Lipoatrophic Panniculitis

Case Report and Review of the Literature

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Background: Lipoatrophic panniculitis (LP) is a rare disease of childhood characterized by eruption of tender erythematous nodules and plaques followed by circumferential bands of lipoatrophy often seen on the arms and legs. This condition has also been known as lipophagic panniculitis of childhood, annular atrophy of the ankles, and partial lipodystrophy.

Observations: A previously healthy 8-year-old boy was evaluated for tender, raised plaques on the ankles, which progressed to circumferential atrophy of the distal lower extremities. Biopsy specimen analysis revealed a dense mixed infiltrate extending into the subcutaneous tissue as well as lipophages within the fatty lobules. A diagnosis of LP was made, and the patient began treatment with prednisone and hydroxychloroquine. Methotrexate was added later to the regimen as a steroid-sparing agent, and the dose was increased over the course of 3 months, by which time the cutaneous disease progression was nearly halted. However, the patient continued to have lower leg pain with bone changes demonstrated on magnetic resonance imaging.

Conclusions: We report this case and review of the literature to call attention to the clinical features of LP and its association with skeletal changes. Our patient's response to combination therapy is of interest and contributes to the limited literature about management of this disease.

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Lipoatrophy refers to the loss of subcutaneous fat and may be classified as generalized, partial, or localized. Lipoatrophic panniculitis (LP) is a form of localized lipoatrophy that typically presents on the extremities with tender erythematous nodules and plaques that enlarge radially and leave residual circumferential bands of lipoatrophy. Clinically, it may resemble many conditions, including granuloma annulare, morphea, erythema nodosum, foreign body granulomatous reaction, deep erythema annulare centrifugum, tumid lupus, erythema migrans, cellulitis, and urticarial vasculitis. However, it can be differentiated from other disorders via characteristic histologic features of lipophagic panniculitis and absence of vasculitis. Reported treatments include prednisone, antimalarial agents, saturated solution of potassium iodide, dapsone, and azathioprine, each with different efficacy profiles. We report herein a case of an 8-year-old boy with progressive LP who responded well to a combination of prednisone, hydroxychloroquine, and methotrexate.

A previously healthy 8-year-old boy developed tender, raised plaques on the lateral aspects of his ankles and had been given the diagnosis of granuloma annulare initially. Over the course of 6 months, the lesions progressed circumferentially around the ankles and spread to the calves with edema, thickening, tenderness of the skin, and increased atrophy and inflammation (Figure 1). He remained afebrile during the 6 months, complaining of moderate pain, especially near the advancing borders. The findings from a complete review of systems were otherwise negative. His family history was significant for Crohn disease. There was no adenopathy noted on examination, and the patient had normal range of motion.

Two biopsy specimens were obtained from the right medial calf and dorsal aspect of the right foot. Histopathologic analysis revealed a dense inflammatory infiltrate composed primarily of large histiocytes, multinucleated giant cells, and small collections of neutrophils infiltrating the lower reticular dermis and extend-
ing into the subcutaneous fat (Figure 2). No vasculitis or polarizable foreign body was identified. Numerous lipophages were evident in the fatty lobules. Periodic acid–Schiff, Gomori methenamine silver, acid-fast bacilli, and Warthin-Starry stainings revealed no microorganisms.

Given the patient’s family history of Crohn disease, a workup consisting of abdominal and pelvic computed tomography, upper and lower endoscopy, and biopsies were performed, and all findings were within normal limits. Laboratory results were also within normal limits, with the exceptions of a repeatedly elevated erythrocyte sedimentation rate (ESR) (up to 51 mm/h), mild normocytic anemia, and an elevated platelet count (592 × 10^9/L). (To convert platelets to number/L, multiply by 1.0.) Assay results were also normal for quantitative immunoglobulins (IgA, IgG, and IgM), circulating anti-neutrophil cytoplasmic antibody, peripheral antineutrophil cytoplasmic antibody, anti–Saccharomyces cerevisiae antibody, antinuclear antibody, alpha 1-antitrypsin phenotype, primary immunodeficiency, Lyme disease, and human immunodeficiency virus (HIV) antibody.

Nine months into the course of his symptoms, the patient was referred to our institution, where it was noted that the disease process had skipped to other areas of his body, including new involvement of both wrists and the left buttck and left posterior thigh. These new lesions were accompanied by pain, tenderness, and redness. The patient had a weight of 25.4 kg, height of 1.283 m, and body mass index of 15.4 (calculated as weight in kilograms divided by height in meters squared), which represents approximately the 50th percentile for each characteristic. Findings from the rest of his skin examination were within nor-
mal limits. There were no clinical signs of insulin resistance, such as acanthosis nigricans. He underwent further laboratory evaluations, including complete blood cell counts, a complete metabolic panel, and assays of pancreatic enzymes, thyroid function, tissue transglutaminase antibody, anti-microsomal antibody, C-reactive protein, and ESR. All laboratory test results were within normal limits except the ESR, which was elevated to 30 mm/h.

