

Pediatric Leg Ulcers: Going Out on a Limb for the Diagnosis

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This article exhibits the most common differential diagnoses for pediatric leg ulcers and contrasts the etiologies with the adult population. The diagnoses are further categorized into hematologic, infectious, genodermatoses, and autoimmune etiologies to help the dermatologist deduce the accurate diagnosis in this unique patient population.

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Compared to the adult population with a prevalence of lower extremity ulcers reaching approximately 1% to 2%, pediatric leg ulcers are much less common and require dermatologists to think outside the box for differential diagnoses.¹ Although the most common types of lower extremity ulcers in the adult population include venous leg ulcers, arterial ulcers, and diabetic foot ulcers, the etiology for pediatric ulcers is vastly different, and thus these statistics cannot be extrapolated to this younger group. Additionally, scant research has been conducted to construct a systemic algorithm for helping these patients. In 1998, Dangoisse and Song² concluded that juvenile leg ulcers secondary to causes other than trauma are uncommon, with the infectious origin fairly frequent; however, they stated further workup should be pursued to investigate for underlying vascular, metabolic, hematologic, and immunologic disorders. They also added that an infectious etiology must be ruled out with foremost priority, and a subsequent biopsy could assist in the ultimate diagnosis.²

To further investigate pediatric leg ulcers and their unique causes, a PubMed search of articles indexed for MEDLINE published from 1995 to present was performed using the term *pediatric leg ulcers*. The search yielded approximately 100 relevant articles. The search generated more than 47 different causes of leg ulcers

and produced unusual etiologies such as trophic ulcers of Lesch-Nyhan syndrome, ulcers secondary to disabling pansclerotic morphea of childhood, dracunculiasis, and dengue hemorrhagic fever, among others.³⁻⁶ The articles were further divided into 4 categories to better characterize the causes—hematologic, infectious, genodermatoses, and autoimmune—which are reviewed here.

Hematologic Causes

Hematologic causes predominated in this juvenile arena, with sickle cell disease specifically comprising the vast majority of causes of pediatric leg ulcers.^{7,8} Sickle cell disease is a chronic disease with anemia and sickling crises contributing to a myriad of health problems. In a 13-year study following 44 patients with sickle cell disease, Silva et al⁸ found that leg ulcers affected approximately 5% of pediatric patients; however, the authors noted that this statistic may underestimate the accurate prevalence, as the ulcers typically affect older children and their study population was a younger distribution. The lesions manifest as painful, well-demarcated ulcers with surrounding hyperpigmentation mimicking venous ulcers.⁹ The ulcers may be readily diagnosed if the history is known, and it is critical to maximize care of these lesions, as they may heal at least 10 times slower than venous leg ulcers and frequently recur, with the vast majority recurring in less than 1 year. Furthermore, the presence of leg ulcers in sickle cell disease may be associated with increased hemolysis and pulmonary hypertension, demonstrating the severity of disease in these patients.¹⁰ Local wound care is the mainstay of therapy including compression, leg elevation, and adjuvant wound dressings. Systemic therapies such as hydroxyurea, zinc supplementation, pentoxifylline, and transfusion therapy may be pursued in refractory cases,

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though an ideal systemic regimen is still under exploration.^{9,10} Other major hematologic abnormalities leading to leg ulcers included additional causes of anemia, such as thalassemia and hereditary spherocytosis. These patients additionally were treated with local wound care to maximize healing.^{11,12}

Infectious Causes

Infectious causes of pediatric ulcers were much more varied with a myriad of etiologies such as ulcers from ecthyma gangrenosum caused by *Pseudomonas aeruginosa* to leishmaniasis and tularemia. The most commonly reported infection causing leg ulcers in the pediatric literature was *Mycobacterium ulcerans*, which led to the characteristic Buruli ulcer; however, this infection is likely grossly overrepresented, as more common etiologies are underreported; the geographic location for a Buruli ulcer also is important, as cases are rare in the United States.^{13,14} A Buruli ulcer presents as a well-defined, painless, chronic skin ulceration and most commonly affects children.¹⁵ Exposure to stagnant water in tropical climates is thought to play a role in the pathogenesis of this slow-growing, acid-fast bacillus. The bacteria produces a potent cytotoxin called mycolactone, which then induces tissue necrosis and ulceration, leading to the clinical manifestations of disease.¹⁵ The ulcers may heal spontaneously; however, up to 15% can be associated with osteomyelitis; treatment includes surgical excision and prolonged antibiotics.¹⁴ Given the numerous additional causes of pediatric leg ulcers harboring infections, it is critical to be cognizant of the travel history and immune status of the patient. The infectious cause of leg ulcers likely predominates, making a biopsy with culture necessary in any nonhealing wound in this population prior to pursuing further workup.

Genodermatoses

A number of genodermatoses also contribute to persistent wounds in the pediatric population; specifically, genodermatoses that predispose to neuropathies and decreased pain sensation, which affect the child's ability to detect sensation in the lower extremities, can result in inadvertent trauma leading to refractory wounds. For example, hereditary, sensory, and autonomic neuropathies are rare disorders causing progressive distal sensory loss, leading to ulcerations, osteomyelitis, arthritis, and even amputation.¹⁶ Hereditary, sensory, and autonomic neuropathies are further categorized into several different types; however, the unifying theme of diminished sensation is the culprit for troublesome wounds. Therapeutic endeavors to maximize preventative care with orthotics are vital in allaying recurrent wounds in these patients. Another uncommon hereditary disorder that promotes poor wound healing is caused by an inborn error of collagen synthesis. Prolidase deficiency is an autosomal-recessive condition resulting in characteristic facies, recurrent infections, and recalcitrant leg

ulcerations due to impaired collagen formation.¹⁷ More than 50% of affected patients experience leg ulcers comprised of irregular borders with prominent granulation tissue. Treatment is aimed at restoring collagen synthesis and optimizing wound healing with the use of topical proline, glycine, and even growth hormone to promote repair.¹⁸ Additional genodermatoses predisposing to leg ulcerations include Lesch-Nyhan syndrome due to self-mutilating behaviors and epidermolysis bullosa due to impaired barrier and a decreased ability to repair cutaneous defects.

Autoimmune Causes

Although a much smaller category, ulcers due to autoimmune etiologies were reported in the literature. Fibrosing disorders including morphea and scleroderma can cause extensive disease in severe cases. Disabling pansclerotic morphea of childhood can cause sclerosis that extends into muscle, fascia, and even bone, resulting in contractures and ulcerations.⁴ The initial areas of involvement are the arms and legs, followed by spread to the trunk and head and neck area.⁴ Immunosuppressant therapy is needed to halt disease progression. Pediatric cases of systemic lupus erythematosus also have been associated with digital ulcers. One case was thought to be due to vasculitis,¹⁹ and another resulted from peripheral gangrene in association with Raynaud phenomenon.²⁰ Albeit rare, it is important to consider autoimmune connective tissue diseases when faced with recurrent wounds and to search for additional symptoms that might yield the underlying diagnosis.

Conclusion

Pediatric leg ulcers are a relatively uncommon phenomenon; however, the etiologies are vastly different than adult leg ulcers and require careful contemplation surrounding the cardinal etiology. The main categories of disease in pediatric leg ulcers after trauma include hematologic abnormalities, infection, genodermatoses, and autoimmune diseases. The evaluation requires obtaining a thorough history and physical examination, including pertinent family histories for associated inheritable disorders. If the clinical picture remains elusive and the ulceration fails conservative management, a biopsy with tissue culture may be necessary to rule out an infectious etiology.

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