4 Common Dermatological Conditions

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Introduction

Newborn Skin

Shortly after birth (and removal of the vernix caseosa), the skin of a full-term neonate is typically soft and smooth. There are a variety of physiologic skin conditions that appear in the first few days to weeks of life that disappear in a short time. For example, desquamation of newborn skin, which appears as fine thin scaling, begins in the first 1–2 days of life and may not be complete until 3 weeks of age. Cutis marmorata, a bluish-purple lacy mottling of the skin, occurs in the first 1–2 days of life and is a reflection of immature temperature regulation in the skin that then normalizes in the first few months of life.

In addition to physiologic skin changes, there are a number of skin eruptions and skin lesions that can be present at birth and are often the source of anxiety and concern for parents. Birthmarks can present as a red, blue, brown-black, or white lesion; they can be flat or raised and hairy or warty and occur as single or multiple lesions or distributed over a segment of the body. Fortunately, regardless of color or shape, the vast majority of congenital skin lesions or "birthmarks" are a benign, isolated finding and parents can be reassured. Similarly, there are several skin eruptions that are common in the first few weeks of life that are benign and self-limited. It is critical to differentiate these benign and self- limited conditions, from those that require further work-up and systemic treatment. The following clinical cases describe several common skin conditions seen in newborns and discuss their appropriate work-up and management.

Case Presentation

The mother of an otherwise healthy 2-day-old boy born via natural spontaneous vaginal delivery, with Apgar scores of 9 and 9 calls for a pediatrician prior to discharge. She is concerned about several scattered pink blotchy macules, papules, and few pustules on his face and trunk as shown (Fig. 4.1). He is otherwise well.

What is the most likely diagnosis?

1. Transient neonatal pustular melanosis
2. Erythema toxicum neonatorum
3. Congenital cutaneous candidiasis
4. Bacterial folliculitis

This case demonstrates a typical presentation of erythema toxicum neonatorum (ETN). ETN is a common, benign, self-limiting skin eruption

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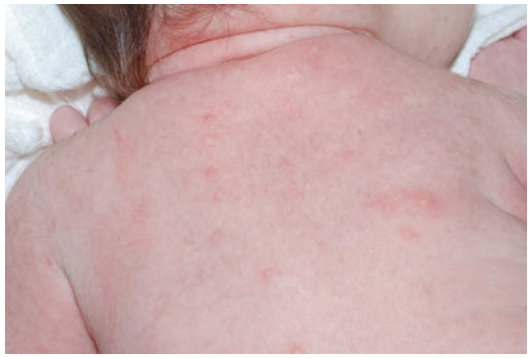

Fig. 4.1 Erythema toxicum neonatorum on the trunk of a newborn. Note the typical pink papules with surrounding erythema

seen in full-term newborns. It is more common in term neonates and is rare in premature babies. Skin lesions usually present at 3–4 days of age but can be seen as early as the first 24 h and up to 10 days of age. Lesions start as splotchy pink macules that evolve to having a central papule or pustule and self-resolve without sequelae. They are typically found on the face, trunk, and extremities with notable sparing of the palms and soles. The diagnosis is usually made clinically and a biopsy is rarely necessary. Table 4.1 [1] shows other diagnoses and helpful clinical and laboratory features for distinguishing between them.

Answer: 2

How would you counsel the parents?

1. Treatment with topical antifungals is required
2. Treatment with topical corticosteroids is required
3. Treatment with topical antibiotics is required
4. No treatment is required

You can reassure parents that although we do not know exactly what causes this eruption, it is a benign, self- limiting condition which heals without sequelae. New crops of lesions can appear for 5–7 days, but each individual lesion resolves in 1–2 days and does not recur. No treatment is required. The presence of this eruption is not linked to future skin disease.

Answer: 4

How can a definitive diagnosis be made?

1. A skin biopsy
2. A potassium hydroxide (KOH) prep
3. A bacterial culture
4. Clinical recognition

The diagnosis is usually made clinically. A Wright's stain [combination of acid dye (red "eosin") and a basic dye (blue "methylene blue")] on a skin scraping would highlight eosinophils, and occasionally there is associated peripheral eosinophilia. A skin biopsy is rarely necessary, however if performed would show a dense infiltrate (usually perifollicular) and subcorneal pustules composed of eosinophils.

Answer: 4

Case Presentation

You stop in to check on a 10-h-old baby whose delivery you attended that morning. On examination, the baby appears well. On the skin you notice scattered superficial pustules without surrounding redness. Some of these pustules have ruptured, leaving a circular rim of scale and/or a peeling edge (collarette). There are also scattered hyperpigmented macules on the face and a few pustules on his palms.

How do you explain this condition to the baby's family?

1. This is an infection that he acquired in utero.
2. This is a non-worrisome condition that will go away on its own.
3. This is an infection that he acquired during delivery.
4. This is the result of trauma during delivery.