Based on the clinical features and classic histologic finding of lipophages within the fatty lobules, the diagnosis of LP was made. The patient began treatment with prednisone (20 mg/d, approximately 1 mg/kg) and hydroxychloroquine (100 mg/d) and showed a rapid initial response of decreased edema and erythema. However, his disease relapsed when the prednisone dose was tapered to 10 mg/d, resulting in increased tenderness and erythema. Ten months into the illness, methotrexate was added to the treatment regimen as a steroid-sparing agent, given as 15-mg intramuscular weekly injections, then gradually increased to 25 mg weekly over the course of

Figure 3. Clinical arrest of panniculitis after 3 months of therapy. A-D, There remains circumferential lipoatrophy of ankles and lower calves as well as isolated areas of lipoatrophy on the posterior left thigh and left buttock.
3 months. The prednisone dose was gradually tapered over the course of the next 6 months. His ESR decreased to 2 mm/h, with clinical cessation of the progression of his panniculitis but with focal areas of atrophy remaining (Figure 3).

Despite the improvement of his skin lesions, the patient continued to have pain localized to his lower legs. Magnetic resonance imaging of the calves revealed increased T2-weighted signal from the subcortical and cortical bone within the mid shaft of both tibiae, most consistent with a stress reaction. However, no definite fracture was identified. A bone mineral density measurement showed normal status for chronologic age. At last follow-up, the patient had cessation of lipoatrophy maintained for 12 months and continued to respond well to methotrexate therapy.

Progressive LP is also known as lipophagic panniculitis of childhood, annular atrophy of the ankles, and partial lipodystrophy. It has a distinctive clinical presentation and histologic findings but usually lacks systemic findings. Clinically, there are eruptions of erythematous nodules and plaques followed by a striking circumferential band of lipoatrophy, principally of the arms and legs. Associated laboratory findings include elevated ESR, thrombocytosis, and microcytic anemia. The end-stage atrophic phase of disease is chronic, but this condition is otherwise self-limited and not fatal. Differential diagnoses include “noninflammatory” lipoatrophy and inflammatory lipoatrophy or lipodystrophy. Dunnigan-

<table>
<thead>
<tr>
<th>Source</th>
<th>Cases, No./Sex/Age, y</th>
<th>Affected Areas</th>
<th>Associated Diagnoses</th>
<th>Treatment; Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winkelmann et al²</td>
<td>12/F and 5/M Age range, &lt;1 to 11³</td>
<td>Legs (n = 14), feet (n = 2), thighs (n = 10), arms (n = 9), trunk (n = 5), face (n = 4)</td>
<td>NR</td>
<td>Observation (n = 6); remission in 1 of 6</td>
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<td></td>
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<td>Prednisone (n = 8); remission in 8 of 8</td>
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<td>Chloroquine (n = 1); remission in 1 of 1</td>
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<td></td>
<td></td>
<td></td>
<td>Prednisone and chloroquine (n = 2); remission in 0 of 2</td>
</tr>
<tr>
<td>Martinez et al⁷</td>
<td>1/F/3</td>
<td>Arms, legs, buttocks</td>
<td>Chromosome 10q26 abnormality</td>
<td>Prednisone and azathioprine; good response (complication, avascular necrosis of bilateral femoral heads)</td>
</tr>
<tr>
<td>Billings et al⁵</td>
<td>1/M/3 1/F/6</td>
<td>Arms, legs, arms, legs</td>
<td>Rheumatoid arthritis Type 1 DM, Hashimoto thyroiditis</td>
<td>Prednisone; complete response</td>
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<tr>
<td></td>
<td>1/M/9</td>
<td>Legs</td>
<td>Type 1 DM</td>
<td>Potassium iodide solution; no response</td>
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<tr>
<td>Roth et al³</td>
<td>1/F/4</td>
<td>Ankles, thighs, knees</td>
<td>NR</td>
<td>Combined prednisone and dapsone; halted disease progression</td>
</tr>
<tr>
<td>Madasserri et al⁴</td>
<td>1/F/4½</td>
<td>Ankles, calves</td>
<td>NR</td>
<td>Combined prednisone and dapsone; halted disease progression</td>
</tr>
<tr>
<td>Dimson and Esterly⁶</td>
<td>1/F/6</td>
<td>Ankles, calves</td>
<td>Graves disease, alopecia areata</td>
<td>Observation; atrophy remained localized and stable</td>
</tr>
<tr>
<td>Shelley and Izumi⁹</td>
<td>1/F/6</td>
<td>Ankles</td>
<td>NR</td>
<td>Corticosteroid cream under occlusion and cold quartz light; skin appeared normal, and atrophic bands remained unchanged</td>
</tr>
<tr>
<td>Falcini et al¹⁰</td>
<td>1/F/8</td>
<td>Legs</td>
<td>NR</td>
<td>Prednisone; complete response</td>
</tr>
<tr>
<td>Melchiorre et al⁶</td>
<td>1/F/12</td>
<td>Calves</td>
<td>NR</td>
<td>Prednisone and pentoxifylline for 3 mo; good response</td>
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<tr>
<td>Handfield-Jones et al¹²</td>
<td>1/F/24</td>
<td>Cheeks, upper outer arms, buttocks, thighs</td>
<td>Raynaud phenomenon</td>
<td>Hydroxychloroquine (400 mg/d) and prednisolone (30 mg/d); suppressed active lesions, but lesions reappeared on tapering of prednisolone dose to &lt;20 mg/d</td>
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<td>1/F/32</td>
<td>Face, trunk, proximal extremities</td>
<td>NR</td>
<td>Dapsone, azathioprine, and antimalarial agents; unsuccessful</td>
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<td>Nelson¹²</td>
<td>1/F/36</td>
<td>Ankles, calves</td>
<td>NR</td>
<td>Corticosteroids; effective (complication, avascular necrosis of femoral head)</td>
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<td>Umbert and Winkelmann¹¹</td>
<td>1/F/47</td>
<td>Buttocks, thigh, arm</td>
<td>NR</td>
<td>Hydroxychloroquine; remission</td>
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<td>1/F/57</td>
<td>Trunk, legs, arms, breasts</td>
<td>NR</td>
<td>Observation; no new lesions after 2 y</td>
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</table>

