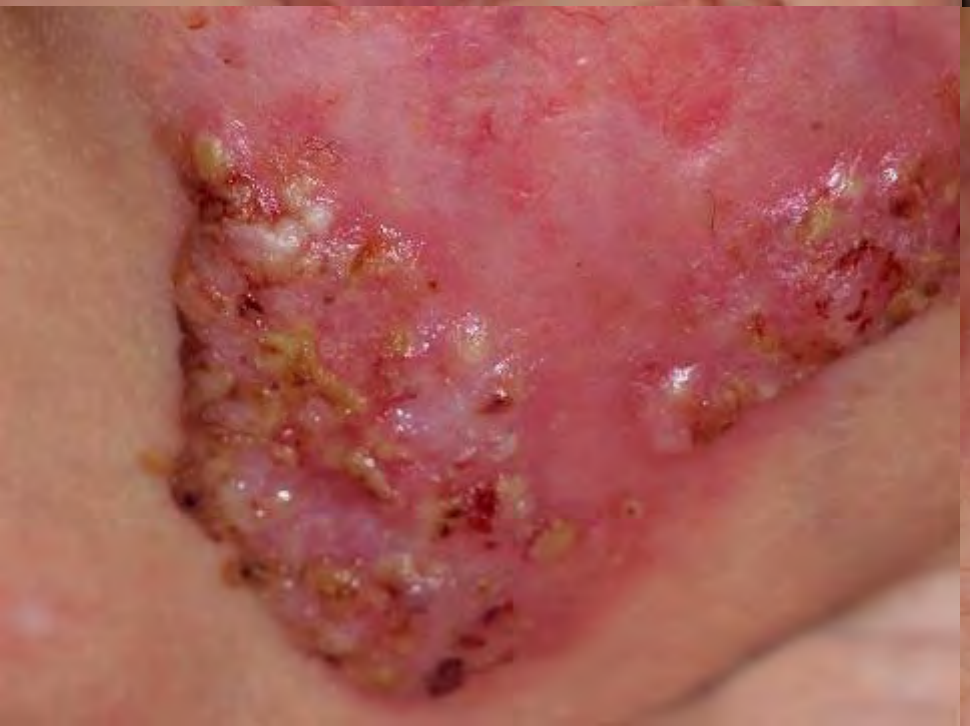
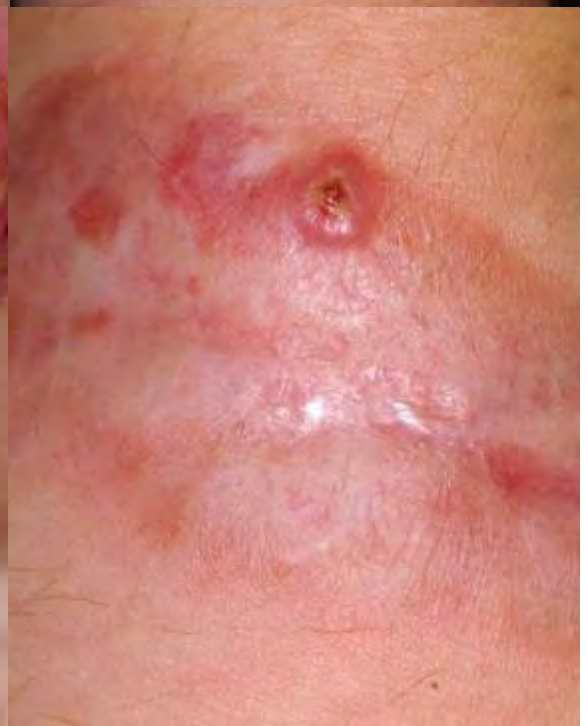
Stage II

Incontinentia pigmenti

- Mutation in the *IKKBKG* (*NEMO*) gene
- *Stage 1* (vesicular); *Stage 2* (verrucous); *Stage 3* (hyperpigmented); usually resolve during infancy/adolescence; *Stage 4* (hypopigmented atrophic) onset in adolescence or adulthood
- "Painful subungual tumor": possibly a type of keratoacanthoma
- *Differential diagnosis with other vesiculobullous eruptions in newborns and young children:*
  Toxic erythema of newborn; Transient pustular melanosis; Neonatal cephalic pustulosis; Congenital candidiasis; Langerhans cell histiocytosis; Infantile acropustulosis; other rare causes of vesiculobullous eruptions



F, 4. Since the age of 2 months vegetating, ulcerated lesions on the face and upper extremities. Radiologic investigations negative; blood investigations within normal limits.

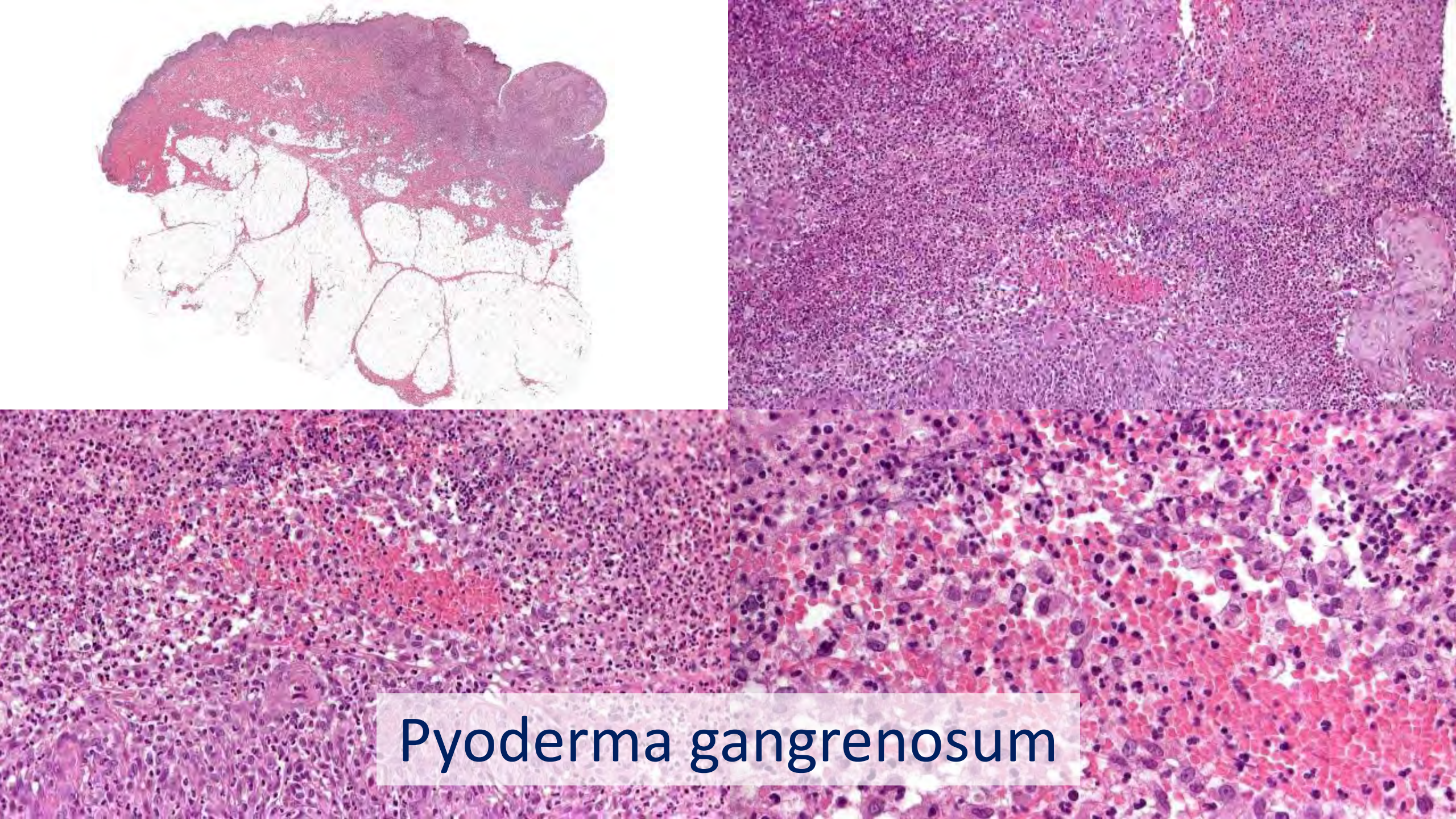
Between 1 and 2 years of age treated with steroids, cyclosporin, infliximab with only partial response.

At age 2 a biopsy was diagnosed with "non-X malignant histiocytosis"; treatment with vincristine, cyclophosphamide, prednisone without effect (short-term improvement was noted by the mother after every prednisone administration).

At age 3 two more biopsies did not provide a clear-cut diagnosis; treated with low-dosage radiotherapy without effects.

At age 4 two new biopsies.

The family of the patient comes to Graz for a second opinion (this picture taken during the visit; old biopsies reevaluated).

