Papular and Nodular Skin Lesions in Children

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ABSTRACT

A child may present to plastic surgery for treatment of a wide range of cutaneous lesions. Accurate clinical diagnosis of any skin lesion prior to considering excision results in an optimal outcome. This review discusses the most common papular and nodular skin lesions in children and addresses indications for removal as well as relative contraindications, alternative treatment options, and necessary further diagnostic work-up. Lesions are classified into five categories: expected spontaneous regression without treatment intervention; elective surgical removal guided by clinical circumstances, with a subgroup of these indicating possible underlying syndromes; further diagnostic imaging indicated prior to treatment intervention; and malignancy requiring complete surgical removal or adjuvant therapy (Fig. 1)

KEYWORDS: Pediatric skin tumor, spontaneous regression, elective surgical removal, underlying syndrome, further diagnostic imaging

Figure 1 offers an overview of factors that should be considered in the evaluation of papular and nodular skin lesions in children.

SPONTANEOUS REGRESSION

Spontaneous regression is expected with:

Infantile digital fibromatosis (Fig. 2)
Juvenile xanthogranuloma (Fig. 3)
Solitary mastocytoma (Fig. 4)
Calcified ear nodule (of Winer)/heelstick calcinosis

Infantile Digital Fibromatosis

One lesion with well-documented potential for spontaneous regression is the infantile digital fibroma, also known as recurring digital fibroma of childhood. This arises as a firm, smooth, flesh-colored to slightly erythematous, broad-based nodule on the lateral or dorsal

aspect of a digit. It is found more commonly on fingers than toes, and several digits can be involved, but the thumbs and great toes are usually spared. Lesions typically develop shortly after birth, the majority by 12 months of age.¹ Differential diagnosis includes subungual exostosis, calloused pad, digital mucous cyst, and fibrosarcoma. Diagnosis should be confirmed by biopsy, revealing characteristically whorls and interdigitating sheets of elongated fibroblasts as well as eosinophilic perinuclear cytoplasmic inclusion bodies.

Indications for excision of these lesions are controversial because they have a tendency for both spontaneous regression and recurrence after incomplete surgical intervention. The literature supports a conservative, noninterventional approach.² Local excision may be advocated on the basis of the risk of flexion and deviation deformities if the tumor continues to grow. However, it is reasonable to await spontaneous regression over a period of several years, avoiding surgical intervention unless joint deformity or functional impairment or both

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Figure 1 Factors to consider in the evaluation of papular and nodular skin lesions in children.

occur. With a high recurrence rate after surgical excision of up to 60%, the risks and benefits of any surgical procedure need to be carefully considered.³ There is currently no defined standard of care. Case reports have stated the successful use of intralesional fluorouracil injections and Mohs micrographic surgery, both with no recurrence at 2-year follow-up.^{4,5}

Juvenile Xanthogranuloma

Juvenile Xanthogranuloma (JXG) arises as a well-demarcated, firm, 0.5- to 2-cm dome-shaped papule. Most commonly, the clinical course shows spontaneous involution within several years, and no treatment is required. JXGs show a predilection for the head, neck, and trunk and evolve over time from slightly erythematous to yellow-brown. It is the most common non-Langerhans cell histiocytosis of childhood, with a slight male predominance, and is 10 times more prevalent in white than black children.⁶ Five percent to 35% arise at birth, 40 to 70% within the first year of life, 88% by 5 years, and 95%

by 10 years.⁶⁻⁸ Despite the name “xantho”-granuloma, there is no association of these lesions with hyperlipidemia or other metabolic abnormalities. Differential diagnosis includes atheroma, lipoma, xanthoma, and Langerhans cell histiocytosis. Histologic appearance varies with stage of disease, but diagnosis can generally be confirmed by characteristic biopsy, consisting of an accumulation of histiocytes without Birbeck granules or Touton-type giant cells and S-100 negativity on staining. With rare exception, JXGs arising early in life

Figure 2 Infantile digital fibroma.

Figure 3 Juvenile xanthogranuloma.