Transient neonatal pustular melanosis (TNPM, *syn transient neonatal pustulosis, lentigines neonatorum*) is an idiopathic, benign, self-limiting skin eruption that occurs in 5% of darkly pigmented neonates. It is much less common in Caucasian newborns. Skin lesions are typically

Table 4.1 Differential diagnosis of neonatal vesiculopustular eruptions

Diagnosis	Typical age of onset	Clinical features	Diagnosis/laboratory
Erythema toxicum neonatorum (ETN)	DOL 1–2	Common, ~50% of full-term neonates	Clinical diagnosis; Wright stain (skin and peripheral blood smear): eosinophils; bacterial and viral cultures are negative
		Small papules and pustules surrounded by a flare of erythema	
		Spares palms and soles	
Transient pustular melanosis	Birth	Lesions progress through 3 phases: superficial pustules, collarettes of scale, hyperpigmented macules	Clinical diagnosis; gram stain shows neutrophils, bacterial culture is negative
		Widespread involvement including the palms and soles	
Congenital candidiasis	Birth–6 days	Monomorphic papulovesicles that evolve to pustules typically on face, palms, and soles; can be widespread or only involve the nail	Fungal stain shows pseudohyphae and budding yeast
		Majority present at birth	
Neonatal candidiasis	>1 week	Scaly red patches, papules, satellite pustules	Fungal stain shows pseudohyphae and budding yeast
		Affects diaper area and oral mucosa, intertriginous areas	
Miliaria rubra	1–12 weeks	Monomorphic small pink papules and pustules in areas that are wrapped or heated; or areas covered with thick emollients	Clinical based on appearance and location; when in doubt culture can rule out candida or other infection
Neonatal acne (a.k.a. neonatal cephalic pustulosis)	3–4 weeks	Pink papules and pustules, notably lack of comedones; typically on the face but can extend to scalp, shoulders, and upper back	Clinical diagnosis; potassium hydroxide (KOH) scraping may demonstrate yeast

present at birth and can be found anywhere on the skin but have a predilection for chin, neck, back, and legs. Lesions are often seen on palms and soles. These eruptions evolve through three characteristic phases. In the first phase, variably sized (2–10 mm) superficial pustules with minimal or no surrounding erythema are seen. In the second phase, there are faint hyperpigmented macules with fine collarettes of scale at sites of ruptured pustules. In the third phase, brown hyperpigmented macules, representing post-inflammatory hyperpigmentation, are seen at sites of previous pustules. These light brown macules may persist for months. The first two phases may occur in utero [2].

Answer: 2

How do you make the diagnosis?

1. A skin biopsy
2. A KOH preparation
3. A bacterial culture
4. Clinical recognition

The diagnosis of TPNM is usually made clinically; a gram stain and/or biopsy is rarely necessary. When in doubt or when the surrounding erythema is significant and an infection is considered, a swab of pustule contents for gram stain and culture can be helpful. A gram stain would show neutrophils and a bacterial culture is typically negative. A KOH preparation is not indicated. A skin biopsy would show spongiosis and intra- or subcorneal pustules containing neutrophils, fibrin, and rarely eosinophils. See Table 4.1 for the differential diagnosis of TPNM.

Answer: 4

What is the treatment?

1. Topical antifungal
2. Topical corticosteroid
3. Topical antibiotic
4. No treatment is required

Infants with TPNM are otherwise well and no treatment is necessary. Parents should be

reassured that the eruption will self-resolve without sequelae. The residual hyperpigmented lesions will resolve but may take up to several months.

Answer: 4

Case Presentation

A one-week-old presents with yellow discoloration and thickening of the nail plates of several fingernails as shown in Fig. 4.2. Her mother states that these have been present since birth.

Analysis of the fingernail is most likely to show?

1. Gram-positive cocci
2. Pseudohyphae and budding yeast
3. Hyperkeratosis and parakeratosis
4. Neutrophils and fungal hyphae

Thickening and yellow discoloration of the nail plates may be the only manifestation of congenital cutaneous candidiasis (CCC). Histologic examination with a periodic acid-Schiff (PAS) stain of the nail plate is most likely to reveal pseudohyphae and budding yeast typical of *Candida albicans* infection. Gram-positive cocci would be seen in bacterial nail infections, and neutrophils and fungal hyphae are seen in dermatophyte infection of the nail. Hyperkeratosis and parakeratosis are seen in nail psoriasis.

Answer: 2

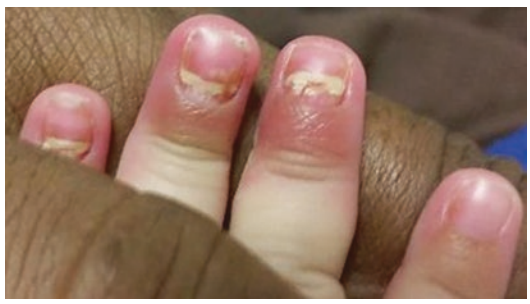

Fig. 4.2 Congenital cutaneous candidiasis present in several fingernails

How does congenital cutaneous candidiasis (CCC) present on the skin?

1. Vesicles on an erythematous base on mucous membranes
2. Superficial pustules some coalescing, extensor surfaces and palms and soles
3. Pink eczematous plaques with overlying yellow crusty scale
4. Papules, pustules, and desquamation in the diaper area

The typical rash of CCC consists of generalized 2–4 mm pink macules, papules, and/or pustules that evolve and sometimes coalesce into larger "lakes of pus." [3] Lesions are in different stages contributing to the appearance of diffuse erythema with overlying desquamation or a fine scale. The back, extensor surfaces, and skin folds are the typical areas affected, but the diaper area and oral mucosa are relatively spared. CCC often involves palms and soles (in contrast to ETN and TNPM) [3]. As in the case presented, some neonates have yellow discoloration and transverse ridging of the nail plates as the only manifestation of congenital cutaneous candidiasis. Congenital cutaneous candidiasis (as opposed to neonatal candidiasis) occurs earlier in life, presenting at birth or up to DOL 6. The diaper area and oral mucosa are spared. Table 4.2 highlights the key differences between congenital cutaneous candidiasis and neonatal candidiasis. Papules, pustules, and desquamation in the diaper area are typical of neonatal candidiasis. Vesicles on an erythematous base are seen in herpes simplex. Pink eczematous plaques with overlying yellow crusty scale are seen in infantile seborrheic dermatitis. Papules, pustules, and desquamation in the diaper area are typical of neonatal candidiasis.