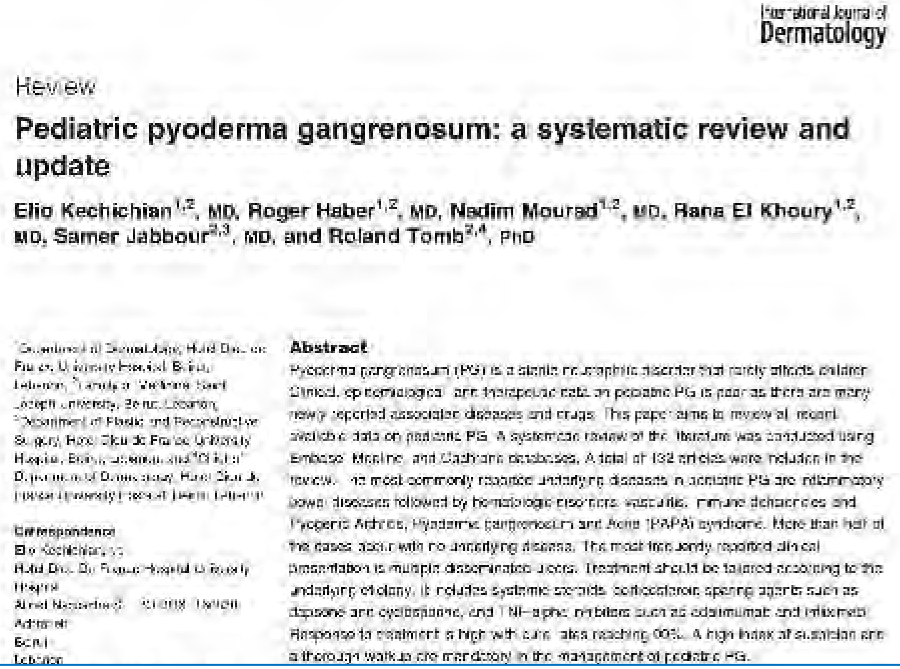


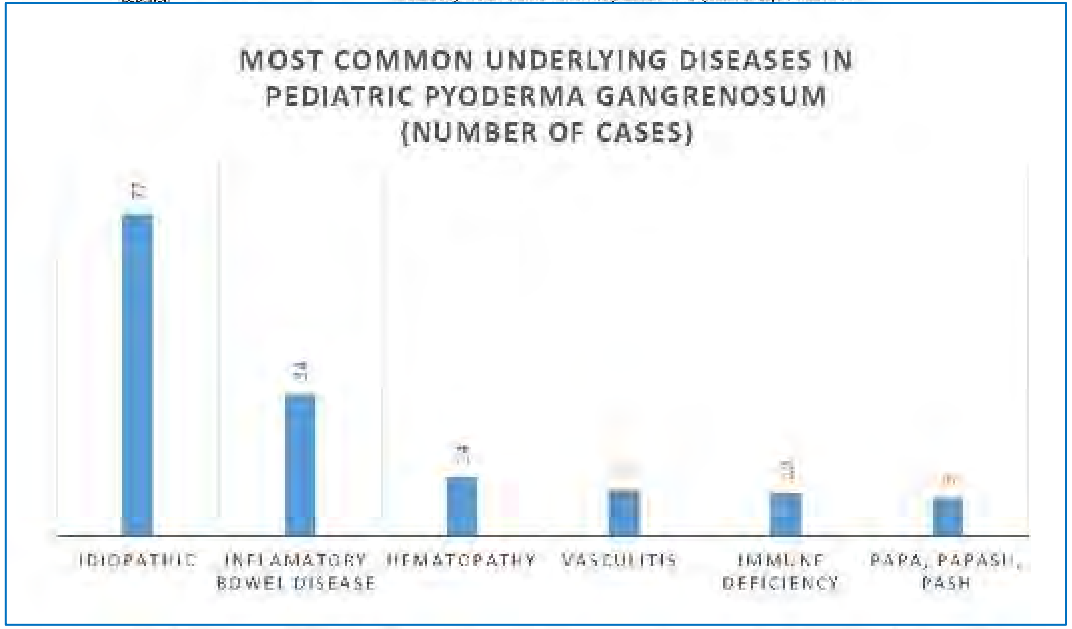
Pyoderma gangrenosum

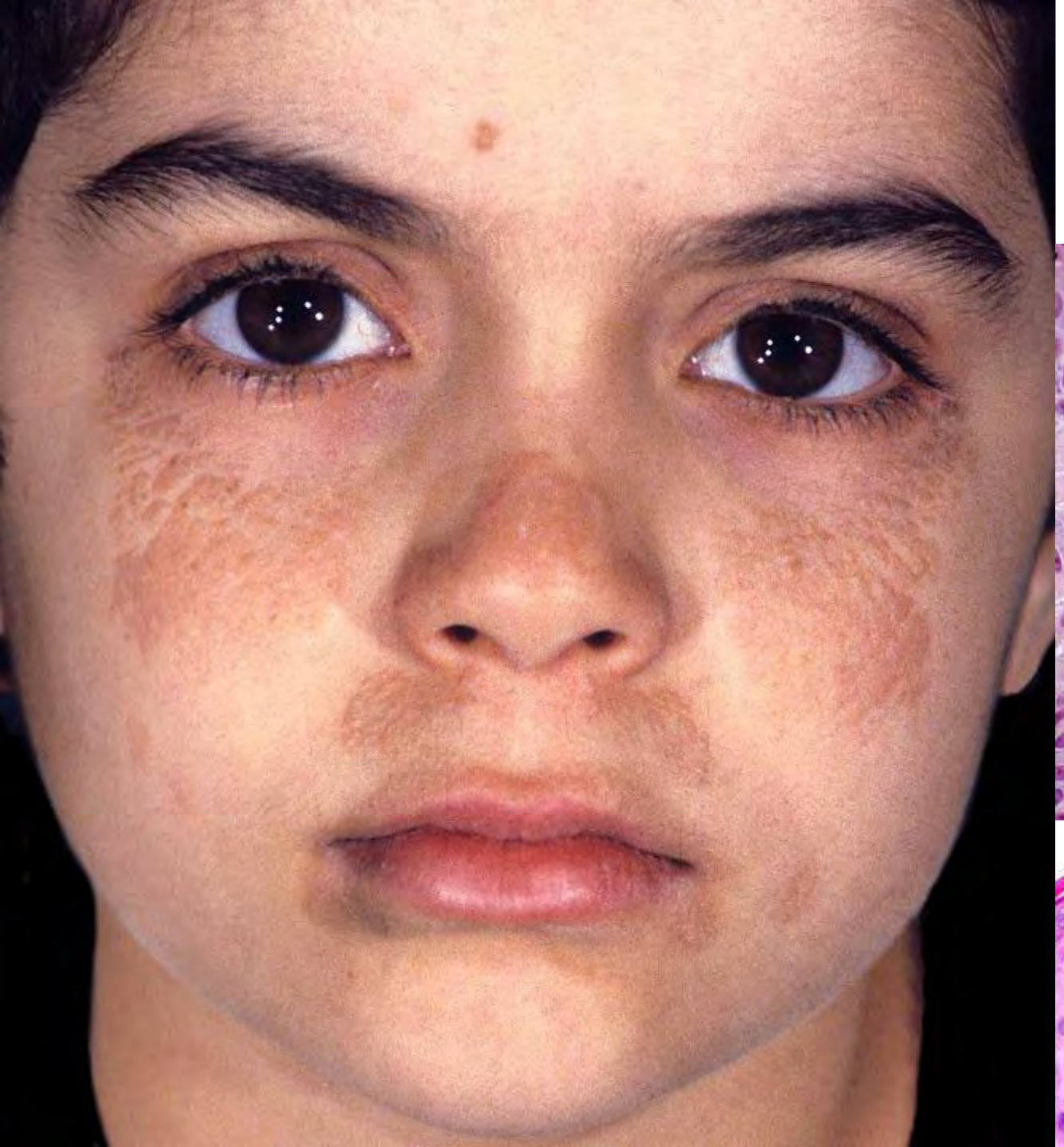
Severe pyoderma gangrenosum in children

- Head & face lesions more common than in adults; often genital lesions in infants and small children (perineum)
- May be associated with systemic diseases (ulcerative colitis, rheumatoid arthritis, etc.); the majority of cases however idiopathic
- May be part of PAPA *(pyogenic arthritis, PG & acne)*, PAPASH *(pyogenic arthritis, PG, acne, & suppurative hidradenitis)*, or PASH *(PG, acne, suppurative hidradenitis)*
- In many cases controlled by systemic steroids
- Severe, recalcitrant cases pose a difficult therapeutic problem


Images in paediatrics
Dramatic case of paediatric pyoderma gangrenosum
Figure 1
Figure 2
REFERENCES
Check for updates
BMJ


International Journal of Dermatology
Review
Pediatric pyoderma gangrenosum: a systematic review and update
Elio Kechichian, MD, Roger Haber, MD, Nadim Mourad, MD, Rana El Khoury, MD, Samer Jabbour, MD, and Roland Tomb, PhD
Abstract


MOST COMMON UNDERLYING DISEASES IN PEDIATRIC PYODERMA GANGRENOSUM (NUMBER OF CASES)
IDIOPATHIC
INFLAMATORY BOWEL DISEASE
HEMATOPATHY
VASCULITIS
IMMUNE DEFICIENCY
PAPA, PAPASH, PASH



F, 7

Severe sunburn after sun exposure without sunscreen in the mountain (1,500 meters elevation above sea level). The eruption developed within 7—10 days.

Juvenile colloid milium

Juvenile colloid milium

Immunohistochemical and ultrastructural studies

Hashimoto K, Nakayama H, Chimenti S, Carlesimo O A, Calvieri S, Iacobelli D, Bianchi L. J Cutan Pathol 1989: 16: 164–174.

