Yellow and yellow-brown papules and plaques: Differentiating look-alikes in children's dermatology

ABSTRACT

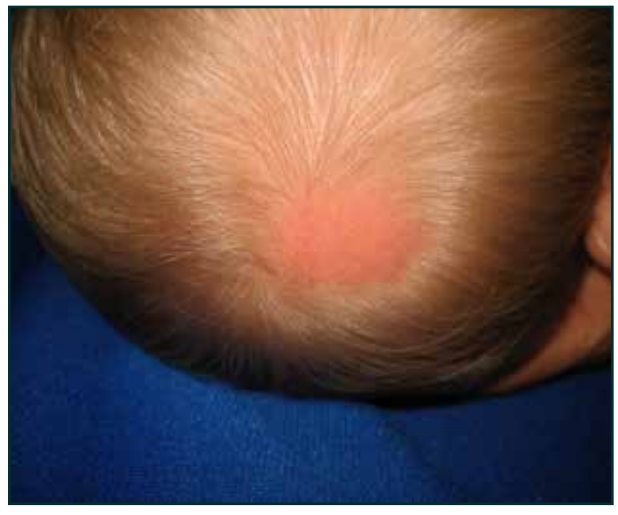
Yellow-hued papules and plaques in children can be difficult to differentiate as many causes are rare and may not be frequently outside of specialty pediatric dermatology settings. We will review some of the common and concerning yellow-brown papules and plaques found in infants and children and discuss appearance and distribution, pathophysiology, associated findings, and management.

KEYWORDS: dermatology, pediatric, yellow lesions

Introduction

Yellow and yellow-brown papules and plaques represent an array of underlying pathophysiology in children's dermatological diseases. The evaluation of these lesions can be challenging if they are not commonly encountered in practice. Understanding an approach to distinguishing yellow-brown lesions and related findings is important for practitioners to make timely diagnoses and appropriate referrals. Congenital or acquired appearance, and the number and distribution of lesions are important factors to aid in diagnosis. We will examine both common and uncommon lesions for practitioners to be aware of.

Figure 1: Nevus sebaceous on the vertex of the scalp with circumscribed hair loss



1. Congenital Lesions

1.1 - Nevus Sebaceous

A nevus sebaceous is a hamartoma—a benign tumour—of the sebaceous glands. Nevus sebaceous presents as a thin,

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sharply demarcated yellow to red plaque commonly presenting at birth. They are oval to linear in shape ranging from a few millimetres to a few centimeters. The surface may appear verrucous or waxy. About half of the lesions occur on the scalp, but can also occur on the face and neck. They are less common on the upper chest or arms. When on the scalp, the overlying area is usually hairless, making it one of the most common causes of congenital hair loss in children.[1]

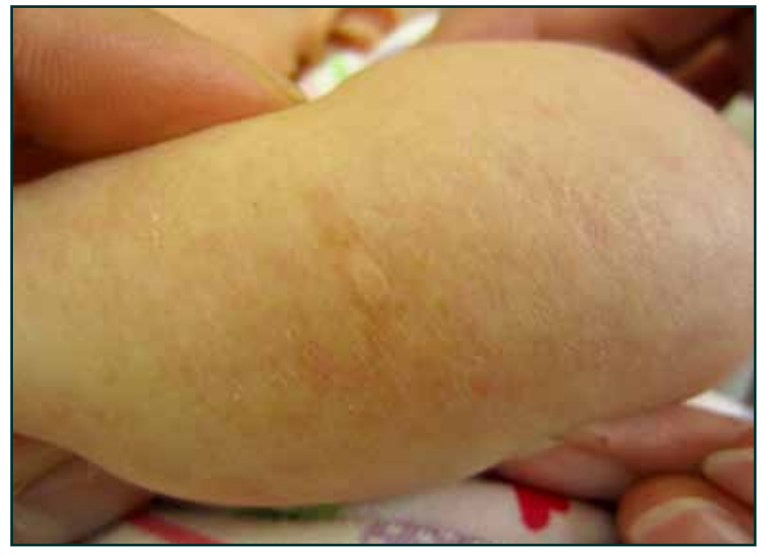
In adulthood, androgenic stimulation to the sebaceous glands within the lesion may cause the plaque to become verrucous. There is a small chance that benign tumors (1.6-2.8%) or malignant but slow growing basal cell carcinoma (0.9%) will grow within the lesion.[2] Rapidly growing nodules or plaques should be biopsied for pathologic evaluation, but is not needed for stable lesions. Barring cosmetic concerns, excision can be postponed until the teen or young adult years when they child can make an informed decision about removal, and general anesthetic can be avoided.

