68 Skin Necrosis in Children: Vascular Causes and Angioma

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68.1 Ulcerated Infantile Hemangioma

Infantile hemangiomas (IH) are the most common vascular tumors during infancy (5% of infants) [1, 2]. They appear during the first weeks of life and have typically an early rapid proliferation phase, followed by stabilization and finally a progressive spontaneous regression. Complications can be seen in 10–15% of cases [3, 4]. Ulceration is the most common complication (up to 15% of IH) [5]. These ulcerations are painful, with a risk of bleeding (mainly mild and benign), infection, and persistent scarring due to skin necrosis.

68.1.1 Physiopathology

- Pathogeny of IH is not yet fully elucidated. The trigger factor of endothelial cells proliferation seems to be hypoxic stress, leading to overproduction of angiogenic factors through lowered VEGFR1 expression [5, 6].

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68.1.2 Clinical Presentation

- Ulcerations appear most of the time during the proliferation phase of IH with the highest risk between the age of 4 and 6 months (median age of 4 months).
- Ulcerations usually start with a central gray coloration appearing on the IH. This can be triggered by a local trauma.
- IH with ulcerations are more likely large, superficial/mixed or segmental and localized on lower lip, neck/ head, or anogenital area (Fig. 68.1a–c).
- All ulcerated IH will lead to significant scarring due to wound healing process.
- Moisture, maceration, and friction seem also to have a role in the appearance of these ulcerations [7–10].

68.1.3 Diagnosis

- The diagnosis of IH is mostly clinical [10, 11].
- In atypical subcutaneous IHs, a doppler ultrasonography (US) by a radiologist experienced in vascular anomalies, can help confirming the diagnosis. Doppler US during the proliferation phase shows hyper vascular high flow tumor, with a stromal or tumoral component. In some cases, a magnetic resonance imaging is needed, especially to delimit the extent of the IH. A skin biopsy showing GLUT-1 staining gives a definite diagnosis.

L. Téot et al. (eds.), *Skin Necrosis*, https://doi.org/10.1007/978-3-031-60954-1_68

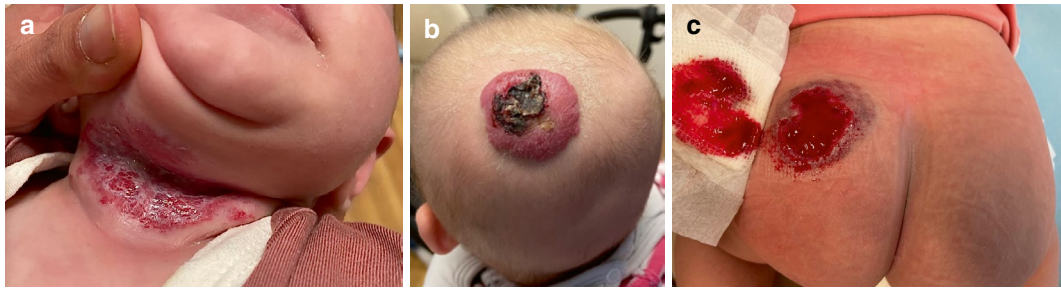

Fig. 68.1 (**a**) Cervical ulcerated infantile hemangioma. (**b**) Ulcerated infantile hemangioma with necrosis of the vertex. (**c**) Ulcerated infantile hemangioma of the genital area with bleeding