A 7-year-old Italian girl with juvenile colloid milium was studied with histological, immunohistochemical, and electron microscopic methods. This patient had a well-documented history of severe sunburn and developed the lesions on the face shortly afterward. Numerous apoptotic keratinocytes were observed in the lower epidermis. These cells began their degeneration with filamentous whorl formation (or filamentous degeneration) of tonofilaments. In the papillary dermis the colloid substance was resolved by the electron microscopy into either wavy, thin filaments derived from the epidermal keratinocytes or typical amyloid filaments. Many desmosomes and gap junctions were found in the colloid substance. Polyclonal antikeratin antibody (DAKO) was positive in the colloid substance, particularly in the parts close to the epidermis. These findings suggested that juvenile colloid milium is different from adult colloid milium despite clinical similarities and that the former belongs to the group of actinic amyloid K, i.e. amyloidoses due to actinic degeneration of keratinocyte and its keratin.

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Colloid milium is currently classified into three different subtypes; (a) adult type (1–7), which occurs on sun-exposed areas such as face, ears, neck and dorsum of hands as small or confluent semi-translucent papules, (b) juvenile form (8), which has been attributed to keratinocyte degeneration and (c) pigmented colloid milium (9) associated with exogenous ochronisis due to hydroquinone bleaching cream among South African blacks. A vague entity called nodular colloid degeneration (10–12) or paracolloid of the skin (13) may represent a tumefactive nodular amyloidosis which is now characterized as an accumulation of light chain of immunoglobulins. (14, 15).

We encountered an interesting case of juvenile colloid milium which was initiated by a severe sunburn. This report consists of immunohistochemical and ultrastructural analyses of this case to elucidate the nature of so called juvenile colloid milium.

Clinical history

The patient is a 7-year-old Italian girl presenting several small confluent papules, brownish-colored, occurring symmetrically on the zygomatic prominences, nose and perioral region (Fig. 1). The onset of her illness coincided with a very severe sunburn which she sustained during mountain skiing in the Italian Alps (1,500 meters elevation above sea level) in February, 1984. The sun exposure without sunscreen lasted 2–3 h/day for one week. The first eruption developed within 7–10 days. Only a slight improvement has been noticed after the diagnosis and avoidance of sun-exposure. No history of similar illness is noted in her family.

Material and methods

A biopsy specimen was divided into 2; the first part was fixed in 10% formalin and routinely prepared for diagnostic H & E stain and the second part for electron microscopy. Some sections from the first part were used for PAS stain, alkaline Congo red stain, Dylon stain (16) and immunohistochemical stain for amyloid P component and keratins. Amyloid P component (17) is present in all types of amyloid as well as in elastic fiber microfibrils (17). NKH-1 was used to detect proteins related to elastic fiber microfibrils (18). Monoclonal and polyclonal

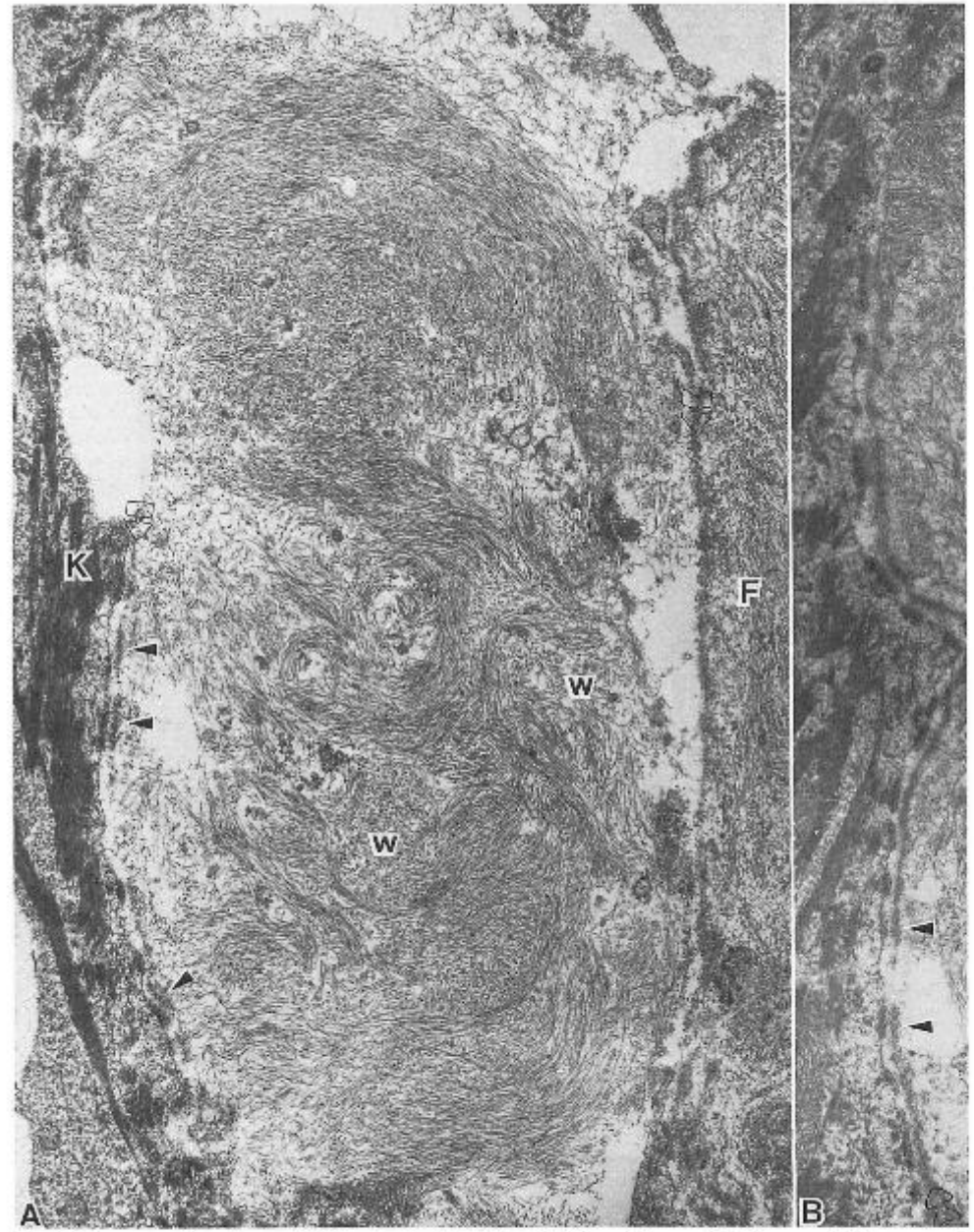
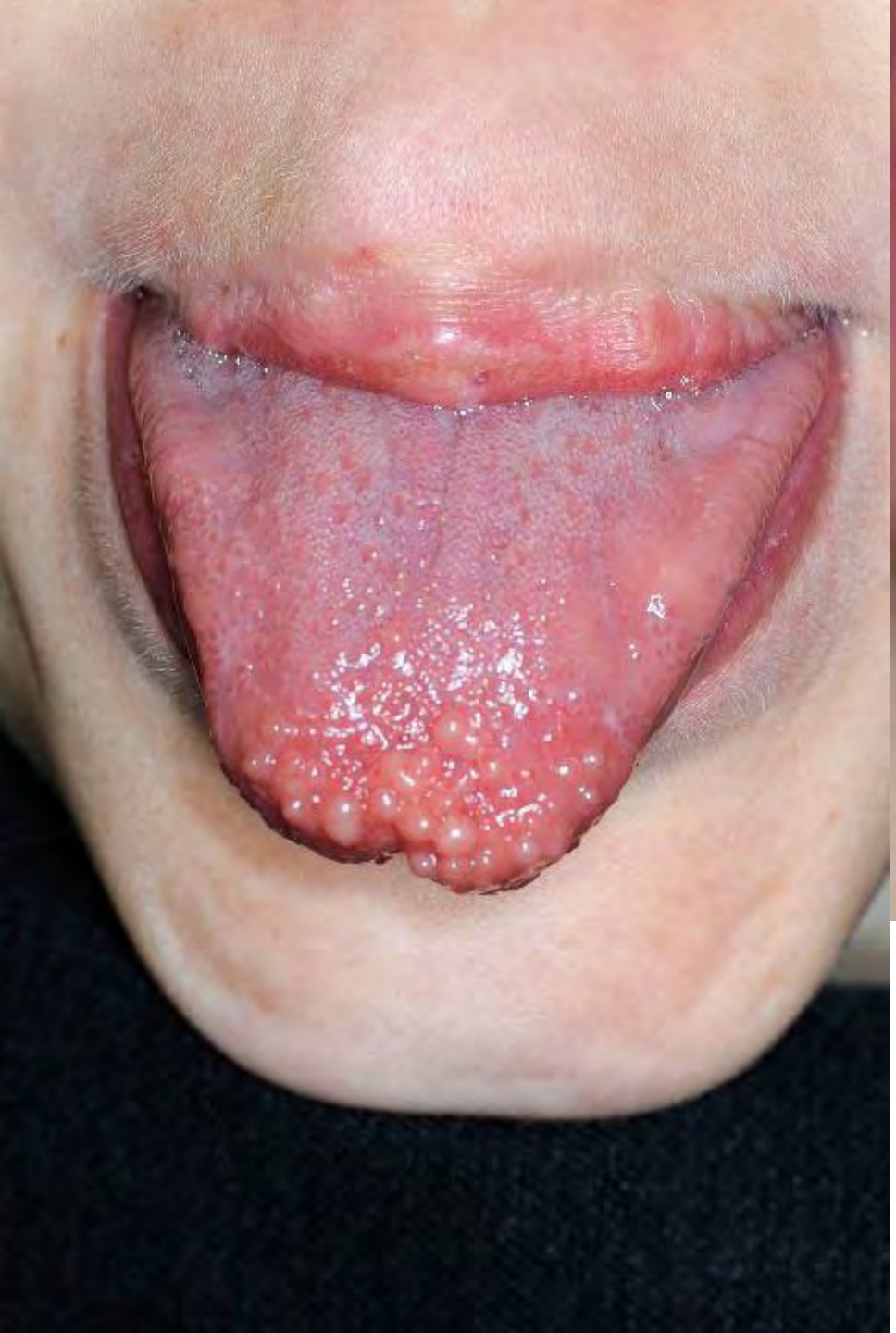
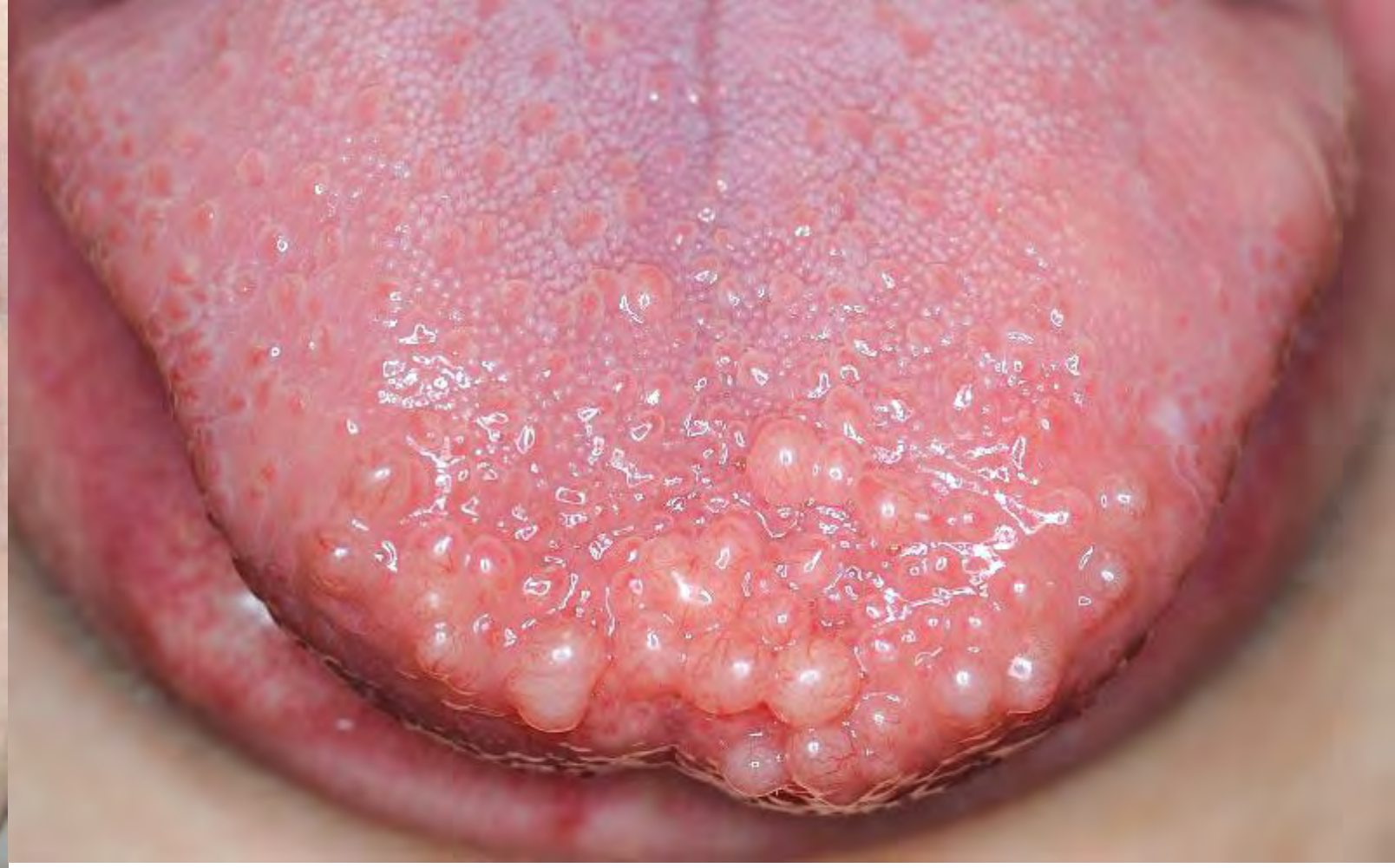