Infants with large nevus sebaceous on the face or scalp (larger than 10cm) should be screened for musculoskeletal, neurologic, ocular and cardiovascular involvement, which may be indicative of nevus sebaceous syndrome (also known as Schimmelpenning syndrome). Nevus sebaceous syndrome is characterized by neurologic abnormalities and potential ocular diseases. Some examples include seizures, developmental delay, hemiparesis, hypotonia, deafness, scoliosis, facial bone deformity, macrocephaly, and corneal changes. Treatment of nevus sebaceous syndrome is challenging and requires a multi-disciplinary approach.[3]

1.2 - Focal dermal hypoplasia

Focal dermal hypoplasia is a rare, X-linked disorder found predominantly in females. Lesions develop due to a lack of fibrous dermins, allowing the yellow subcutaneous fat to be visible through the skin. Cutaneous lesions appear at birth as red-yellow reticular streaks of thinned dermis, often with associated telangiectasias. As babies develop more fat, the yellow hue of the lesions increases.[4] Lesions may also appear with focal fat herniation, hypo-or hyper-pigmentation, papillomas, or ulcerations. Affected children may also have abnormali-

Figure 2: Focal fat herniation and streaky, atrophic yellow-red hued dermis on the leg in focal dermal hypoplasia



ties of tissues arising from the ectoderm, including sparse hair, thin nails, hypodontia or enamel hypoplasia.[3]

Children should be screened for skeletal, ocular, and neurologic abnormalities, as well as umbilical or inguinal hernias, and cleft lip or palate.

Skin biopsy can be used for diagnosis if the clinical picture is unclear. Long bone X-ray can also be used; parallel linear striations in the metaphysis of long bones at or near the epiphyseal junction is found in all cases of focal dermal hypoplasia.[3] Children should be screened for skeletal, ocular, and neurologic abnormalities, as well as umbilical or inguinal hernias, and cleft lip or palate. Genetic counselling later in life is recommended, as even mildly affected children have a high risk of severely affected offspring.[3]

Dermatological treatment options include surgical intervention to remove skin or mucous membrane papillomas, and pulsed dye laser to reduce telangiectasia.[3]

2. Congenital or Acquired Lesions

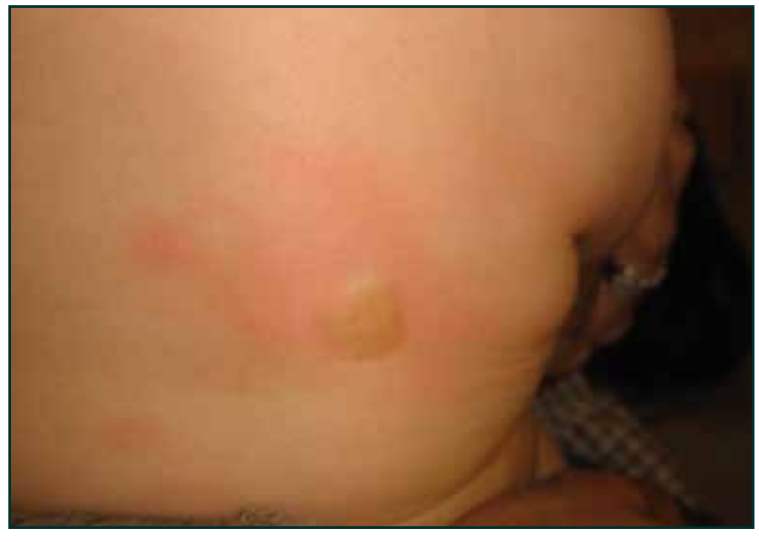
2.1 - Solitary Mastocytomas

Mastocytomas are a form of mastocytosis, a general classification for conditions arising from an accumulation of mast cells under the skin. Solitary mastyocytomas appear as solitary yellow brown papules and plaques. They can be identified by eliciting Darier's sign, whereby rubbing the lesion triggers urticaria in the area. These lesions may be confused for lentigines or melanocytic nevi.[3]