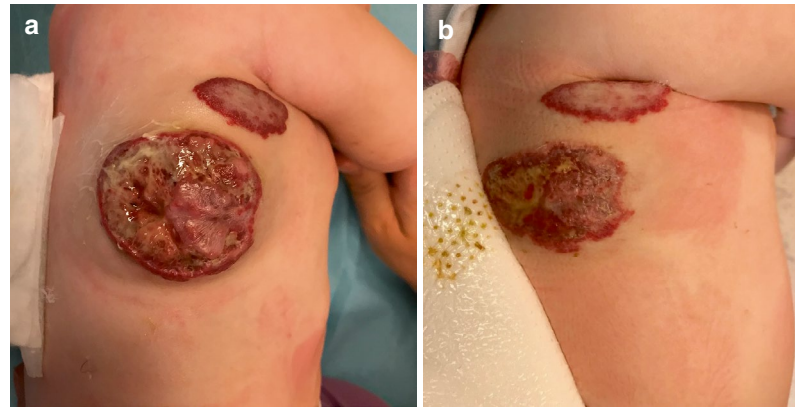

Fig. 68.2 (**a**) Ulcerated infantile hemangioma of the trunk. (**b**) Eight days after propranolol initiation (2 mg/kg/days)

68.1.4 Treatment

- **Wound care** is central in the treatment of ulcerated infantile hemangioma [12]. It should be adapted to the type, localization, and size of ulceration. The wound should be protected and covered with atraumatic dressing to enhance the healing process and reduce the pain.
- If infection is suspected, local antibiotic can be applied.
- If the ulceration bleeds, hemostatic dressing can be used.
- **Pain control** with paracetamol should be considered.
- **Oral propranolol**: As for all complicated IH, oral propranolol is the first choice of treatment as it shortens the proliferation phase [4, 13] (Fig. 68.2a, b). Usually, it is administered at 2–3 mg/kg/day in 2 or 3 intakes [14, 15]. Some authors suggest that propranolol at this dose could induce or precipitate ulceration through vasoconstriction [16–18]. They propose to consider a lower dosage (up to 1 mg/kg/day or less) of oral propranolol if the IH is ulcerated (as it is used to treat segmental IH seen with PHACE syndrome). Topical timolol is not recommended due to the risk of systemic resorption [17].
- Pulsed dye laser can be used but its efficacy is variable and the procedure is painful [12].
- Early surgical resection can be proposed for strawberry-like ulcerated IH, knowing that they will leave sequalae after involution [19, 20]

68.2 Ulcerated Congenital Hemangiomas

Congenital hemangioma (CH) are rare, benign, vascular tumors fully developed at birth. There are three subtypes with common features: unique red or purple lesion, covered with telangiectasia with surrounding pallor. Rapidly Involuting Congenital

Hemangiomas (RICH) looks typically at birth as a large exophytic firm tumor with rapid regression during the first months of life (7–14 months) [21]. One third do not completely regress and are named Partially Involuting Congenital Hemangiomas (PICH) [22]. Ulceration is frequent in PICH. The third type of CH is called Non Involuting Congenital Hemangioma (NICH) which are usually flat at birth and do not regress [2].

68.2.1 Physiopathology

The pathophysiology of CH remains unclear. Histological features resemble pyogenic granulomas (PG) suggesting that an in-utero local vascular accident could trigger an abnormal vascular reparative process, as seen in PG [23]. The same missense mutations in *GNAQ* and *GNA11* are found in the three subtypes of CH suggesting that another post-natal phenomenon could induce spontaneous involution [6].