Fig. 6. A degenerated keratinocyte is filled with whorled (w) bundle of wavy filaments. This is surrounded by a normal keratinocyte (K) on the left and by another degenerated cell (F) on the right in A. Along the border of these cells basal lamina-like dense layer (arrow) is formed and hemidesmosome–like junctions are produced in A and B. At such junctions the basal lamina-like layer become thicker and denser (arrowheads). It seems that the basal lamina-like layer represent modified cell membrane of the degenerated cell. A and B; × 30,000.





F, 8

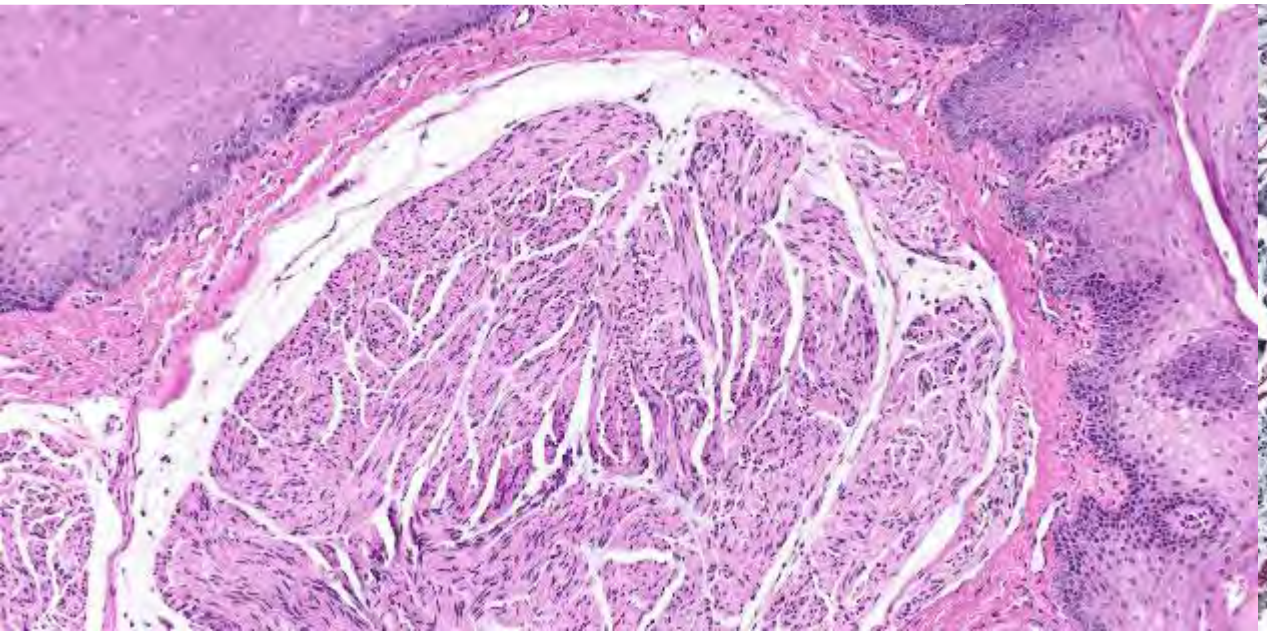
According to the mother lesions on the tip of the tongue present "forever". No other relevant information reported in the chart.

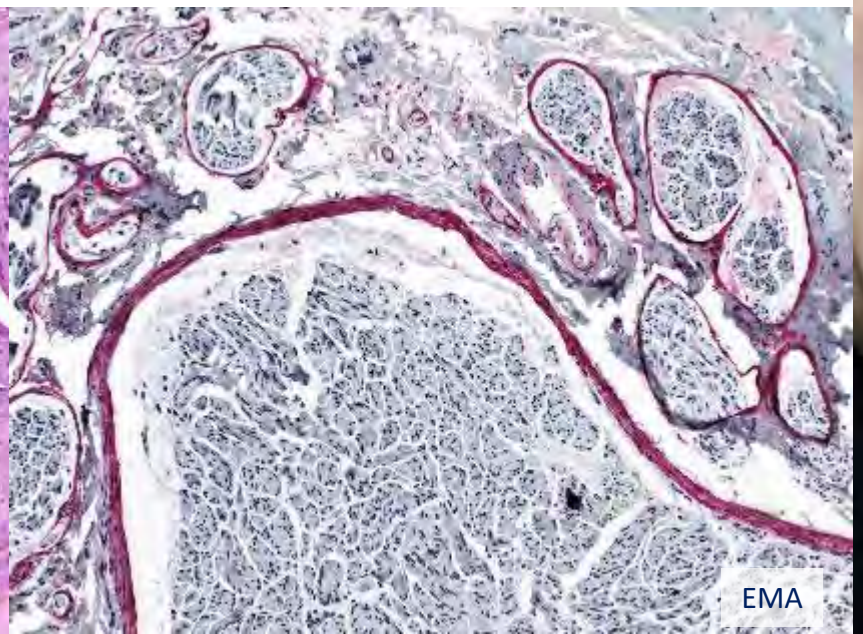
Several lesions are removed surgically under the clinical diagnosis of "lymphangiomas, retention cysts, or papillomas".