Lesions may be present at birth or arise during the first few months of life.[5] Most children are asymptomatic, however they may experience prutitis or flushing due to the release of mast cell mediators including as histamine, eicosanoids, and cytokines. These symptoms may become more prominent with exercise, heat, or trauma to the lesions.[1]

A rare variant is diffuse cutaneous mastocytosis (DCM), which may appear as a yellow-brown plaque or thickening of skin with peau d'orange appearance, without discrete lesions. Children may be

Figure 3: Yellow-brown plaque of solitary mastocytoma on the upper back



pruritic and exhibit Darier's sign where they develop urticaria as a response to local trauma.[1] These children are at risk for more severe symptoms including flushing, pruritis, hypotension, anaphylactic shock, diarrhea, and GI bleeding as a result of the high mast cell load in the entire skin.[5]

Onset of mastocytomas in childhood is most often benign and spontaneously remits prior to puberty.[4] Children should be monitored yearly through physical exam specifically looking for hepato- or splenomegaly, lymphadenopathy, osteoporosis, and elevated serum tryptase levels.[5] Serum tryptase levels greater than 20 ng/mL, hepatomegaly, or splenomegaly are concerning for systemic mastoctyosis.[6]

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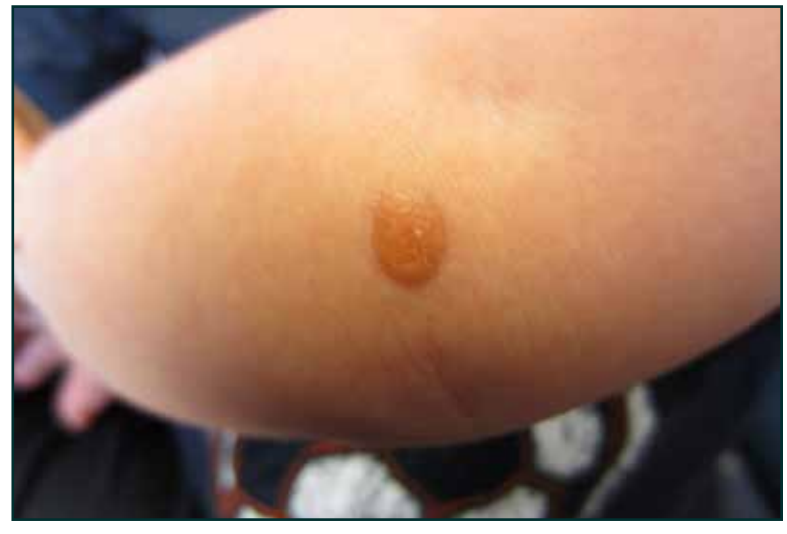
Therapy is usually unnecessary in solitary mastocytosis. For cosmetic complaints, topical steroids under occlusive dressing could be considered in children over two years of age. For children with cutaneous mastocysotsis complaining of itch, redness, or swelling, oral antihistamines (H1 and H2 blockers) may be used.[7] Avoidance of mast-cell degranulation triggers, such as anesthetics and physical stimulation of lesions is also warranted as these may result in a large local or systemic adverse reaction.[1]

2.2 - Juvenile Xanthogranuloma

Juvenile xanthogramuloma (JXG) are a common, benign form of non-langerhans cell histiocytosis. Sharply demarcated, yellow-orange papules and plaques or soft nodules are characteristic, which are usually smaller than two centimeters in size. They often occur on the head and neck area. Lesions contain lipid, which is responsible for the color. They occur in childhood most often under two years of age, and usually spontaneously involute after 2-5 years. Rarely, they are present in newborns. On average, children present with 5-10 lesions at a time.[4] Despite what the name might suggest, JXG is not associated with abnormalities in lipid or triglyceride levels.