Answer: 2

What is the treatment of CCC?

1. Intravenous antifungals and intravenous antibiotics until culture results are in
2. Intravenous antifungals for 10 days

Table 4.2 Key differences between congenital cutaneous candidiasis and neonatal/infantile candidiasis

	Congenital cutaneous candidiasis	Neonatal/infantile candidiasis
Onset of skin lesions	Birth up to DOL 6	2 weeks of life
Acquisition	Rare	Common
	Acquired in utero	Acquired through the birth canal or postnatally
Risk factors	Prematurity, foreign body in cervix, premature rupture of membranes, maternal history of vaginal candidiasis	Maternal history of vaginal candidiasis
Clinical features	Small pink macules and papules that evolve into pustules and desquamate	Scaly red macules, papules, and pustules usually localized to the intertriginous areas (body folds) with characteristic "satellite pustules" outside the folds
	Papules, pustules and desquamation often present at birth	
	Lesions are often at various stages	Affects diaper area (diaper dermatitis), oral mucosa (oral thrush), and intertriginous areas
	Widespread including palms and soles	
	Yellow discoloration and thickening of nail may be the only manifestation	
Diagnosis	Gram stain is negative KOH reveals budding yeast and pseudohyphae Fungal cultures from blood, urine, and CSF are usually negative	
Treatment	Depends on gestational age: <1500 gm or <27 weeks: bacterial, fungal, viral cultures; and IV antifungal is required Full term, healthy Topical antifungal Any systemic symptoms: IV antifungals	Topical antifungals usually sufficient Watch premature and low birth weight infants closely Use systemic antifungals if any sign of systemic infection Cases with oral candidiasis, recurrent or recalcitrant cases may require systemic antifungal therapy, such as nystatin solution or oral fluconazole

3. Depends on age and hemodynamic status of neonate
4. Topical antifungals only

Treatment of CCC depends on the newborn's gestational age and hemodynamic status. Premature neonates less than 1500 g or less than 27 weeks' gestation will require bacterial, fungal, and viral cultures and should be treated with empiric IV antifungal therapy [4]. If the neonate is full term and hemodynamically stable, topical antifungals such as clotrimazole or ketoconazole cream to affected areas on skin twice daily should suffice. For affected nails, topical antifungals such as ketoconazole 2% cream twice daily should clear the infection in several months. In a cohort of mostly premature neonates, prompt systemic antifungal treatment at the time of presentation and treatment duration for ≥14 days prevented fungal dissemination and mortality. Delaying systemic treatment, use of oral or topical nystatin, and treating for <10 days was associated with dissemination of candida to the bloodstream [5]. Fortunately, systemic dissemination of cutaneous infection is rare occurring in ~5% of affected neonates; however, if there is any sign of systemic infection, there should be a low threshold for starting IV antifungals [4].

Answer: 3

Case Presentation

A 3-week-old baby boy is brought into your newborn follow-up clinic because his mother is concerned he has acne. He is otherwise well and thriving. On exam you note tiny superficial pustules and pinpoint pink papules on the posterior neck, scalp at the hairline, and her upper back (Fig. 4.3).

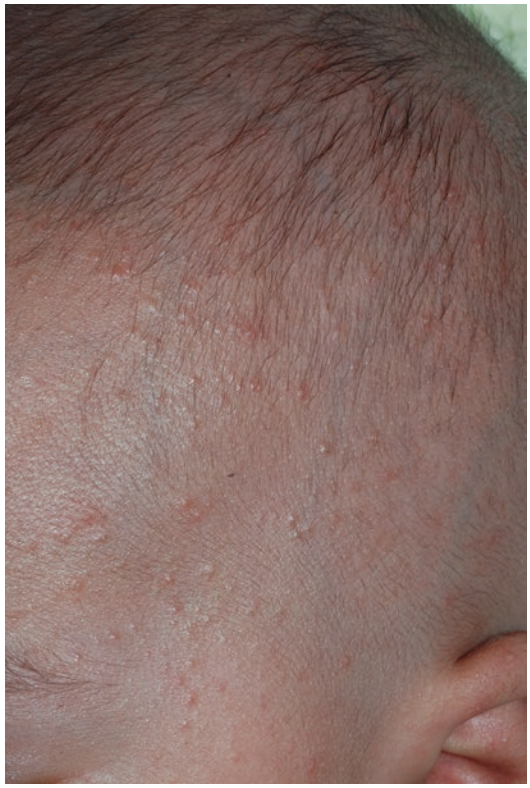

Fig. 4.3 Miliaria rubra on the scalp of a neonatal boy

What is the diagnosis?

1. Neonatal acne
2. Miliaria rubra
3. Seborrheic dermatitis
4. Transient neonatal pustular melanosis

Miliaria rubra is a common condition that is usually seen after the first week of life. Miliaria occurs more commonly in the neonatal period due to the immaturity of the sweat (eccrine) ducts which results in obstruction. Superficial obstruction results in miliaria crystallina, which is a clear superficial pinpoint vesicle with no surrounding pinkness. A slightly deeper obstruction of the eccrine duct results in miliaria rubra, a small papulovesicle with surrounding erythema, as demonstrated in this patient. Miliaria is more common in warmer climates. Typical lesions are located on the forehead, scalp, posterior neck, and upper back as opposed to neonatal acne where lesions are found on nose and cheeks. Pustules are usually sterile. Conditions that can look similar to miliaria are listed in Table 4.1. Neonatal acne presents with acneiform papules and pustules and occurs on the face, commonly on the cheeks. Seborrheic dermatitis is characterized by pink eczematous plaques with greasy yellow scaling.