Multiple mucosal neuromas

(in the original report diagnosed as "neurofibromas")

(Thanks to the Institute of Pathology, Graz, for providing the specimens)





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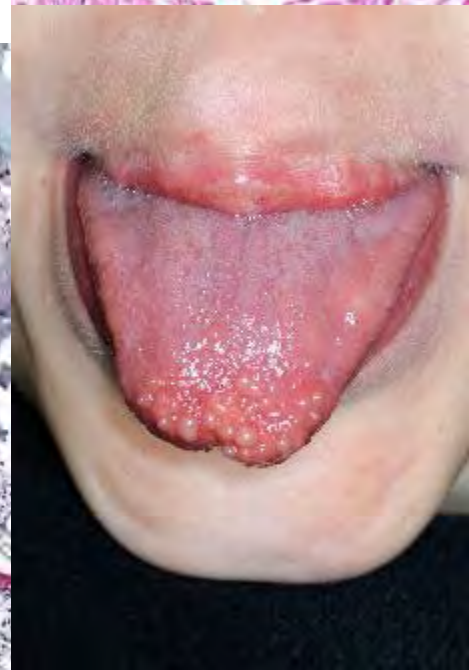
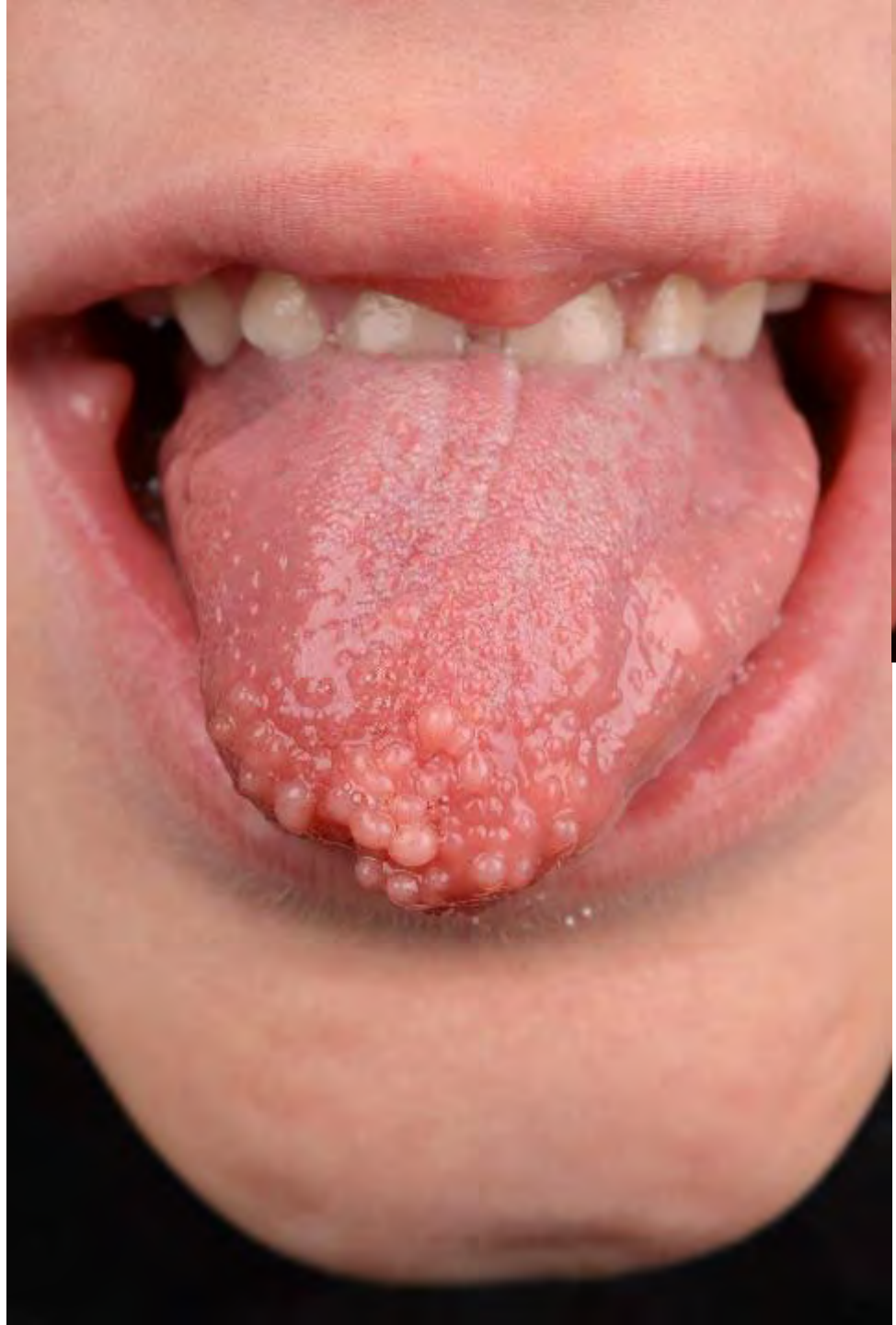
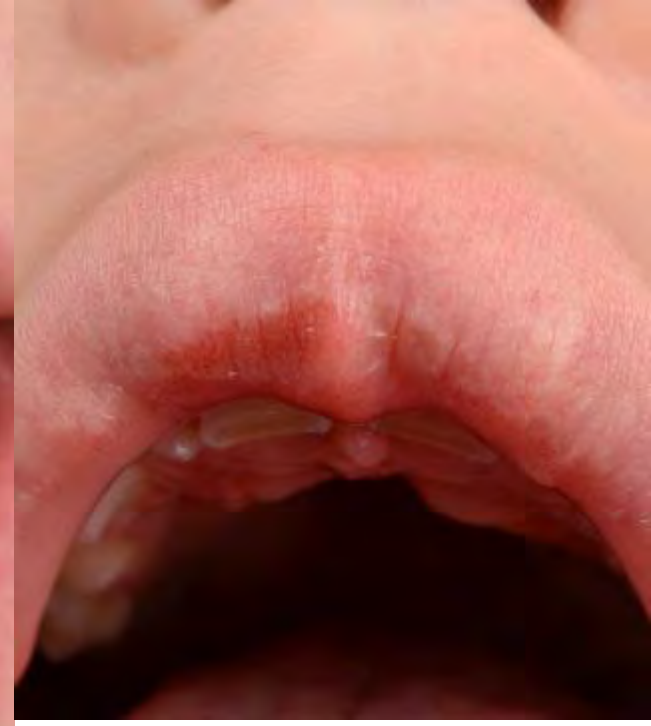


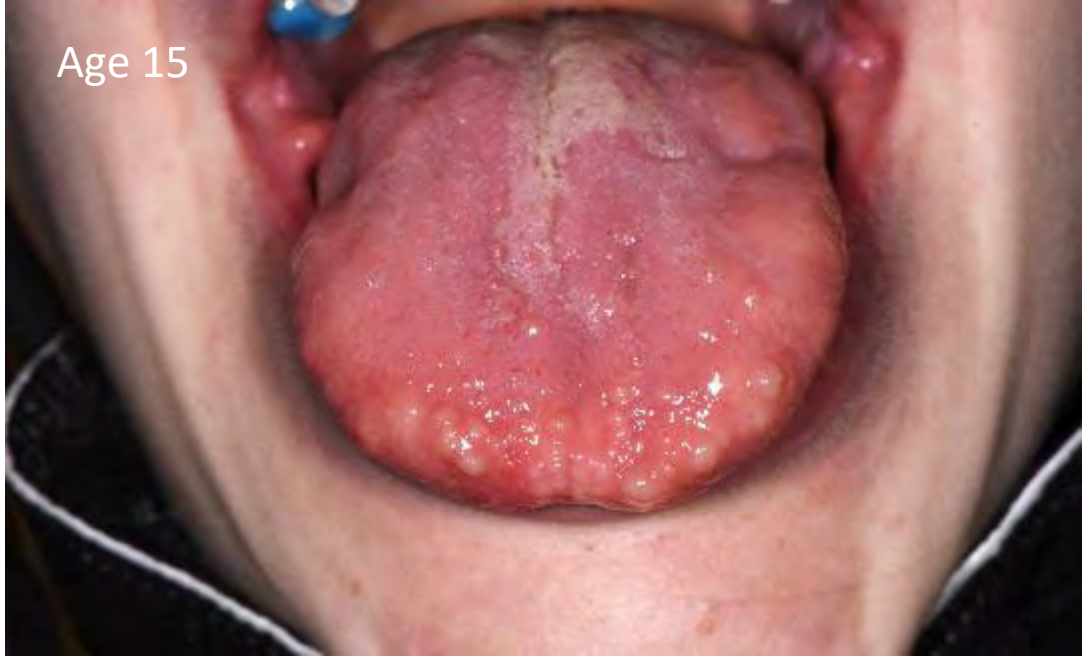
One year previously (age 7)





Four years previously (age 4) had presented at the Pediatric department; a diagnosis of "multiple retention cysts" had been made; a dermatological consultant made the diagnosis of "multiple oral papillomas and retention cysts". No treatment was administered.