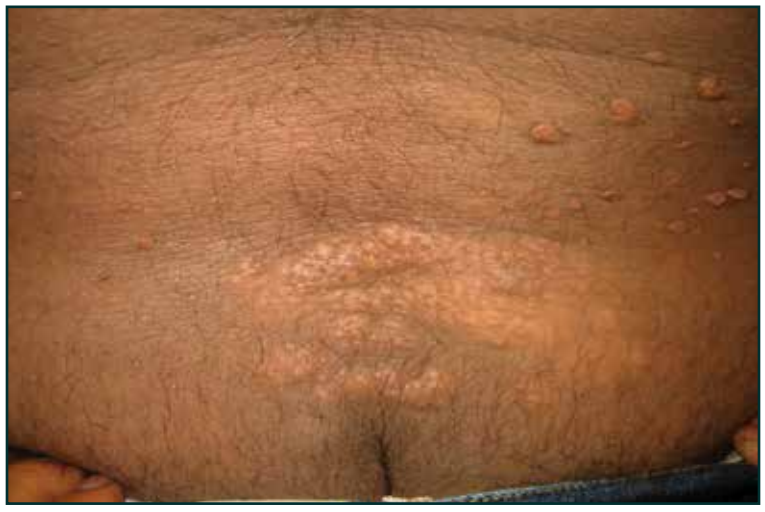
Figure 4: Yellow-orange papule of juvenile xanthogranuloma on the arm



Multiple JXG in children under two years of age have been associated with development of JXG in the iris, which may cause vision loss. Affected children may have eye redness or complain of irritation or photophobia.[3] Rarely, JXG can be found in internal organs, including the testes, lung, liver, spleen, and pericardium. Around 20% of children with JXG also have café au lait macules, which is associated with neurofibromatosis type 1. Multiple JXG and café au lait macules occurring in a child has also been associated with an increased risk of chronic myeloid leukemia in few case reports. Though rare, children presenting with JXG should be monitored for development of leukemia.[3]

Treatment is not necessary for skin-limited JXG; most lesions will spontaneously resolve on their own over 3-6 years.[3] Surgical excision can be performed for cosmetic purposes or to aid in diagnosis. Children presenting with multiple lesions under two should be referred to an ophthalmologist to rule out hyphema and glaucoma.[3]

Figure 5: Shagreen patch (connective tissue nevus); yellow to flesh colored papules coalescing into a plaque on the mid lower back of a patient with tuberous sclerosis



2.3 Connective tissue nevus

Connective tissue nevi are a hamartoma (benign tumor) of the dermal collagen or elastic fibers. They present as smooth, flesh-colored to yellow-brown papules which may coalesce into plaques. They may be solitary, grouped, linear, or irregularly distributed. Lesions may appear congenitally or be acquired, typically appearing before puberty.[3]

Connective tissue nevi may occur spontaneously, but are also characteristic of underlying genetic diseases.[1] Tuberous sclerosis (in which the lesion is referred to as a shagreen patch) is commonly associated with connective tissue nevi occur on the lower back. Children with tuberous sclerosus may also present with leaf-shaped white macules, angiofibroma, and periungal fibroma. Tuberous sclerosis is a neuro-cutaneous syndrome leading to benign tumor formation in the skin, brain, heart, lungs, and kidneys. Similarly, Buschke-Ollendorf syndrome is an autosomal-dominant condition presenting with disseminated connective tissue nevi and osteopoikilosis, a sclerosing dysplasia of bone.[3]

SUMMARY OF KEY POINTS

Nevus sebaceous typically grow in proportion with patients in early childhood. Excision should be deferred until adolescence to avoid the use of general anesthetic and an informed decision can be made by the child.

Benign cephalic histiocytosis and juvenile xanthogranuloma are both forms of non-Langerhans cell histiocytosis and are benign and self limited.