Abbreviations: DM, diabetes mellitus; NR, not reported.

³Age reported as range only for entire study population; youngest patient was aged 0.67 years.
type familial partial lipodystrophy type 2 and juvenile dermatomyositis are examples of conditions mimicking LP in addition to the inflammatory conditions listed herein. Lipoatrophic panniculitis is distinct from these entities in that there are no other systemic disease processes present. Histologically, a characteristic feature of lobular panniculitis with histiocyte and lipophage replacement of the fat is seen. There is notable absence of vasculitis or phlebitis.

Very few pediatric cases of LP have been documented to date (Table). Although the cause is unknown, an association with autoimmune conditions has been proposed. Billings et al have described 3 patients with LP in addition to autoimmune diseases such as diabetes mellitus type 1, Hashimoto thyroiditis, and juvenile rheumatoid arthritis. Dimson and Esterly also reported the case of a 6-year-old girl with a history of Graves disease and alopecia areata who subsequently developed annular lipoatrophy of the ankles. It has also been proposed that a genetic link may exist, as evidenced by a chromosome 10q26 abnormality in a 3-year-old girl with a 12-month history of rapidly progressing acquired lipoatrophy.

Lipoatrophic panniculitis may also have associated joint and skeletal findings. Shelley and Izuumi first reported radiographic changes in a 6-year-old girl with annular atrophy of the ankles: radiography revealed increased growth lines in the underlying tibiae (representing bone regrowth after temporary cessation of longitudinal growth) but no bone cysts. Melchiorre et al reported the case of a 12-year-old girl with lipophagic panniculitis with painful bilateral ankle synovitis and erythema along the peroneal tendons. Radiography did not reveal any bony abnormalities, but magnetic resonance imaging showed extensive edema of the distal lower extremities, including the joint, subcutaneous tissue, and sheath of the posterior tibialis tendon. Similar arthritis symptoms have also been reported in an adult case by Umbert et al, which included painful joint swelling in addition to tender subcutaneous nodules.

While LP is quite rare and more commonly seen in children, it has also been reported in adults (Table). Nelson reported the case of a 36-year-old woman with edema and erythema of both legs that was originally attributed to deep venous thromboses, but her disease eventually progressed to annular atrophy around both ankles extending to the mid calf. Handfield-Jones et al reported 2 cases of chronic LP that showed some response to full doses of antimalarial agents, allowing subsequent repair of the defects with plastic surgery.

Lipoatrophic panniculitis is a diagnosis of exclusion that requires evaluating the patient for infection (with, eg, fungus, acid-fast bacilli, spirochetes), autoimmune conditions, other causes of panniculitis (eg, pancreatic disease, alpha-1-antitrypsin deficiency), hepatitis or liver failure, vasculitis, immunodeficiency, local trauma or foreign body, and HIV. Treatment options include prednisone, antimalarial agents, saturated solution of potassium iodide, and dapsone, all of which have varying degrees of efficacy. Our patient responded well to a combination of prednisone, hydroxychloroquine, and methotrexate. We present our case to contribute to the growing body of literature on this relatively uncommon entity and to call attention to potential associated skeletal problems. Further studies are needed to determine the efficacy of various treatment options for this progressive disease.

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Author Contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the case report.

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REFERENCES