Three years later, at the time of these pictures (1 year before biopsy), still no change in the diagnosis.



Constipation and abdominal pain described already at birth (and in subsequent visits), with diagnosis of "congenital megacolon" made at birth (no other investigations performed).

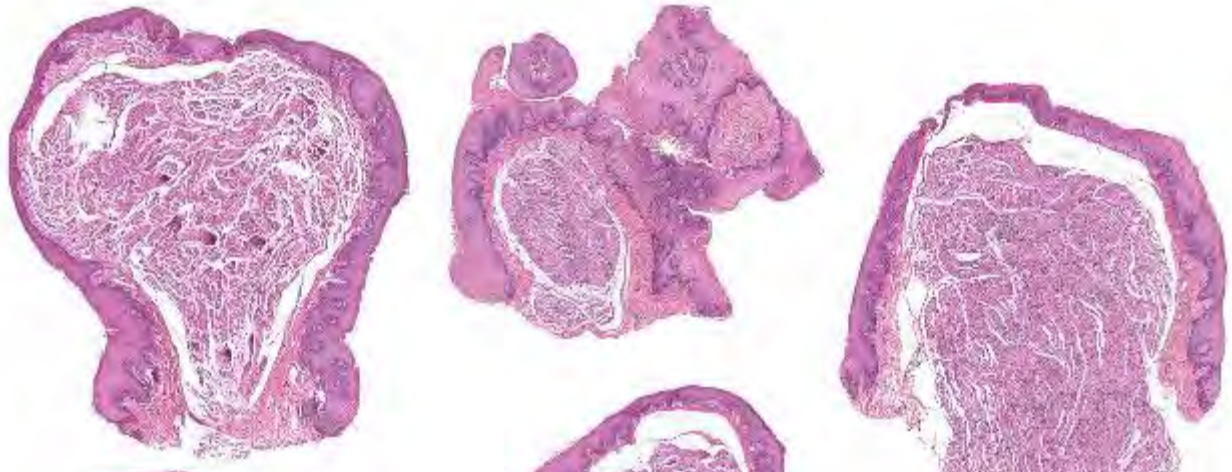
First description of oral lesions in a Hospital chart at the age of 4.

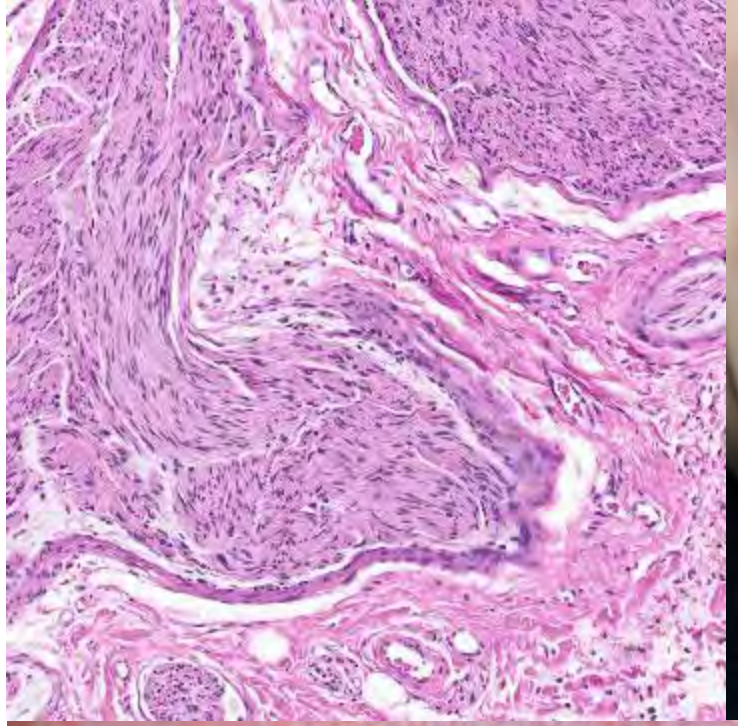
At 9, one year after the excision of some oral lesions, diagnosis of multifocal medullary thyroid carcinoma with lung and vertebral metastases; only at this time a diagnosis of MEN type 2b has been made (spontaneous mutation p-Met 918 THR).

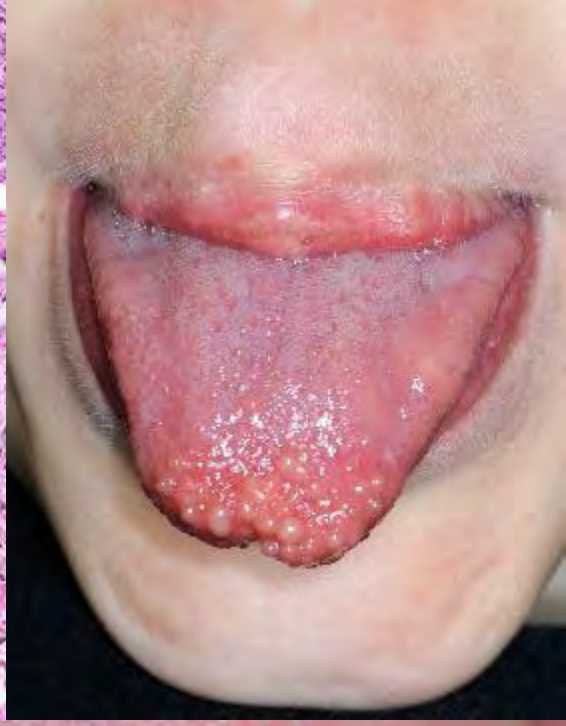
During the years the oral lesions were slowly growing in number with appearance of neuromas also on the hard palate and gingiva.

At 15 new metastases detected, than stable disease.

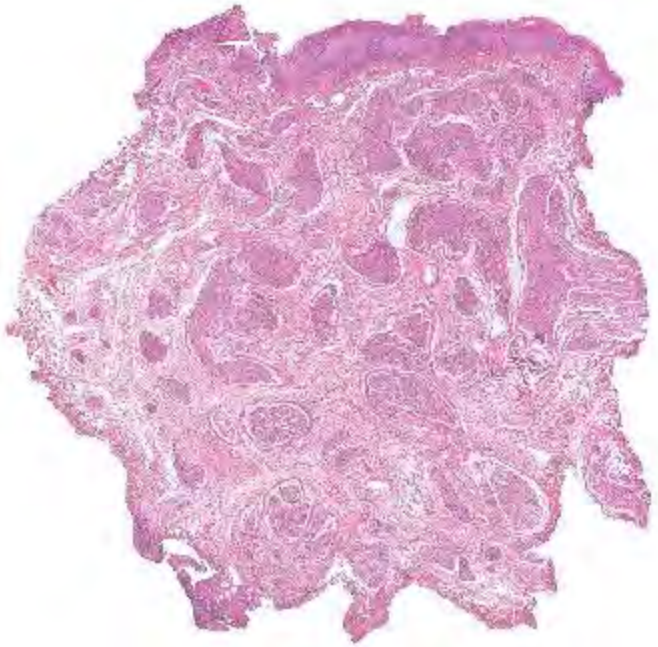
At present (age 19) serum calcitonin 4760 (+++).