Consider a diagnosis of tuberous sclerosis in any child presenting with connective tissue nevi, especially if white macules, angiofibroma, or periungual fibroma are also found.

Screen children with necrobiosis lipodica for retinopathy and neuropathy.

Biopsy of the lesion can be considered if the diagnosis is unclear.[3]

Connective tissue nevi are asymptomatic and do not require surgical excision. They are typically not cosmetically concerning.

3. Acquired lesions

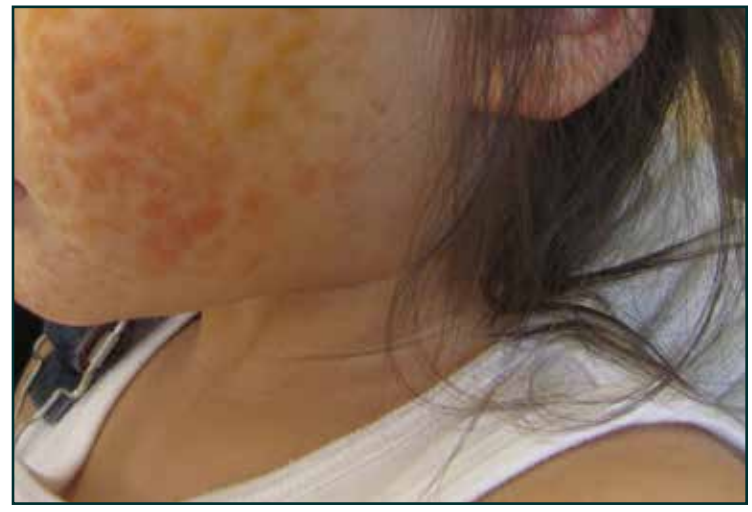
3.1 - Benign cephalic histiocytosis

Benign cephalic histiocytosis (BCH) is a rare, potentially under-recognized form of non-Langerhans cell histiocytosis.[8] It can be identified by raised, orange-red or red brown thin papules appearing on the upper face including eyelids and cheeks of infants. Lesions are typically one to eight millimetres in diameter. Additional lesions can appear for many months over the entire head, ears, occiput, and neck, and potentially on the shoulders and arms. As few as two to upwards of 100 lesions may appear. Lesions usually spontaneously fully resolve in a few years, and may not scar, or may leave a flat, atrophic pigmented scar.[1,3]

When in doubt, the diagnosis can be confirmed with biopsy. This may be useful if the clinical picture is not clear, as there may overlap with other non-Langerhans cell histiocytosis such as JXG.[3] Some have now hypothesized that BCH and JXG are both manifestations of the same condition, with BCH being the earlier presentation.[9]

There are no known complications of BCH, and no investigations are necessary if it can be differen-

Figure 6: Orange-red grouped papules on the cheek in benign cephalic histiocytosis



tiated from xanthomas, JXG, and flat warts.[1] There have been a few case reports of associating BCH with diabetes insipidus and diabetes mellitus, but so far there is no known link between these conditions and further investigation is not necessary.[8] No treatment is necessary, but clinical follow up to monitor for progression or systemic involvement of the condition is prudent.[3]

3.2 - Cutaneous Xanthoma

Cutaneous xanthomas are the manifestation of a collection of lipid filled histocytes in the dermis. They appear as yellow-hued papules, plaques, or nodules. Nodules may present in different locations. Tendon xanthomas are deep, flesh to yellow colored hard nodules located within peripheral tendons. Eruptive xanthomas appear as multiple yellow-pink papules suddenly appearing on extensor surfaces and the buttocks. Flat xanthomas appear on the eyelids are referred to as xanthelasmas.[1]

Xanthomas are a cutaneous manifestation of an alteration in lipid metabolism, and in many cases may be the first manifestation of the underlying disease.[10] Tendon and other cutaneous xanthomas are more likely to present in children with hyperlipidemia, such as familial hypercholesterolemia.[11] Screening lipid profiles and family history of lipid disorder should be sought.

