Lupus erythematosus panniculitis in a 10-year-old female child with severe systemic lupus erythematosus

A case report

Ruolin Zhang, PhD, Xiqiang Dang, MD, PhD, Lanjun Shuai, MD, PhD*, Qingnan He, MD, PhD, Xiaojie He, MD, PhD, Zhuwen Yi, MD, PhD

Abstract

Rationale: Lupus erythematosus panniculitis (LEP) is a rare subset of lupus erythematosus. The incidence of LEP in systemic lupus erythematosus (SLE) ranges from 2% to 5%. In the previous literature, most LEP patients were women aged from 20 to 60 years, while pediatric cases were rare, all of whom appeared on their own without SLE. A rare LEP in a 10-year-old female child with severe SLE is presented.

Patient concerns: A 10-year-old girl was admitted to our hospital for marasmus and fatigue without other typical manifestations of SLE well before the appearance of skin lesions. The only proof to support the SLE is that we observed a weakly positive antinuclear antibody (ANA) in serum at the onset.

Diagnoses: A 10-year-old girl diagnosed to the Division of Nephrology, Department of Pediatrics, the Second Xiangya Hospital, Central South University, for LEP with severe SLE.

Interventions: The patient was administered with high-dose corticosteroids and cyclophosphamide.

Outcome: The patient died of severe lung involvement despite the use of high-dose corticosteroids and cyclophosphamide.

Lessons: This report highlights an unusual manifestation of LEP associated with SLE in a child. It also suggests that pediatricians should be aware of occult onset of SLE, such as unclear marasmus and fatigue found in this case. Repeat tests of antinuclear antibody and anti-double strand DNA antibody (anti-dsDNA) as well as renal biopsy in a timely manner will be effective to achieve early recognition and immediate treatment for saving lives.

Abbreviations: ALT = alanine aminotransferase, ANA = antinuclear antibody, anti-dsDNA = anti-double strand DNA antibody, AST = aspartate aminotransferase, DLE = discoid lupus erythematosus, ESR = erythrocyte sedimentation rate, LEP = lupus erythematosus panniculitis, SLE = systemic lupus erythematosus.

Keywords: fatigue, lupus erythematosus panniculitis, marasmus, renal biopsy, systemic lupus erythematosus

1. Introduction

Lupus erythematosus panniculitis (LEP) with systemic lupus erythematosus (SLE) in a 10-year-old female child is an extremely rare presentation. LEP manifests as recurrent nodules or plaques involving subcutaneous tissues. It is viewed as a variant of lupus erythematosus, which may be a single manifestation or appear with discoid lupus erythematosus (DLE) or SLE.[1,2] In the described series, most of the patients were adults in the age group of 20 to 60 years. LEP is rare in children, especially when it is associated with SLE.[1,2] We report here a case of LEP in a female child with atypical severe SLE.

2. Case presentation

A 10-year-old female child was referred to our department for marasmus and fatigue for approximately 1 year and painful rash on her limbs for nearly 2 weeks. Unclear marasmus and fatigue appeared 1 year previously and became progressively aggravated. Half a year ago, she went to the local hospital, where she had a systemic medical examination. Her alanine aminotransferase (ALT) level was 234.4 U/L, aspartate aminotransferase (AST) level was 485.3 U/L, erythrocyte sedimentation rate (ESR) was 51 mm/hour, the titer of antinuclear antibody (ANA) was 1:80, and anti-double strand DNA antibody (anti-dsDNA) was negative. There was no evidence of infection of hepatic virus or tubercle
bacillus, and no tumors. The diagnosis was not clear, and therapy for liver protection was given, but this was not effective. Two weeks before she went to our hospital, some tender plaques and subcutaneous nodules appeared on her limbs, which were mostly around the joints, part of which were ulcerative. She also suffered from intermittent fever, cough, sputum, alopecia, and oral ulcers in the past year. However, malar rash, arthralgia, or photosensitivity did not appear in the patient. There was no family history of autoimmune disorders.