Figure 4 Solitary mastocytoma.

undergo complete spontaneous regression, usually within 3 to 6 years.⁶ Minimal residual changes such as hyperpigmentation, atrophy, or anetoderma may persist. Given the self-limited benign prognosis, no treatment is required for patients with disease limited to the skin. If surgical excision is performed for diagnostic or cosmetic purposes, recurrence is uncommon, although it has been documented.^{6,7}

An exception is children who develop multiple lesions in the skin and rarely at extracutaneous sites.^{7,8} In these patients the eyes are involved in 0.3% of cases, and if the lesions are left untreated they can result in acute hyphema, uncontrolled glaucoma, or blindness.⁹ Patients may initially present with eye redness, irritation, or photophobia. Any child younger than 2 years with more than three lesions should be referred to ophthalmology for slit-lamp examination.⁶ Other extracutaneous sites reported include the bone, nasal cavity, orbit, tongue, and bronchus.⁸ However, screening for visceral lesions in patients with cutaneous disease is not routinely recommended, as they remain asymptomatic with rare exceptions.⁶ A link between neurofibromatosis-1 (NF-1), JXG, and juvenile chronic myelogenous leukemia (JCML) is well recognized. Children with NF-1 and JXG have a 20- to 32-fold higher risk of developing JCML than patients with NF who do not have JXG.¹⁰ Therefore, the presence of JXG in an infant with café-au-lait macules, particularly in the case of a family history of NF, should alert to this potential association and warrant further work-up.

Solitary Mastocytoma

Mastocytomas represent abnormal accumulations of mast cells in the skin and arise as one to five flesh-colored-pink or yellow-tan ovoid papules, nodules, or plaques, 0.5 to 3 cm in diameter, typically on the arms, neck, and trunk and with smooth or peau d'orange

surface texture. They most commonly arise at birth or during early infancy. Differential diagnosis includes JXG, xanthoma, and melanocytic nevus. A helpful diagnostic clue is the presence of Darier's sign, in which rubbing of the lesion releases mast cell mediators such as histamine, resulting in local pruritus, erythema, edema, urtication, and blistering and rarely mild systemic symptoms such as flushing and diarrhea. Diagnosis can be made clinically, but if biopsy is performed, it will reveal mast cell hyperplasia.

The prognosis for a solitary mastocytoma in a child is excellent, with the majority following a mild course with ultimately complete resolution, generally before adulthood.^{11,12} Surgical excision is rarely necessary if local symptoms cannot be adequately controlled with topical corticosteroids or oral H1 and H2 antagonists.^{13,14} Patients and their families should be advised to avoid potential triggers of mast cell degranulation, such as physical stimuli, aspirin, shellfish, and iodine-containing contrast medium. The solitary mastocytoma needs to be differentiated from multiple or extensive presentations, the spectrum of which includes urticaria pigmentosa, diffuse cutaneous mastocytosis, telangiectasia macularis eruptive perstans, and systemic mastocytosis. Even with extensive disease, the prognosis remains more favorable in the pediatric population with only rarely progression to systemic disease or malignancy.¹⁵

Calcified Ear Nodule (of Winer)

This solitary nodule on the pinna or earlobe represents idiopathic calcinosis and most commonly arises in the newborn. It is firm, measures on average 3 to 10 mm, and may show surface ulceration and discharge of chalky material. It is usually asymptomatic without systemic abnormalities, and if spontaneous resolution is not observed, it tends to respond favorably to cryotherapy or curettage. Differential diagnosis includes molluscum contagiosum, syringoma, and inclusion cyst.

Heelstick Calcinosis

These localized, calcified, almost punctate, yellow-white papules occur along the heel of a young infant. They may be unilateral or bilateral and solitary or more commonly slightly clustered, and they represent deposits of calcium following phlebotomy in the neonatal period, particularly in premature infants. As these papules migrate to the skin surface, they tend to appear larger and may extrude chalky material. They usually remain asymptomatic and resolve spontaneously over several months. If they are bothersome, gentle cryosurgery and curettage are curative. Topical retinoids may further hasten spontaneous resolution.

Figure 5 Epidermal nevus.