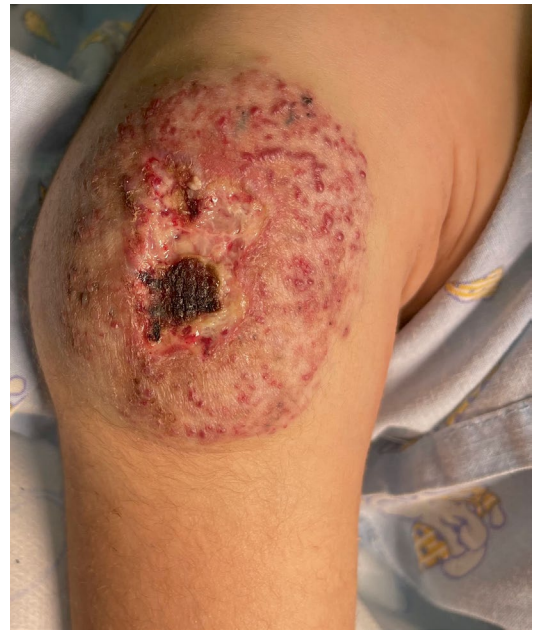

Fig. 68.3 Ulcerated congenital hemangioma of the shoulder

68.2.2 Clinical Presentation

- CH and especially RICH are hyper vascularized lesions. Ulceration is a possible complication. Severe and life-threatening bleeding are rare but described, sometimes needing radiological embolization. The cause of ulceration can be secondary to the erosion of large superficial vessel sometimes seen in CH. Ulceration can be a predictor for incomplete involution in RICH [24, 25].
- Heart failure, transient thrombocytopenia, and coagulopathy are also described [26, 27]. Associated thrombocytopenia can be a diagnostic challenge with sometimes a difficult differential diagnosis with a Kasabach-Merritt Phenomenon (KMP) as seen in Kaposiform Hemangioendotheliomas (KHE).

68.2.3 Diagnosis

- Unlike IH, CH are present and fully grown at birth. The diagnosis can be suspected during antenatal ultrasonography. Clinical presentation differs from an IH and is usually sufficient to make the diagnosis (Fig. 68.3).
- Doppler US (and in some atypical cases, magnetic resonance imagining) can be used to confirm the diagnosis and to evaluate the size and depth of the lesion. CH are highly vascularized tumors with many enlarged veins and arteries [24, 25].
- Differential diagnosis includes infantile fibrosarcomas, KHE, or tufted angioma (TA). A skin biopsy can help make the correct diagnosis if needed. Histopathological findings are similar in the three subtypes: capillary lobules and extralobular abnormal large superficial vessels (veins or lymphatic vessels), surrounded by fibrous tissue [28]. Endothelial cells from CH are negative for GLUT-1 immunostaining.

68.2.4 Treatment

In case of ulceration or severe hemorrhage, selective vascular embolization and/or surgical excision are recommended [24, 25]. Oral beta-blockers do not seem to be effective.

68.3 Arteriovenous Malformations

Arteriovenous malformations (AVMs) are congenital vascular anomalies, characterized by an abnormal connection between arteries and veins without the usual capillary network. This abnormal connection, known as the nidus, creates a direct pathway for blood flow between the high-pressure arteries and low-pressure veins. Those congenital lesions evolve over time with a progressive aggravation and invasion of surrounding healthy tissues [2, 29]. There seems to be a hormonal influence as some cases appeared or aggravated during pregnancy. Aggravation of the AVM is more frequent during adolescence, supporting the theory of hormonal influence [29].

68.3.1 Physiopathology

The precise underlying physiopathology is not known. AVMs seem to result from a hyperactivation of the RAS/RAF/MEK/ERK pathway [6]. Mutations involving the MAPK-pathway causing sporadic AVMs are published in the literature [30, 31]. There seems to be a genotype–phenotype correlation showing that *KRAS* mutated AVMs cause more diffuse and extended facial AVMs [32].

68.3.2 Clinical Presentation

AVMs present as a red warm lesion (Fig. 68.4). Clinical examination can reveal abnormal palpated arteries or a thrill. Although congenital, AVMs tend to evolve over time and become only visible during childhood or later in life. Local aggravation can be triggered by hormonal changes, local trauma, incomplete embolization, or surgery. If present at birth or in early childhood, differential diagnosis with CH or IH is not always easy (Fig. 68.5). Clinical presentation can be very similar, consisting of a red-violaceous warm lesion, that can grow over time and cause local ulcerations (Fig. 68.6), although ulceration will more likely appear later during childhood or adolescence, as opposed to IH. AVM presenting initially as a red mass with ulceration in early