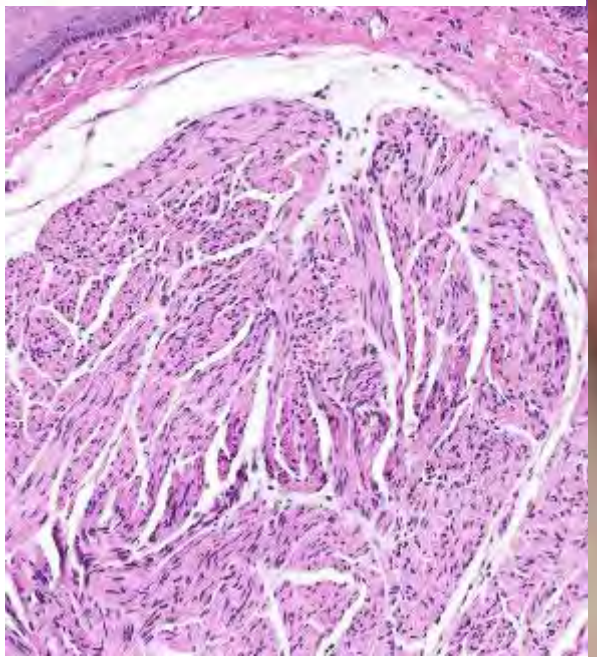


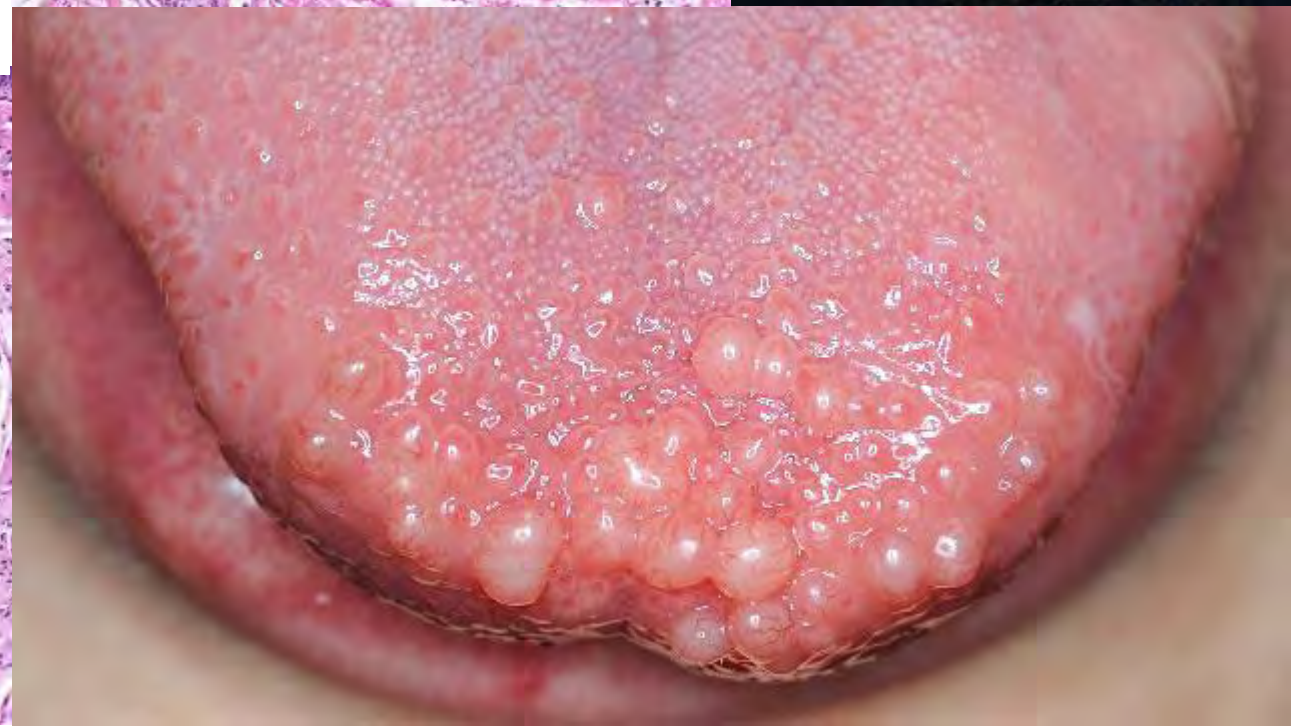


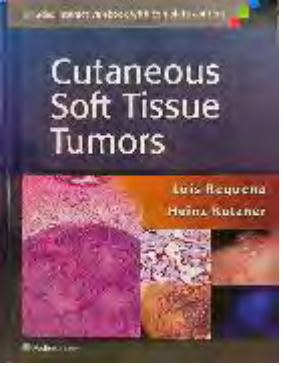


Multiple mucosal neuromas in MEN type 2b









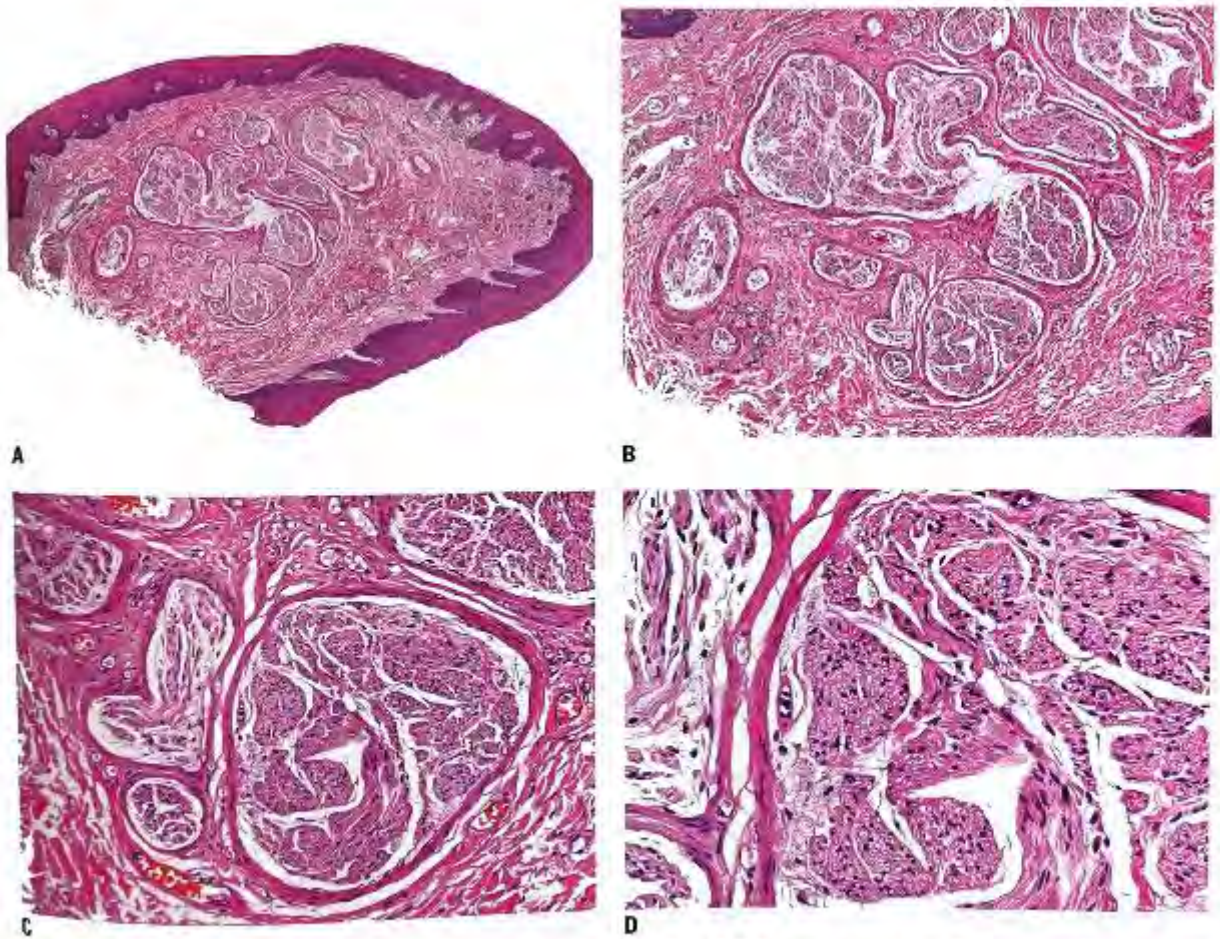


FIGURE 113-14. Histopathology of a neuroma of the tongue in a patient with the MEN 2b syndrome and multiple mucosal neuromas. **A:** Many nerve fascicles are seen in the propria of the mucosa. **B:** Each fascicle is ensheathed by perineurium. **C:** The lesion consists of mature nerve fascicles. **D:** Detailed image of one of the fascicles. Tiny "empty" holes correspond to axons, ensheathed by eosinophilic Schwann cells.

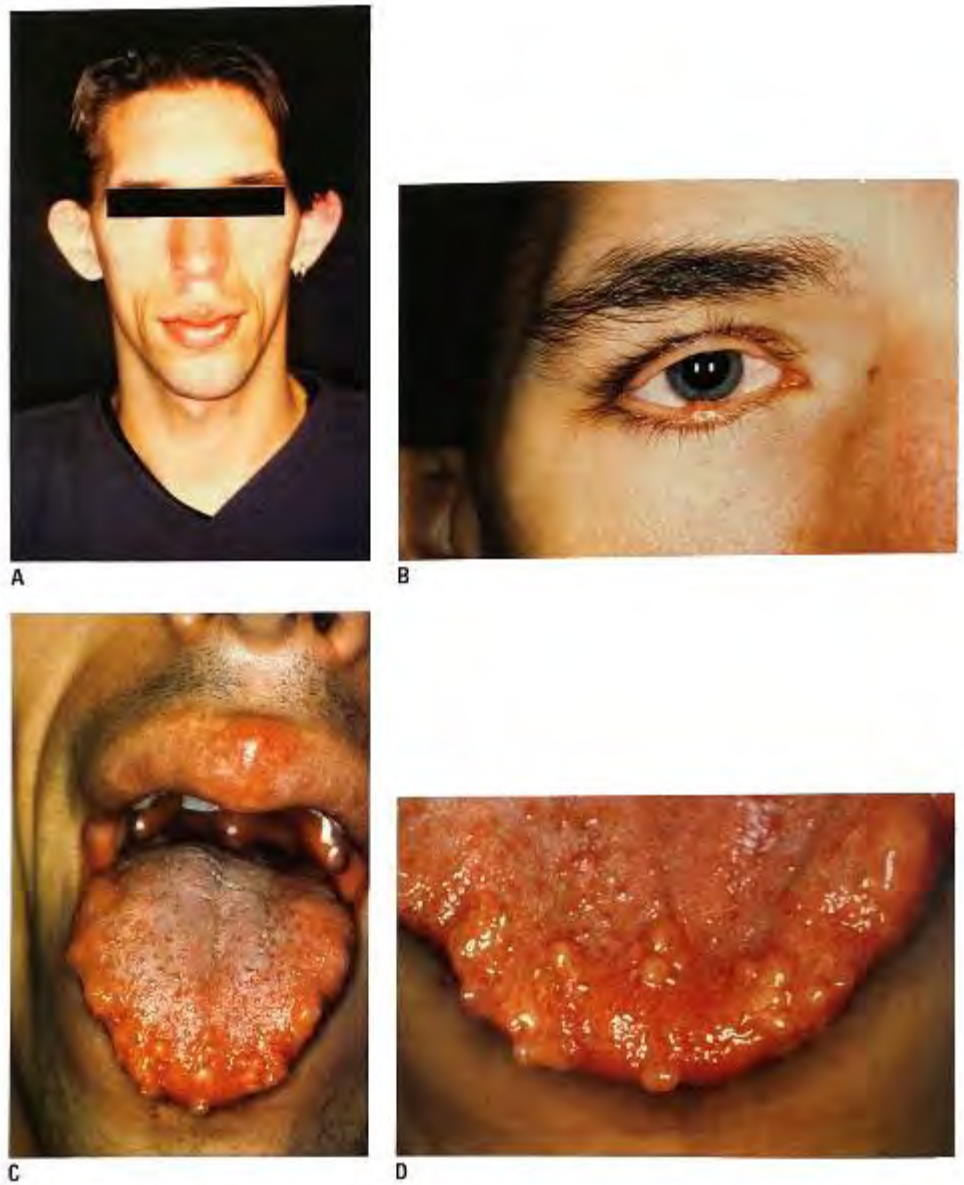
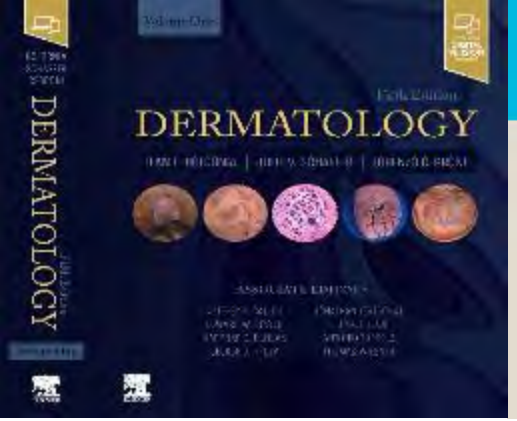