Biopsy is not necessary for diagnosis, but if performed demonstrates foam cells, which are lipid-containing macrophage.[1]

Treatment for xanthomas is dependent on the underlying cause, and typically involves dietary modification and statin or fenofibrate use to lower lipid levels.[10]

Figure 7: Tendon xanthomas; yellow and red nodules and tumours over tendons in the bilateral feet

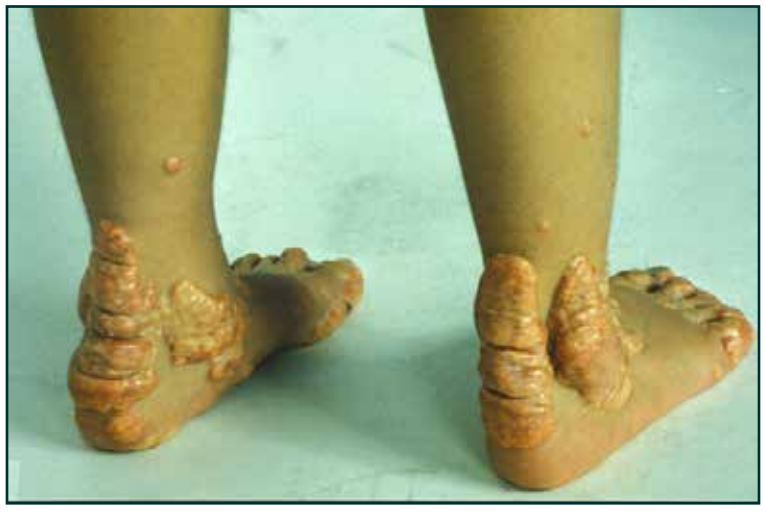


Photo courtesy of Dr. Maureen Rogers

Necrobiosis lipoidica

Necrobiosis lipoidica is a condition in which granulomatous inflammation causes collagen degeneration. It often presents in people with diabetes mellitus, though may also be associated with other autoimmune diseases. The exact cause remains unknown.[12] Necrobiosis characteristically presents a well circumscribed yellow brown plaque with dilated blood vessels and central epidermal atrophy. Lesions first appear as non-specific erythe-

matous papules and may slowly evolve over years before presenting to medical care. Later, lesions may ulcerate, becoming painful. They commonly occur on the anterior lower legs.[1]

Although biopsy can aid in diagnosis, the lesions are characteristic, and diagnosis should be possible to make clinically. It is best to avoid surgical procedures in this location considering wound healing challenges in patients with diabetes.

It is estimated that around three quarters of patients presenting with necrobiosis have a diabetes diagnosis, yet under one percent of patients who have diabetes are affected. The mean age of onset is in the fourth decade of life, however there are case reports among children.[3] Necrobiosis in children with diabetes may suggest a higher risk for nephropathy and retinopathy, thus is it important to have regular screening and management by an endocrinologist.[3] Healthy children presenting with necrobiosis should be screened for diabetes mellitus, and other autoimmune diseases should also be considered.[1]

Treatment of necrobiosis is challenging; the primary goals are controlling blood glucose in patients with diabetes, and wound care if ulceration of the lesions is present. Topical treatment options for active lesions include topical corticosteroids and topical calcineurin inhibitors. Phototherapy and systemic therapy with anti-TNF immunologic agents have also been reported as successful treatments, but unfortunately there is no consensus on best treatment practices.[3,12]

Conflicts of Interest
Lauren Schock and Dr Lam do not have any potential conflict of interest, real or perceived. There is no honorarium, grant, or other form of payment given to me or the coauthor.

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CLINICAL PEARLS

Use your hands – rub a suspected lesion of mastocytosis; if urticaria is elicited (a red, itchy, swollen papule or plaque), you have found Darier's sign. Mastocytosis is likely. Be prepared to treat the child with antihistamines if needed.

Juvenile xanthogranulomas are more common under two years of age, and typically appear on the head and neck. Cutaneous xanthomas often occur overlying tendons, or as grouped papules over the extensor surfaces and buttocks.

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