REMOVAL ELECTIVE AND GUIDED BY CLINICAL SCENARIO

Extensive lesions may indicate underlying syndrome with:

- Epidermal nevus (Fig. 5)
- Connective tissue nevus (Fig. 6)
- Pilomatricoma (Fig. 7)
- Epidermal inclusion cyst (Fig. 8)
- Nevus sebaceus (Fig. 9)

Epidermal Nevus

Epidermal nevus is a common hamartomatous lesion that arises as a gray to yellow-brown well-circumscribed papule or plaque, often in a linear configuration, with a velvety, granular, verrucous, or papillomatous texture. It has a predilection for the extremities but may occur anywhere on the skin surface at birth or in early childhood. Histologically, it is characterized by hyperplasia of keratinocytes and skin appendages. Prognosis is benign, although removal is often sought for cosmetic purposes. Surgical treatment should be guided by expected cosmetic outcome and may not be a feasible approach for large lesions. For more extensive lesions,

Figure 6 Connective tissue nevus.

Figure 7 Pilomatricoma.

superficial destructive therapies using the CO₂ laser or for smaller lesions the erbium:yttrium-aluminum-garnet (YAG) laser may be considered as alternative treatment modalities.^{16,17}

In some cases, multiple systematized epidermal nevi are present along lines of Blaschko in a linear, arcuate, or wavy pattern that is speculated to result from migration of skin cells with a common origin during embryogenesis. These epidermal nevi represent cutaneous manifestations of a different mosaic phenotype and, if extensive, may be associated with neurological, ocular, skeletal, cardiovascular, and endocrine abnormalities constituting the epidermal nevus syndrome. Examples include Proteus syndrome, congenital hemidysplasia with ichthyosiform erythroderma and limb defects (CHILD) syndrome, Becker nevus syndrome, nevus comedonicus syndrome, and phakomatosis

Figure 8 Epidermal inclusion cyst.

Figure 9 Nevus sebaceus.

pigmentokeratotic.¹⁸ A unique variant of epidermal nevus, the inflammatory linear verrucous epidermal nevus, arises with waxing and waning erythematous and intensely pruritic scaly verrucous papules that coalesce into linear plaques along the lines of Blaschko. The differential diagnosis primarily includes psoriasis. Such lesions are often troublesome to the patient because of unremitting symptoms despite topical treatment with corticosteroids and calcipotriol. Other options include cryotherapy, CO₂ or pulsed dye laser, and full-thickness surgical excision.^{19,20}

Connective Tissue Nevus

Connective tissue nevus (CTN) is an asymptomatic, flesh-colored dermal plaque, usually smooth and subtle, but at times thicker, with a leather-grain, peau d'orange, cobblestone, or cerebriform appearance. It arises at birth or develops during early childhood and can occur anywhere on the skin. Multiple lesions, if present, tend to be symmetrically distributed on the back, buttocks, or extremities. This hamartoma develops as a result of excessive deposition of dermal collagen or elastin, or both. Differential diagnosis includes a smooth muscle hamartoma. Biopsy can confirm the clinical diagnosis and should include a small wedge of uninvolved skin to facilitate histologic differentiation. Surgical excision, other than for cosmetic reasons, is generally unnecessary. CTNs in various forms can be seen as part of several syndromes, most notably tuberous sclerosis,²¹ trisomy 21,²² Proteus syndrome,²³ and Buschke-Ollendorff syndrome,²⁴ where such lesions are also known as shagreen patches, fibrous forehead plaques, collagenomas, and palmoplantar cerebriform hyperplasia.

Pilomatricoma

Pilomatricoma (PMC), also known as calcifying epithelioma of Malherbe, typically arises as a rock-hard bluish

subcutaneous nodule on the head or neck, ranging in size from 5 mm to 5 cm. It usually develops during early childhood or by the end of the second decade of life, grows slowly, and may at times display tenderness, inflammation, and erythema or discharge a chalky material. On physical examination the "teeter totter sign" is present, which refers to the manner in which downward pressure at one end causes the other end to elevate because of tethering of the lesion in the mid-dermis. PMC is the most common adnexal tumor of childhood and has a female predominance.^{25,26} Although it is usually not hereditary, familial occurrence has been documented.²⁷ This benign neoplasm is derived from hair follicle matrix cells, and differential diagnosis includes epidermal inclusion cyst, dermoid cyst, calcified lymph node or hematoma, branchial cleft remnant, parotid gland tumor, and hemangioma. Surgical excision is recommended, with clear margins including the overlying skin to which the tumor may be adherent. Recurrence after complete excision is as low as 1.5 to 6%.²⁶ Lesions are multiple in 2 to 26% of patients^{26,27} and in our experience typically do not signify any underlying disorder. However, case reports of association with myotonic dystrophy,²⁸ Gardner syndrome,²⁹ Rubinstein-Taybi syndrome,³⁰ trisomy 9,³¹ and Turner syndrome³² exist and may warrant further work-up in some patients.