Answer: 2

How do you treat and counsel the family?

1. This condition is lifelong and will come and go
2. Use topical antibiotic ointments twice daily until clears
3. This condition spontaneously improves without treatment
4. This condition will improve if dairy is eliminated from the diet

You can reassure parents that miliaria is a benign self-limited condition which can be caused by excessive swaddling, heat, fever, and occlusive dressings. These factors trigger obstruction of the premature eccrine sweat ducts and the resultant fluid accumulation in the dermis leads to an inflammatory response that is seen clinically as the surrounding redness on the skin. This condition spontaneous resolves with cooling and continued avoidance of triggers described above. It is important to counsel the family to use lightweight cotton clothing and to avoid overuse of occlusive emollients. Miliaria usually resolves later in infancy; topical antibiotics and removal of dairy do not treat miliaria.

Answer: 3

Case Presentation

A 2-week-old infant girl presents with a smooth, 1.5 cm circular patch of smooth alopecia on the scalp as shown (Fig. 4.4). Her parents report that it was a superficial erosion at birth and healed quickly. The surrounding hair appears normal.

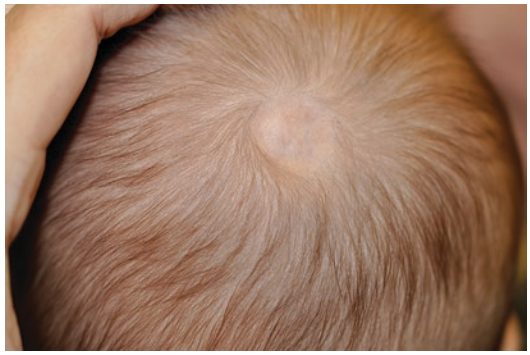

Fig. 4.4 Aplasia cutis congenita on the scalp

She was born via normal spontaneous vaginal delivery without the use of instrumentation.

What is the diagnosis and what is the cause?

1. Superficial abrasion from trauma during delivery
2. Nevus sebaceous
3. Ulcerated infantile hemangioma
4. Aplasia cutis congenita

Aplasia cutis congenita (ACC) is a congenital defect that results from a localized area of absent skin at birth. There is absence of the epidermis and dermis in the affected area, but occasionally underlying subcutaneous tissue, bone, and dura can also be missing. ACC is usually seen on the scalp as a single well-circumscribed area of alopecia. Less commonly, ACC presents as multiple areas of alopecia on the scalp or can be found on the face, trunk, or extremities. Most cases of ACC are sporadic and the exact etiology is unknown. A popular hypothesis suggests that ACC is the result of compromised vasculature of the placenta [6].

While the scenario above describes a typical patient with ACC, other common presentations at birth include a well-formed hairless scar and ulceration with a granulating base, a superficial erosion, or a translucent, glistening membrane ("membranous aplasia cutis" – uncommon variant). Lesions are usually sharply demarcated, oval, circular, or stellate and measure 1–3 cm in diameter [6].

Answer: 4

What is the management of ACC and is an additional work-up necessary?

1. A skin biopsy should be performed
2. Surgical correction is highly recommended
3. Depends on size, location, and presence of "hair collar."
4. MRI/MRA of head and neck

When a lesion of ACC is identified, a detailed and complete physical exam should be performed. ACC is an isolated defect in the majority of cases, but it can be associated with other developmental anomalies or be a feature of a variety of syndromes. In addition, a ring of long, dark hair around membranous aplasia cutis (the hair collar sign) is thought to herald an underlying neural tube defect. If the lesion appears large, deep, or stellate or if it is located in the midline, a radiologic evaluation to assess for an underlying defect is necessary [6]. In this case, a complete physical exam was normal and the lesion was small with no surrounding thick "hair collar" and not located in the midline. Therefore no additional work- up was needed.

When ACC presents with a superficial wound at birth, simple wound care with gentle cleansing, ointments, or antibiotic ointments and nonstick dressings will help heal most small defects quickly. The prognosis of ACC is excellent and most lesions heal completely in the first weeks to months of life. Lesions may heal with scarring. Alopecia may be of cosmetic concern when large or in a highly visible area. Most scars become inconspicuous as the hair and scalp grow. However large or very obvious scars may require plastic surgery correction in the future.

Answer: 3

Case Presentation

You are examining a 2-day-old baby girl at mother's bedside and notice a 3 cm oval, thin, yellow-tan hairless plaque as shown (Fig. 4.5). Her mother is now concerned and asks if it will need to be removed.

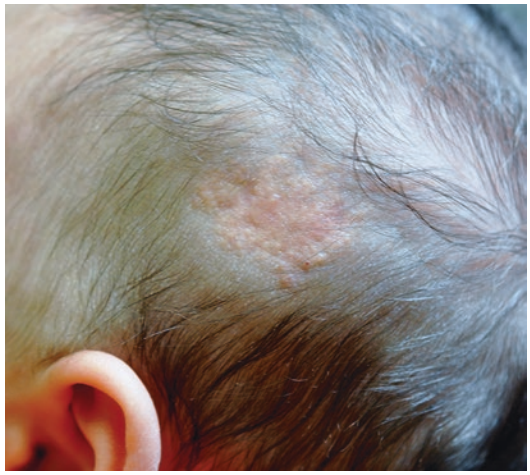

Fig. 4.5 Nevus sebaceous on the scalp

What is the diagnosis?