FIGURE 113-13. A patient with MEN 2b syndrome. **A:** Typical facies with prominent lips. Note the similarity with the patient in the previous figure. **B:** Neuromas on the free border of the eyelids. **C:** Multiple mucosal neuromas on the tip and lateral borders of the tongue. **D:** Detailed image of the multiple mucosal neuromas on the tip of the tongue.



Other Genodermatoses 63

Susan J. Bayliss, Monique G. Kumar, Ángela Hernández-Martín, Bernard A. Cohen, Teresa Martínez-Menchón, Encarna Guillén-Navarro, and Virginia P. Sybert

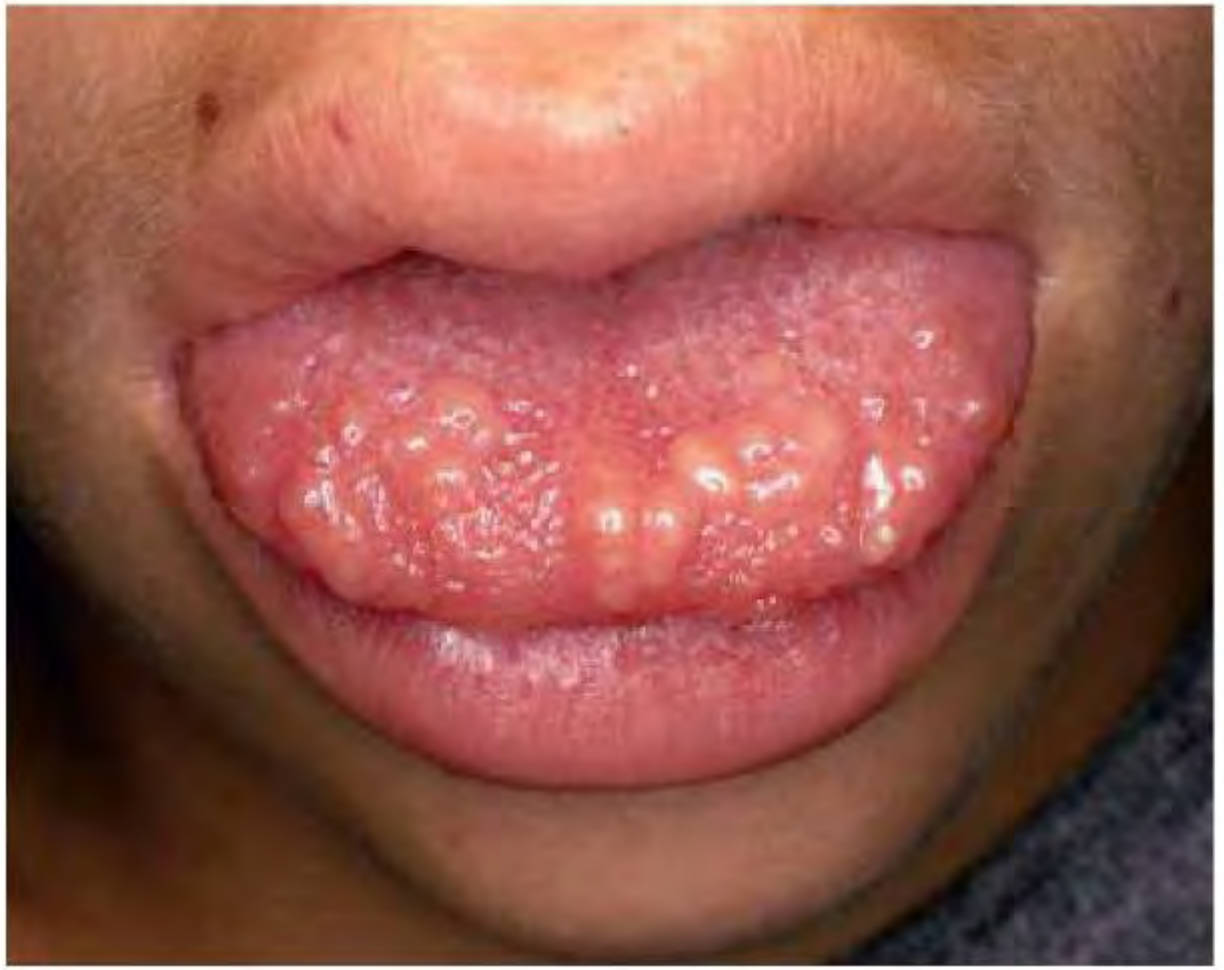
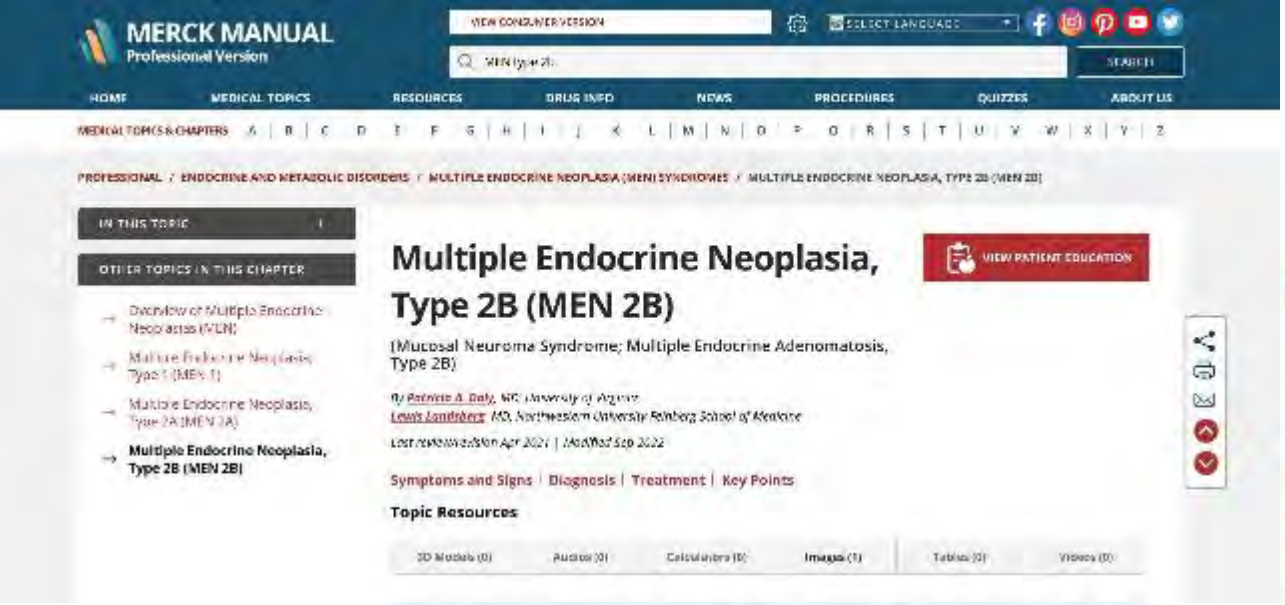


Fig. 63.2 Multiple endocrine neoplasia type 2B. Enlarged lips and multiple neuromas on the tip of the tongue.



The clinical symptoms of MEN2B include mucosal neuroma, Marfan-like habitus, thyroid carcinoma (especially medullary thyroid carcinoma), pheochromocytoma, gastrointestinal symptoms, and specialized facial features. MEN2B combined with GI symptoms mainly includes abdominal pain, constipation or diarrhea, and often includes megacolon disease.