Epidermal Cyst

Also termed epidermal inclusion cyst, this solitary, slow-growing, papular or nodular lesion often arises around puberty but may also be seen in very young children. It varies in size considerably from 2 mm to several centimeters and most commonly appears on the face, scalp, neck, trunk, and scrotum. A central punctum is the clue to the diagnosis, and foul-smelling debris may be extruded. Rupture of the cyst wall may cause inflammation and at times secondary infection. Complete surgical resection with removal of the epithelial lining of the cystic sac is curative and prevents recurrence. Multiple cysts may serve as a cutaneous marker of Gardner's syndrome, an autosomal dominant intestinal polyposis syndrome.

Nevus Sebaceus/Nevus Sebaceus of Jadassohn

Nevus sebaceus, a congenital hamartoma of the skin, arises as a well-circumscribed, irregular, yellow-orange, round or linear, waxy, pebbly-surfaced, hairless plaque on the scalp or face. It appears to flatten in childhood and then become more prominent and raised during puberty secondary to androgenic influence.³³ Incidence is sporadic, although a familial form has been reported.³⁴ Histologically, disordered sebaceous glands, hair follicles, and apocrine glands may be seen. Differential

diagnosis includes cutis aplasia, verrucae vulgaris, and linear epidermal nevus.

Management is controversial. Prophylactic removal was previously recommended because of a high incidence of basal cell carcinoma developing in these lesions. However, the recent literature indicates that the potential for malignancy is as low as 0.8%, and in the absence of clinical signs of malignant transformation (e.g., appearance of a discrete nodule) prophylactic surgical removal should not be systematically performed.³⁵ Elective excision remains the most common treatment approach because of cosmetic concerns and the potential for growth, particularly under hormonal stimulation in puberty. Options include surgical excision in preadolescence under local anesthesia versus removal in infancy under general anesthesia. The latter is preferable for large, cosmetically disfiguring or symptomatic lesions. For temporal scalp lesions, Davison et al reported superior results with a temporal flap compared with a primary linear closure after excision.³⁶ Giant nevus sebaceus, covering extensive areas on the head and scalp, may be associated with central nervous system, ophthalmologic, and skeletal abnormalities as well as malignancies, in linear nevus sebaceus syndrome. Margulis et al described a surgical approach to excision and reconstruction in such patients.³⁷

Further Diagnostic Imaging

Further diagnostic imaging is warranted with:

Nasal glioma

Dermoid cyst (Fig. 10)

Figure 10 Dermoid cyst of the lateral eyebrow.

Figure 11 Congenital midline nasal lesion, which on imaging proved to be an encephalocele.

Nasal Glioma

The nasal glioma (NG) arises as a firm, smooth, non-compressible, flesh-colored nodule, sometimes with a blue-red hue, at the root of the nose, which does not transilluminate. NGs may be extranasal (60%), intranasal (30%) simulating a nasal polyp, or a combination of both (10%).^{38,39} The NG may widen the nasal bridge, mimicking hypertelorism. This rare congenital anomaly occurs in 1 of 20,000 to 40,000 live births, with a 3:2 male predominance.^{38,39} It represents heterotopic neuroglial tissue, which results from herniation of brain tissue and meninges anteriorly during embryologic development, but it may not be recognized until later in life. Differential diagnosis includes other midline nasal lesions, such as dermoid cyst and encephalocele (Fig. 11), as well as nasal polyp, hemangioma, and other neoplasms and malformations. It is differentiated from a cephalocele in that it is separated from the underlying frontal lobe by the closure of cranial sutures. Thus, no fluctuation in size occurs with maneuvers that increase intracranial pressure such as crying or straining. NGs can be distinguished from hemangiomas in their lack of rapid proliferation. If the diagnosis is still in question, ultrasonography or Doppler flow studies, or both, may help with further differentiation.³⁸