1. Nevus sebaceous
2. Aplasia cutis congenita
3. Congenital melanocytic nevus
4. Congenital alopecia

A nevus sebaceous (NS) is an easily recognizable yellow- to tan-colored, hairless, thin plaque that has a fine pebbly surface. An NS is a common congenital benign tumor predominantly composed of large and malformed sebaceous glands. NS can occur anywhere on the body but greater than 95% of lesions occur on the head and neck, most often on the scalp. Although usually localized, as in this patient, occasionally, a more extensive NS along the lines of Blaschko can be present. In such instances, NS can be associated with ocular or CNS abnormalities. NS occurs sporadically. If a dermatoscope is available, visualizing bright yellow dots and an absence of hair follicles can help make the definitive diagnosis, before the characteristic features become apparent.

Answer: 1

What is the natural history of a nevus sebaceous?

1. Rapid growth in the first year of life followed by involution
2. Spontaneous regression
3. Remains quiescent in childhood and thickens at puberty
4. Remains a flat hairless plaque throughout life

An NS is thought to result from a defect in cutaneous embryologic development; its exact etiology is unknown. Lesions are usually yellow to tan and mildly elevated with a pebbly surface at birth. Occasionally, NS can be thicker or have papillomatous projections, simulating a wart. It can also present as a large pedunculated lesion at birth. After infancy, lesions flatten, become more inconspicuous, and grow proportionately with the child. At puberty, under the influence of androgens, NS thicken, become darker yellow or brown, more papular or verrucous, and can be friable or itchy. Warty growths, representing secondary adnexal neoplasms, may develop within a NS during adolescence or later. The area will remain hairless.

Answer: 3

What is your recommendation for management?

1. Immediate complete excision
2. Clinical observation yearly
3. Complete surgical excision around puberty
4. Skin biopsy if growths appear within the lesion

When an NS is identified, the first step should be a complete physical examination to assess for other congenital defects and determine the extent of NS. Complete surgical removal remains the treatment of choice for NS given the concern for warty proliferation, permanent alopecia, and the development of secondary tumors after puberty. More recent investigations have shown that the risk of developing a malignant neoplasm within an NS is quite low [7]. Recommendations for timing of excision vary. Advantages of removing the lesions in infancy are greater laxity of tissues, smaller size of the lesion, and removal of any cosmetic impact on the developing child. The main disadvantage to early removal is the

need for general anesthesia. Most often, smaller NS are removed in late childhood, prior to the onset of puberty, when the patient is able to cooperate with excision under local anesthesia. At this time the NS has not yet thickened under the influence of androgens. In cases of an extensive or widespread NS, a thorough medical history and physical examination should be performed with special attention to the ocular, neurologic, and musculoskeletal systems. Radiologic evaluation and further work-up should be symptom directed. Various ablative treatments including cryotherapy and electrodessication have been used to treat NS, but these do not remove the risk of neoplasia and can still leave areas of alopecia.

Answer: 3

Case Presentation

You are examining a 2-day-old newborn boy who was born with the lesion shown (Fig. 4.6). On examination, this area measures 3 × 2 cm and is a homogeneous brown color with smooth borders. He is otherwise well, and there is no family history of skin cancer or skin disease.

What is the diagnosis?

1. Epidermal nevus
2. Congenital melanocytic nevus
3. Café au lait patch
4. Mongolian spot

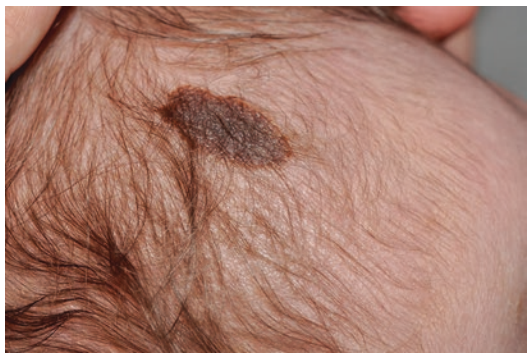

Fig. 4.6 Medium-sized congenital melanocytic nevus on the scalp

The lesion shown is a medium-sized congenital melanocytic nevus. Nevi present at birth or those that develop within the first 2 years of life are considered congenital melanocytic nevi (CMN). CMN have melanocytes that are located deeper down into the dermis surrounding hair follicles and nerves than those in acquired nevi and have characteristic dermoscopic features. CMN are classified according to their predicted final adult size as small, medium, or large. Small CMN have a final size of <1.5 cm in largest diameter. Medium CMN have a final size of 1.5–20 cm in greatest diameter. Large (or giant) CMN have a predicted adult size of >20 cm (equivalent to ≥9 cm on the head of an infant or ≥6 cm on the body of an infant). A newer classification scheme proposed in 2013 has further subdivided medium (M1: 1.5–10 cm; M2 > 10–20 cm) and large (L1″ > 20–30 cm; L2 > 30–40 cm) categories and added a "giant" category for lesions >40–60 cm (G1) and those >60 cm (G2). In addition, descriptive features such as heterogeneity, hypertrichosis, surface rugosity, and number of satellite lesions were added to the categorization schema to better describe CMN and provide more specific melanoma risk earlier in life [8]. Small or medium CMN are common and occur in 1–3% of neonates, whereas large CMN are estimated to occur in 1 in 20,000–50,000 neonates [9].