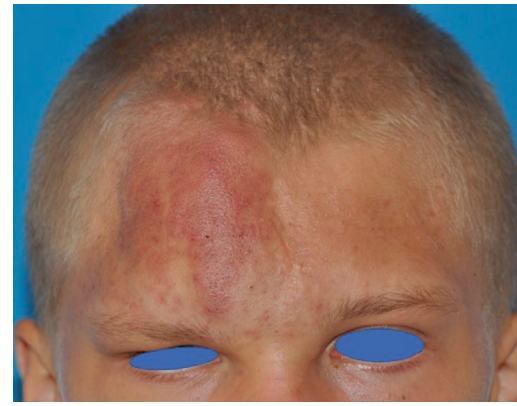

Fig. 68.4 Arteriovenous malformation (AVM) of the forehead presenting as a red, warm mass with abnormal palpated arteries and a local thrill

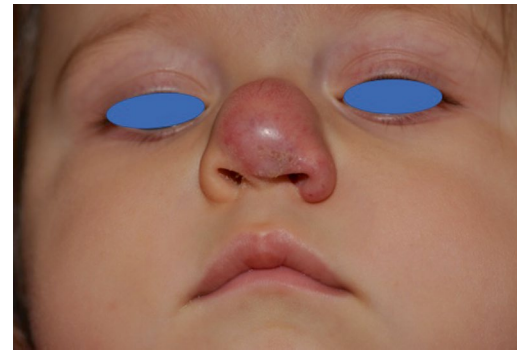

Fig. 68.5 Arteriovenous malformation (AVM) of the nose sends to our center for vascular anomalies with an initial diagnosis of infantile hemangioma (IH)

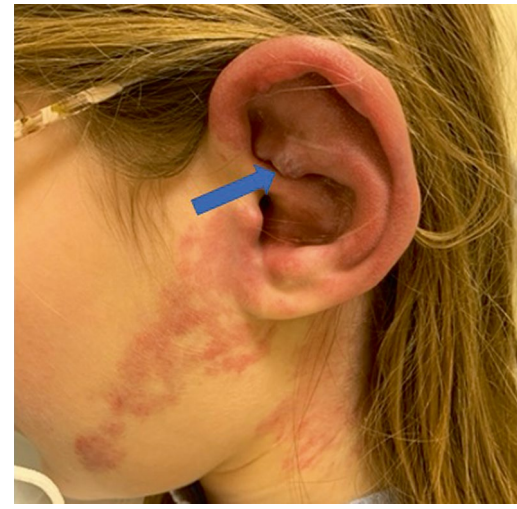

Fig. 68.6 Arteriovenous malformation (AVM) of the left ear. Blue arrow pointing at the ulceration site

childhood is very rare, but must be part of a differential diagnosis of an ulcerated vascular anomaly in pediatric patients.

68.3.3 Diagnosis

- Diagnosis can be clinical, with a red warm lesion or swelling associated with abnormally palpable arteries surrounding the lesion. Drainage veins will have a high blood flow velocity due to the vascular shunting and can cause a thrill that can be palpated.
- It can be confirmed with doppler US that will show high blood flow velocities, with lowered vascular resistance and very few or absent stromal tissue, as opposed to hemangiomas.
- Arteriography is essential to identify the afferent arteries and efferent veins before considering invasive treatments. It will show hypertrophic or abnormal arteries, rapid venous opacification, and a local blush which is consistent with the nidus.

68.3.4 Treatment

The only effective treatment is complete surgical excision with oncological-like margins to avoid local recurrence. Surgical excision can be associated with selective radiological embolization.

Embolization only is used in palliative cases if surgical resection is not an option. The long-term efficacy of embolization alone in AVMs is still under debate as late local recurrence can occur (up to 5 years).

Antiangiogenic treatments are becoming more and more used in adult patients. Thalidomide and trametinib seem to be the most promising medications [33, 34], although clinical pediatric trials are still lacking.

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