Imaging is mandatory for all midline nasal lesions⁴⁰ to define the exact location, differentiate from other midline developmental masses, exclude intracranial extension, fully visualize any cranial defects, and plan a surgical approach. Skull radiographs should be obtained, as well as a computed tomography (CT) or magnetic resonance imaging (MRI) study, with most opting for MRI.³⁸ Optimal management involves prompt neurosurgical or ear, nose, and throat (ENT) referral for resection and reconstruction. Although these lesions are benign, early excision is extremely important to prevent further deformity of the immature facial bones, visual sequelae, and infections.^{38,41} Reports of a successful transnasal endoscopic approach exist.^{39,42} Complete

removal is crucial, as the recurrence rate may be as high as 4 to 10%.^{38,39}

Dermoid Cyst/Congenital Inclusion Dermoid Cyst/Dermoid Sinus Cyst

A dermoid cyst arises as a nontender mobile subcutaneous nodule and most commonly occurs on the lateral third of the eyebrow. They tend not to have any deeper extension in this location,⁴³ but because of local growth, complications include pressure erosion of the bone, proptosis, and eyelid displacement. Only 4 to 12% of head and neck dermoids occur in the nasal midline, but they represent the most common congenital midline mass.⁴⁰ A sinus opening or punctum may be present, with intermittent discharge of sebaceous material or recurrent infection, and is considered pathognomonic for intracranial connection. Any congenital midline lesion should be imaged to assess for this complication even when no such cutaneous markers are noted because the incidence of underlying connection may be as high as 45%.⁴⁴ Dermoid cysts do not transilluminate or show fluctuation in size with Valsalva maneuvers. Most are diagnosed in infancy and childhood.⁴⁴ They arise from a developmental epithelium-lined tract that extends inward from the surface of the skin along embryonic fusion lines and contain both dermal and epidermal derivatives.

Differential diagnosis of nasal dermoids includes other congenital midline lesions such as the NG or hemangioma. Treatment of choice is early surgical excision of the entire lesion as well as any punctum or tract.⁴⁰ In lesions with little or no cutaneous involvement, endoscopic removal has been performed successfully.⁴⁵ Incomplete excision has been shown to result in a recurrence rate from 30 to 100%, but with presumably complete excision, a retrospective study at Children's Hospital Boston showed a 12% postoperative recurrence.⁴⁴

Other Lesions for Which Removal Is Elective and Guided by Clinical Scenario

Other lesions for which removal is elective and guided by clinical scenario include:

Smooth muscle hamartoma (Fig. 12)
Fibrous hamartoma of infancy
Lipoma

Smooth Muscle Hamartoma

Smooth muscle hamartoma (SMH) arises at birth or shortly afterward as a localized, lightly pigmented, slightly elevated plaque with prominent vellus hairs,

Figure 12 Smooth muscle hamartoma.

usually on the trunk or extremities. This lesion represents a disorganized proliferation of arrector pili muscle within the reticular dermis. Contraction of this muscle when the lesion is stroked creates a transient elevation or rippling movement, referred to as “pseudo-Darier’s sign.” Prevalence is 1 in 2600 with a slight male predominance.⁴⁶ They are commonly single and sporadic, although a familial form with multiple lesions in similar body sites has been reported.⁴⁷

Differential diagnosis includes solitary mastocytoma, connective tissue nevus (CTN), congenital melanocytic nevus, and Becker nevus. Biopsy reveals smooth muscle fibers and CD34 positivity. Although surgical excision is curative, it is rarely necessary, as these lesions are benign, remain asymptomatic, are rarely of cosmetic significance, and often become less prominent over time. Extensive diffuse SMHs have been described as part of the extremely rare “Michelin tire baby” phenotype, a disorder associated with numerous transverse skin folds on the limbs, mental retardation, and seizures, among other extracutaneous defects thought to result from abnormal elastic fiber formation.⁴⁸

Fibrous Hamartoma of Infancy

This is a rare, benign soft tissue tumor that usually arises as a solitary 2- to 5-cm, asymptomatic, flesh-colored subcutaneous nodule or nodular plaque on the axillae, shoulders, or upper chest. On palpation there may be a lumpy texture. This lesion most often appears by 2 years of age, with 25% arising at birth and 90% by 1 year of age, and the incidence is higher in males. Growth is generally slow, although rarely a rapid

increase in size has been reported. Biopsy reveals a characteristic histologic triad of adipose, fibrous, and myxoid mesenchymal tissue. Treatment of choice is complete surgical excision if possible, and the recurrence rate is less than 15%. Recurrence is common, however, with incomplete removal. If the lesion is left untreated, its growth usually stops by 5 years of age, although there is no tendency toward spontaneous resolution.