Answer: 2

What changes can occur in CMN over time?

1. Darkening
2. Hair growth
3. Thickening
4. All of the above

At birth, CMN present as tan to light or dark brown/black, flat or raised macules or papules of varying size that then enlarge in proportion to the child's growth. Over time CMN, can become darker or lighter in color, develop a mottled pigmentation, increase in thickness, and even spontaneously regress. Surface changes such as hypertrichosis, verrucous changes, and proliferative nodules can also occur.

Answer: 4

What is your recommendation for monitoring and treatment?

1. Complete excision as soon as possible
2. Regular clinical monitoring with discussion about risks and benefits of excision
3. Monitoring by parents at home
4. Excise completely around puberty

Information from larger cohort studies suggests that prophylactic removal of small and medium CMN is not recommended if there are no concerning features and no obstacles to monitoring, because the risk of melanoma is low [10]. Lifetime melanoma risk in small- and medium-sized CMN is 1% and typically presents after puberty [9]. Regular clinical monitoring is often all that is needed. However, decision to perform surgical removal should be individualized taking into account worrisome clinical features, cosmetic or parental concerns, the location and ease of monitoring, the risks of the procedure, and anesthesia versus the benefits of surgical removal. Surgical excision can be performed for cosmetically disfiguring lesions to avoid the potential psychosocial impact of the nevus on the developing child.

Lifetime melanoma risk is estimated at 10–15% for large CMN especially those that are larger than 40 cm, accompanied by satellite lesions. Many of these melanomas will develop in the CNS and not the skin and usually develop in childhood [10]. Patients with large or giant CMN, especially those located on the posterior axis or those with smaller satellite nevi, and patients with multiple medium CMN should be screened for neurocutaneous melanosis with an MRI of the brain and spine ideally before 4–6 months of age. For large CMN, early and complete surgical excision is often recommended and desired by parents [9, 10].

Answer: 2

Case Presentation

You are called to examine a 3-day-old boy and parents ask about the pink red spots on his upper eyelids and his forehead (Fig. 4.7). The lesions become deeper red when he cries or strains.

What is the diagnosis?

1. Nevus simplex
2. Port-wine stain
3. Infantile hemangioma
4. Ecchymosis from birth trauma

This is a nevus simplex (syn. salmon patch, stork bite, angel's kiss), the preferred term for the most common vascular birthmark of infancy. It occurs in 30–40% of newborns. A nevus simplex is typically present at birth as an ill-defined, flat, dull pink or red, blanchable patch most commonly seen on the posterior scalp (aka "stork bite"), glabella (aka "angel's kiss"), forehead, upper eyelids, nose, and/or upper lip. Less often, a nevus simplex can have a more extensive, widespread distribution such as multiple lesions on the back and trunk.

Answer: 1

What is the typical natural history of nevus simplex?

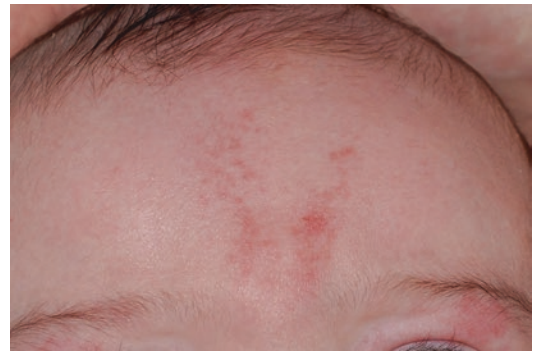

Fig. 4.7 Nevus simplex on the forehead

1. Complete resolution in the first 2 years of life
2. Darkening over time
3. Rapid growth for first year followed by involution
4. Resolution in 2–3 weeks

The etiology of nevus simplex is unknown. Some experts believe it to be a form of persistent fetal circulation rather than a true vascular malformation. Complete resolution within the first 2 years of life is expected for >95% of lesions on the face. Occipital lesions tend to persist for longer, some indefinitely. Lesions become deeper red with crying and physical exertion. No treatment is necessary as most lesions fade; in the uncommon event of persistence, treatment with the pulsed dye laser is highly effective. Port-wine stains (Fig. 4.8) darken and thicken over time; and infantile hemangiomas proliferate rapidly in the first year of life followed by gradual spontaneous involution (Table 4.3).