On admission, physical examination revealed that the patient was extremely thin with the following findings: temperature, 38.6°C; heart rate, 112 beats per minute; respiratory rate, 28 breaths per minute; blood pressure, 90/60 mm Hg; and body weight, 21 kg. Her hair was thin on the top of her head. Multiple tender red plaques were found on her arms, buttocks, and left lateral ankle joint, part of which had already had ulcerations (Fig. 1). She had canker sores sized approximately 0.4 cm × 0.4 cm on her tongue. Bilateral lungs showed some moist rales on auscultation. The liver was enlarged 5 cm below the costal margin, while the spleen could not be palpated on the abdomen.

Laboratory studies showed a white blood cell count of 19,500/μL, granulocyte proportion of 85.9%, lymphocyte proportion of 4.6%, a hemoglobin level of 8.3 g/dL, mean corpuscular volume of 94.0 fl, platelet count of 231,000/μL, a reticulocyte count of 8300/μL, and its proportion was 8.0%. The erythrocyte sedimentation rate and C-reactive protein level were greatly elevated by >140 mm/hour and 21.8 mg/L, respectively. A liver function test revealed a slight elevation in total serum bilirubin level (25.9 μmol/L), a low albumin level (21.5 g/L), and an elevated globulin level (43.4 g/L). Results of urinalysis, electrolytes, renal function, and bone marrow cytology were all within the normal range. Tests for syphilis and anticardiolipin antibody were negative; but anti-β2 glycoprotein 1 antibody was beyond the restrictive range. Results of tests for ANA were positive (1:40) but negative for anti-dsDNA. C3 and C4 levels were lower than normal, and the IgG level was 26.2 g/L (normal range: 7.00–16.00 g/L). A chest radiograph disclosed bilateral lungs with multiple exudation and cavity. A high-resolution computed-tomography scan of the lung showed diffuse bilateral interstitial lesions. An ultrasound scan of the abdomen revealed an enlarged liver.

Histological examination of a skin lesion revealed dense inflammatory cell infiltration within the dermis and subcutaneous fat tissue. The infiltrate included lymphocytes, histiocytes, and some neutrophil granulocytes. In addition, hyaline necrosis of fat lobules and thickening of blood vessel walls were also observed (Fig. 2). Since SLE appeared to be the most likely diagnosis, and a percutaneous renal biopsy was finally taken in spite of no abnormalities of urinalysis and renal function. A light micrograph showed that most glomeruli had segmental endocapillary hypercellularity, mesangial hypercellularity, and mesangial matrix proliferation with deposits, partial atrophy of the tubules, mild interstitial fibrosis, and inflammation (Fig. 3). A direct immunofluorescence study revealed glomerular deposits of immunoglobulin G, immunoglobulin M, immunoglobulin A, C3, and C1q (Fig. 3). Electron microscopy showed diffuse thickening of the glomerular basal membrane, and granular subepithelial electron dense deposits with concomitant mesangial electron dense deposits. All of the above renal pathological changes indicated lupus nephritis. Repeat tests of ANA (1:80–1:160) and anti-dsDNA gradually became positive.

Finally, we diagnosed the patient as having SLE, LEP, lupus pneumonia, and lupus nephritis. Because the patient was in a critical condition, high-dose methylprednisolone (25 mg/kg) combined with cyclophosphamide (10 mg/kg) intravenous pulse therapy were given. Her fever resolved and skin lesions gradually ameliorated. A repeat chest radiograph 20 days later showed slight regression of the exudation. Unfortunately, on hospital day 28, cough and dyspnea were aggravated in the patient, and a chest radiograph revealed more severe exudation. Since the intense antibiotic and breath support therapy were ineffective, the patient died at hospital on day 32.