Lipomas

Lipomas represent a very common benign tumor consisting of mature adipose cells. They most commonly arise around puberty as solitary or multiple lesions and localize preferentially to the subcutaneous tissues of the neck, shoulders, back, and abdomen. They are soft or rubbery on palpation but usually remain asymptomatic. Surgical excision is curative. A subtype of lipoma is the nevus lipomatosus superficialis, which typically arises at birth as an asymptomatic cerebriform cluster of soft, fleshy, yellowish papules or nodules on the buttocks or thighs. This lesion may rarely occur as a giant variant that poses a cosmetic and surgical challenge. If the lesion is tender or painful, the differential diagnosis should include angiolipoma, which is clinically indistinguishable but tends to occur more commonly in teenagers and young adults. Multiple lipomas may rarely be the cutaneous stigmata of patients with syndromic disease such as the Bannayan-Riley-Ruvalcaba syndrome, encephalocraniocutaneous lipomatosis and the Michelin tire baby. All of these syndromes include multiple other cutaneous and noncutaneous features and neurological symptoms that should alert to this rare association.

MALIGNANCY

Cutaneous lesions may be the clinical presenting sign of a primary or secondary malignancy (Fig. 13) with:

Rhabdomyosarcoma (Fig. 14)
 Infantile fibrosarcoma
 Cutaneous neuroblastoma
 Dermatofibrosarcoma protuberans
 Langerhans cell histiocytosis
 Infantile myofibromatosis (Fig. 15)

Rhabdomyosarcoma

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in childhood and infancy^{49,50} and appears as a flesh-colored to erythematous firm papule, plaque, or cyst. Growth ranges from indolent, with minimal signs and symptoms, to a rapidly enlarging swelling. Vascularity may be prominent. Approximately 350 new cases of childhood RMS are diagnosed each year in the United States.⁵¹ Incidence is greatest between 1 and 4 years of age,⁴⁹ and the median age at diagnosis is 5 years.⁵² Despite the fact that it is the most common malignant cutaneous sarcoma, it is actually a tumor of skeletal muscle origin, with a cutaneous appearance secondary to extension from the soft tissue into the dermis.

It is most often confused with a hemangioma, both clinically and radiographically, because of vascular enhancing appearance. Any lesion that is firm on palpation or otherwise suspicious for RMS requires biopsy, even if the radiographic features support the diagnosis of hemangioma. Differential diagnosis includes other vascular malformation, cutaneous neoplasms, cysts, infections, and benign growths. Management consists of a combination of surgery, radiation, and chemotherapy,

Figure 13 Warning signs of malignancy.

Figure 14 Rhabdomyosarcoma.

based on extent of disease and the predicted sequelae of each modality of treatment. Timely diagnosis and referral are crucial and have significantly improved survival with this malignancy.^{49,51,52} Punyko et al found a 5-year survival rate of 83% in children with localized disease. Poor prognostic variables included diagnosis during infancy (age < 1 year) or adolescence (age 10 to 19 years), metastatic disease at the time of presentation, alveolar histology, and tumors of the extremities, retroperitoneum, and trunk.⁵¹

Infantile Fibrosarcoma

Fibrosarcoma (FS) is the second most common childhood sarcoma involving the skin and the most common soft tissue sarcoma in children younger than 1 year.⁵³ There are two peaks of incidence: one in infants and young children, with its own unique behavior, and another in older children, which more closely resembles the behavior of adult lesions.⁵³ In contrast to adult-type FSs, most infantile FSs are painless and rapidly growing but have a very low rate of metastases and a lower

Figure 15 Solitary myofibroma.

mortality.⁵³ Infantile FS occurs in 5 per million infants.⁵⁴ It arises as a dome-shaped mass, with an often vascular appearance and a predilection for the distal extremities. The overlying skin is tense, shiny, erythematous, and ulcerated.⁵³ Skin involvement is usually secondary to involvement of underlying deep soft tissues.