Answer: 1

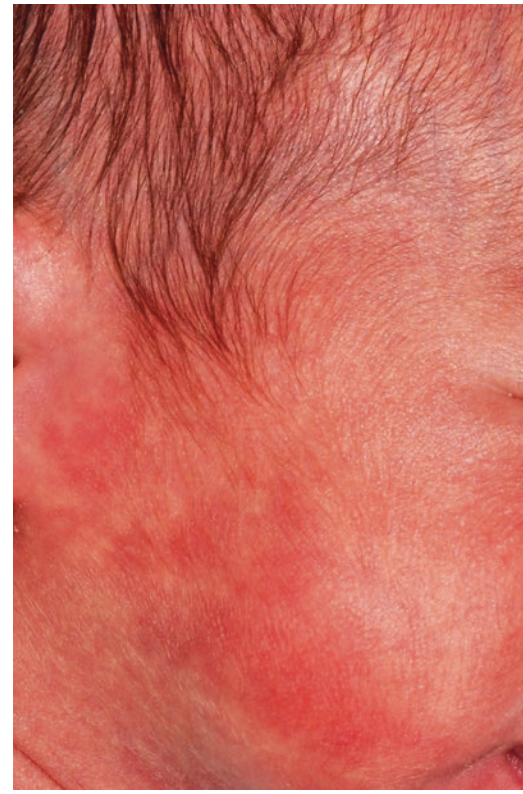

Fig. 4.8 Port-wine stain on the right cheek

Table 4.3 Key differences among the most common neonatal vascular birthmarks

	Nevus simplex	Port-wine stain (Fig. 4.8)	Infantile hemangioma
Age of onset	Birth	Birth	Absent at birth, precursor (flat pink or bruise-like patch) lesion may be present
Location	Glabella, forehead, nape of neck/posterior scalp	Head and neck most common; but can be anywhere	Head and neck most common; but can be anywhere
Clinical features	Ill-defined, light pink, blanches	Well demarcated	Rapid volumetric growth in first few weeks of life
		Dark pink	
		Darkens over time	
Natural history	Darkens with crying or exertion, most fade completely over first 2 years of life	Darken and thicken over time, may develop nodules at puberty	Rapid growth, plateau, and spontaneous involution
Treatment	Clinical observation	Pulsed dye laser early and often is the established treatment of choice	Localized treatments for small superficial lesions: timolol 0.5% gel forming solution
			Systemic treatment of choice: propranolol hydrochloride 2–3 mg/kg/day until no longer proliferating

Case Presentation

At her follow-up in the newborn clinic, a 3-week-old girl presents with the bright red, firm, warm plaque (Fig. 4.9). Her mother is alarmed because it was a small flat spot at birth that was barely visible.

How do you explain the diagnosis and natural history of this lesion to this concerned mother?

1. This is a tumor and needs an immediate biopsy
2. This is a benign birthmark that is expected to grow in infancy
3. This is a result of trauma during delivery
4. This is a hereditary birthmark

The lesion described above is an infantile hemangioma (IH), the most common benign tumor of infancy, and while the exact etiology and pathogenesis of IH is unknown. Infantile hemangiomas more common in female infants and low birth weight newborns. Several theories, including a placental embolus, a somatic mutation in a gene-mediating endothelial cell proliferation, or origination from an endothelial progenitor cell (CD34+, CD133+), have been proposed [11].

As seen in the newborn, IH are either not present at birth or a "precursor" lesion that can appear as a bluish bruise-like patch, telangiectasias with a rim of pallor, or a red flat stain. IH have a characteristic natural history consisting of three phases:

1. The rapid proliferation phase. IH experience rapid volumetric growth and are red, firm, and rubbery. This usually begins at 3 weeks of age and lasts until 6–7 months of age depending on the IH. IH with a deep component will proliferate for longer period of time. The most rapid rate of growth is thought to occur between 5 and 8 weeks of age.
2. The plateau (or late proliferative) phase. IH have a slower rate of growth and color changes to dull red or gray and begins to break apart. IH feel soft and spongy. The length of this phase is variable and can begin as early as 7 months and typically lasts until 12 months of age.
3. The involution phase. Involution of IH is a slow gradual process that usually starts at 1 year of age. In this phase, the color continues to fade and lesions flatten. Some lesions involute completely while others leave fibrofatty residua and skin texture changes (Table 4.3).

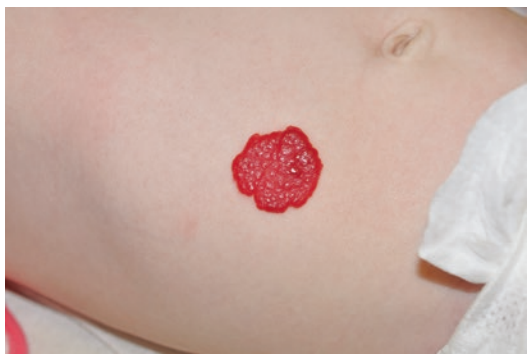

Fig. 4.9 Infantile hemangioma in the early proliferative phase on the right lower abdomen

Answer: 2

Which infantile hemangiomas require treatment?

1. Large function threatening lesions
2. Ulcerated hemangiomas
3. Infantile hemangioma at high risk for cosmetic disfigurement
4. All of the above

The vast majority of IH will proliferate and involute with minimal consequences. In these cases, active nonintervention is the treatment of choice and consists of education on the natural history of IH, close monitoring, and reassurance. There is a significant minority of IH that are high risk for complications and or associated anomalies. It is important to recognize these patterns early so that a work-up can be done and treatment initiated (preferably in the early proliferative phase), so that treatment can have maximal benefit. There are three generally accepted reasons for treatment: (1) ulceration or risk of ulceration, (2) disfigurement or risk of cosmetic disfigurement, and (3) functional impairment. IH at high risk for ulceration can be identified by their location and morphology.

For example, those located in the perineal, axillae, neck, or perioral areas are at higher risk for development of ulceration. Ulceration is heralded by a gray-white surface color during the proliferative phase, and when it occurs, it can be painful and will result in residual scarring.