Differential diagnosis is similar to that of RMS, and it may be mistaken for a hemangioma. If suspicion of malignancy arises, biopsy should be performed for definitive diagnosis. In infantile disease, complete surgical extirpation is the treatment of choice. When complete resection is impossible, some centers are reporting encouraging results with the use of up-front chemotherapy.⁵⁴ The Italian Cooperative Group Studies found a 10-year overall survival of 78.6% for patients younger than 2 years and 51% for patients older than 2 years.⁵³

Cutaneous Neuroblastoma

Neuroblastoma is the most common malignant neoplasm occurring in the neonate and accounts for about 50% of malignancies in infants, with a median age at diagnosis of 22 months.^{55,56} It is derived from primitive neural crest cells of the sympathetic nervous system. Primary cutaneous neuroblastoma is exceedingly rare in children compared with adults. Most commonly, children with this disease present with multiple firm bluish cutaneous nodules representing metastases from a primary adrenal tumor. Classically, there is an enlarging hard abdominal mass related to tumor cell infiltration of the liver, but other dermatologic clues are "raccoon eyes," which represent periorbital ecchymoses from orbital metastases, and an "icy blanch" of cutaneous lesions secondary to local catecholamine release when stroked. Signs of advanced disease include fever, hepatomegaly, and failure to thrive.

Differential diagnosis includes other cutaneous metastases, mastocytoma, angioliipoma, adnexal tumors, blue nevus, cysts, vascular lesions, leukemia or lymphoma cutis, and the "blueberry muffin" baby following intrauterine infection. Neuroblastomas are constantly evolving and changing tumors. Biopsy should be obtained to confirm the diagnosis, but it may be non-diagnostic depending on the timing. If clinical suspicion for this tumor persists, further diagnostic evaluation should be pursued despite negative biopsy. This may include genetic analysis, immunophenotyping, abdominal ultrasonography, and serum and urine catecholamines, which are elevated in the majority of patients. Treatment options include any combination of surgery, chemotherapy, and radiation, depending on the results of a complete systemic work-up. Overall survival with stage IV disease is only 34%, but this tumor exhibits extreme variability in its behavior, and even infants with metastatic disease may still experience complete regression.^{57,58} Factors that have been found to improve

prognosis are age younger than 1 year, favorable pathology, complete tumor resection, no recurrence, and particular genetic subtype.^{57,58}

Dermatofibrosarcoma Protuberans

Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue neoplasm that is indolent, infiltrative, and highly locally destructive and often masquerades as a bumpy scar. It appears as a lumpy nodular ill-defined plaque, with a predilection for the trunk and proximal extremities. Incidence is greatest in the second to fifth decades of life, but pediatric and even congenital cases do occur.⁵⁹ This tumor is believed to have a fibroblastic and histiocytic origin and is considered a low-grade sarcoma.

Differential diagnosis includes hypertrophic scar, keloid, and other fibrous tumor, such as dermatofibroma. If a patient is referred for a suspicious scar, a history of antecedent trauma should be ascertained beyond doubt, and a biopsy should be performed if any clinical suspicion remains. Histologically, the tumor shows spindle cells in a characteristic "cartwheel" or storiform pattern and CD34 positivity. DFSP has a propensity for extensive local infiltration, beyond the assessed clinical margins, through tentacle-like projections of tumor cells. Complete removal can have devastating cosmetic consequences, but inadequate surgery often results in recurrence. Wide excision with 3-cm margins or Mohs results in the lowest recurrence rates and is therefore the standard of care.⁶⁰⁻⁶² Follow-up is recommended at 6- to 12-month intervals.⁶² Metastases from this tumor are extremely rare but have been reported.⁶³

Giant cell fibroblastoma is a rare locally aggressive DFSP variant that is seen predominantly in prepubertal children.⁶⁴ It arises most often on the trunk, as a solitary, slowly enlarging, rubbery, asymptomatic dermal nodule, fixed to the overlying skin. Biopsy is similar to that for DFSP but reveals sinusoidal spaces lined by multinucleated giant cells. Local recurrence after excision is as high as 50%, but metastases have not been reported. Treatment consists of wide surgical excision.

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH), formerly known as histiocytosis X, ranges from clinically very limited cutaneous disease to severe multisystem disease. This disorder represents infiltration of various organs by a clonal proliferation of Langerhans cells, antigen-presenting cells of the skin. Cutaneous manifestations are often the first sign of disease and may include solitary or few crusted papules on the scalp, flexural areas, palms, and soles mimicking scabies. Other cutaneous signs include a persistent scaly erythematous rash mimicking seborrheic

dermatitis, vesiculopustular lesions mimicking varicella or herpes, petechiae with or without associated thrombocytopenia, and red nodules or plaques. The most common extracutaneous site of infiltration is the bone, followed by lymph nodes, pituitary, lung, liver, and spleen. The patient may present with systemic signs of fever, anemia, thrombocytopenia, adenopathy, hepatosplenomegaly, or diabetes insipidus. Incidence is 2 to 5 in 1 million children⁶⁵ and peaks between 1 and 3 years of age.⁶⁶

Diagnosis is confirmed by biopsy, which reveals a diffuse infiltration of Langerhans cells with S100 and CD1a positivity. Electron microscopy shows Birbeck granules. Prognosis varies widely from congenital self-healing LCH, also known as Hashimoto-Pritzker disease, in which congenital skin lesions spontaneously involute over the first year of life, to severe multisystem disease with an approximate 20% fatality rate despite chemotherapy.⁶⁷

Infantile Myofibromatosis

Solitary myofibroma, a rare fibrous tumor of infancy, arises as a nontender firm rubbery well-circumscribed 0.5- to 3-cm subcutaneous or dermal nodule, usually on the head or neck. It is often telangiectatic and dusky red to purple, and ulceration of the overlying skin may occur. Sixty percent of cases present at or soon after birth and 90% within the first 2 years of life.^{68,69} The lesion is approximately twice as common in males as in females.⁶⁹ The majority are solitary, but multicentric or generalized forms are also seen, more commonly in females and in those presenting at birth.⁶⁸ If multicentric, soft tissues are also affected and multiple lytic bone lesions can be seen, potentially with pathologic fractures or spinal cord compression. With severe generalized disease, visceral organs such as the heart, lungs, central nervous system, and gastrointestinal tract may be involved, and the space-occupying effect of the lesions is associated with a high mortality.

Differential diagnosis of a solitary myofibroma includes fibrosarcoma, neuroblastoma, hemangioma, rhabdomyosarcoma, mastocytoma, leiomyoma, and other infantile fibromatoses. Biopsy is usually required to make the diagnosis. Histopathology reveals interlacing fascicles of spindle cells. Most lesions regress spontaneously with some degree of atrophy, and as long as there is no visceral involvement, prognosis is excellent. Resection should be reserved for cases involving vital structures, but if it is performed, the recurrence rate is 7 to 10%.⁶⁸⁻⁷⁰ In cases of visceral involvement, however, a mortality rate as high as 73% has been reported, usually secondary to cardiopulmonary or gastrointestinal complications.⁷⁰ If the patient has only a solitary lesion, the risk is extremely low, and no further investigation is necessary, but multiple cutaneous lesions warrant further work-up including

chest radiography, skeletal survey, and CT or MRI of the thorax and abdomen. Visceral signs or symptoms require referral for complete systemic work-up.⁶⁸⁻⁷⁰ A careful family history should be obtained, as an autosomal dominant mode of inheritance has been proposed in some familial cases, and genetic counseling would then be appropriate.⁷¹

CONCLUSION

Many factors warrant consideration prior to surgical excision of a cutaneous lesion in children to ascertain optimal outcome. Accurate clinical diagnosis of a skin lesion determines the surgical technique and timing of treatment intervention or whether prompt referral for further work-up is indicated. Onset of a skin lesion in the neonatal period, firmness, high vascularity, fixation, ulceration, large size, and fast rate of growth should raise suspicion for malignancy and direct further diagnostic clarification.

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