Further evaluation for underlying anomalies or systemic associations is required for hemangiomas of the following morphologies and/or locations:

1. Large segmental IH (i.e., those with a configuration corresponding to a recognizable and/or significant portion of a developmental segment) on the face >5 cm should be evaluated with MRI/MRA of the head and neck, echocardiogram, and an ophthalmologic evaluation to assess for underlying PHACES syndrome [posterior fossa brain malformations, hemangiomas, arterial anomalies (most often cerebrovascular), cardiac anomalies, eye abnormalities, and sternal cleft or supraumbilical raphe or both].
2. Large segmental IH over the lumbosacral or perineal regions may be associated with underlying spinal dysraphism such as tethered cord and other structural abnormalities as part of the LUMBAR syndrome. This is a rare condition that presents as a hemangioma or several hemangiomas on the lower body in association with other congenital anomalies. These anomalies may include urogenital tract malformation, myelopathy (spinal cord defect), bone deformities, anorectal malformations, and arterial anomalies. Screening should include a spinal ultrasound if less than 3 months and/or an MRI/MRA of the lower back and affected lower extremity.
3. Large hemangiomas on the lower face or "beard" area can be a marker of a deeper laryngeal or airway hemangioma. Patients with IH in this area should be referred early for otolaryngology evaluation [12].
4. Patients with more than five IH are at significantly higher risk for hepatic hemangiomas and should be screened with abdominal US to assess for hepatic or other visceral IH [13]. The risk of visceral hemangiomas increases with increasing number of skin IH [14].

Oftentimes, the large segmental lesions described above that should prompt further work-up will also require systemic treatment because they are at high risk for hemangioma-related complications (disfigurement, ulceration, or visual compromise).

Answer: 4

What is the treatment of choice for infantile hemangioma that requires systemic treatment?

1. Oral corticosteroids
2. Oral propranolol
3. Vincristine
4. Pulsed dye laser

The vast majority of IH do not require active intervention. For small superficial hemangiomas in cosmetically sensitive areas or in an area at high risk for ulceration (perineal, axillae, neck, or perioral), the treatment of choice is timolol 0.5% gel forming solution. Timolol is a nonselective beta-blocker that is highly effective for ulcerated and superficial hemangiomas. The recommended dose of timolol 0.5% gel forming solution is 1 drop twice daily on the IH for at least 3 months for best response.

Other local therapies include intralesional triamcinolone (5–10 mg/mL), a useful option for bulky, localized lesions, and pulsed dye laser (PDL) treatment. This approach is useful for small flat lesions in the early proliferative phase or for residual telangiectasias after most of the IH has involuted.

Systemic therapy is reserved for larger IH with more aggressive growth characteristics that pose a high threat to a vital function, for cosmetic disfigurement, or for those IH not responding to local therapy. The first-line systemic treatment option is propranolol, a nonselective beta-blocker, that has demonstrated superior efficacy and safety compared to systemic corticosteroids. The recommended generic formulation to use is propranolol hydrochloride oral solution 20 mg/5 mL. The branded, infant friendly formulation, Hemangeol™ (propranolol hydrochloride 4.28 mg/mL) was used in several large international multicenter randomized

controlled trials and is FDA approved and indicated for the treatment of IH in patients 5 weeks and older [15].

Practices for propranolol initiation vary. Guidelines published in 2013 recommended a baseline cardiopulmonary assessment with electrocardiogram (ECG) prior to starting propranolol in certain situations (baseline HR low for age; family history of congenital heart disease or arrhythmia; history or presence of arrhythmia) [16]. Monitoring heart rate and blood pressure at baseline and after initiation was also recommended [16]. Since the consensus guidelines were published, large safety studies have shown very low incidence of symptomatic bradycardia and/or hypotension, and thus most practitioners will start propranolol in healthy full-term infants that have a normal clinical cardiac exam (performed by either the prescribing practitioner or pediatrician) and no family history of heart disease [17]. In addition, monitoring HR and BP after initiation or dose escalation is no longer a common practice. However continued anticipatory guidance of potential side effects is imperative [18].

Optimal dosing is based on weight with a goal therapeutic dose of ~2.2 mg/kg/day (range 1–3 mg/kg/day) divided 2–3 times daily with a minimum of 6 hours between doses. Propranolol should be given during the day, with or shortly after a feeding. The most common reported side effects include sleep disturbance, intermittent acrocyanosis, cold hands and feet, gastrointestinal symptoms, and/or respiratory symptoms. Serious side effects are rare and include hypotension, bradycardia, and hypoglycemia. Parents should be educated regarding the symptoms of hypoglycemia and instructed to ensure regular feeding times, avoid prolonged fasts, and discontinue propranolol during times of decreased oral intake or if there is wheezing. Propranolol is usually continued through the growth phase of the IH and then tapered off.

When there is a contraindication to the use of propranolol and the IH requires systemic treatment, oral corticosteroids (prednisone or prednisolone; 2–4 mg/kg/day divided twice daily until growth has stopped) and/or surgical excision are used. Oral corticosteroids must be tapered slowly to avoid rebound growth and adrenal suppression.

Answer: 2

Clinical Pearls

- Most skin lesions and skin eruptions present in the first few weeks of life are benign and self- limited.
- Erythema toxicum neonatorum is a common and self-limited skin condition that can mimic other pustular neonatal skin conditions.
- Transient neonatal pustular melanosis progresses through three characteristic phases and then self-resolves without sequelae.
- Congenital cutaneous candidiasis can present with yellowing of the nail plates as the sole manifestation.
- Miliaria rubra improves spontaneously with cooling.
- Close inspection and visualization of yellow color or yellow dots can help distinguish a nevus sebaceous from aplasia cutis.
- Congenital melanocytic nevi should be classified by size and monitored clinically.
- Nevus simplex should be distinguished from a port-wine stain and an infantile hemangioma early, so parents can be reassured of their eventual resolution.
- Infantile hemangioma may resemble port-wine stains initially, but close monitoring in the first month of life will demonstrate the characteristic growth pattern of an IH.
- Most infantile hemangiomas require no treatment; for those requiring treatment, topical and systemic beta-blockers are offered first.

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