3. Discussion

LEP is a rare subset of lupus erythematosus, which was first described by Kaposi in 1883 and was termed “lupus erythematosus panniculitis” by Irgang in 1940. It may occur on its...
own or be associated with DLE or SLE. However, the incidence of LEP in SLE patients is only 2% to 5%, which confers a less severe disease course. Most LEP patients were women aged from 20 to 60 years, while pediatric cases were rare, all of whom appeared on their own without SLE.

Clinically, a typical lesion of LEP presents as recurrent subcutaneous nodules or plaques, sometimes ulcerated and they often heal with scarring and lipoatrophy. The most common involved sites are the upper outer arms, shoulders, buttocks, trunk, face, and scalp. The legs are rarely involved. Histologically, lobular lymphocytic panniculitis and hyaline fat necrosis are characteristic findings. Other features include calcification, lymphocytic vasculitis in fat lobules, and mucin deposition can also be found. The diagnosis can be made by characteristic pathological findings alone, while excluding other types of panniculitis, deep morphea, and subcutaneous panniculitis-like T-cell lymphoma. A typical clinical course can also be helpful for providing the correct diagnosis.

However, in our patient, the clinical manifestations were not the same as those mentioned above. First, subcutaneous nodules and plaques appeared for the first time, and therefore, scarring and lipoatrophy were not found. Second, her involved sites were around the joints of the forearms and lower legs, which are different from the usual sites. Finally, and most importantly, unclear marasmus and dysfunction of multiple systems (respiratory system: cough, sputum, change in imaging studies; digestive system: enlarged liver, elevation of ALT, AST, and serum bilirubin levels; hematological system: anemia) had already been present for a long time before the appearance of skin lesions. Therefore, the diagnosis was a challenge.

Since manifestations in the patient were characterized by an initial presentation of gradually aggravated marasmus, and then multiple systems injury, we had reason to suspect the diagnosis of a malignant tumor or connective tissue disease. Since an imaging study and bone marrow cytology investigation did not indicate a malignant tumor, a subcutaneous nodular biopsy was then performed, which led to the identification of LEP. As previously described, LEP may appear as an isolated phenomenon or in association with SLE or DLE. Apart from the skin lesions, there were abnormalities of multiple organs and a
weakly positive ANA in our patient, all of which suggested SLE. According to the American College of Rheumatology (ACR) revised criteria for SLE dating from 1982 with a 1997 revision,[7,8] our patient only had oral ulcers, hemolytic anemia, and a weakly positive ANA; the diagnosis was not straightforward as the manifestations did not satisfy 4 of the 11 diagnostic criteria. A percutaneous renal biopsy was then performed, despite no abnormalities of urinalysis and renal function, because renal involvement is the most frequent finding in pediatric SLE and renal pathological findings may not always correlate with clinical manifestations.[9] Interestingly, the renal pathological findings indicated lupus nephritis. SLE was then able to be diagnosed. Positive repeat tests of ANA (1:80–1:160) and anti-dsDNA were also in accordance with the diagnosis. Therefore, finding in our case that it is necessary to monitor ANA and anti-dsDNA for patients suspected of having of SLE, as well as performing a renal biopsy. It is noteworthy that our case confirms that the ACR classification criteria for SLE are not validated until a renal biopsy is taken.[10] A new revision by the Systemic Lupus International Collaborating Clinic (SLICC) group appears to be more applicable for our patient, since our case had oral ulcers, nonscarring alopecia, hemolytic anemia, ANA above the normal laboratory range, low complement and positive anti-β2 glycoprotein 1 antibody, that it, ≥4 criteria according to the SLICC, which are sufficient for the diagnosis of SLE, even if the renal pathology is unknown.[10] However, the SLICC revision also recommends that a patient can be classified as having SLE if the patient has biopsy-proven lupus nephritis with ANA or anti-dsDNA. Therefore, a renal biopsy is equally important in the diagnosis of SLE.

SLE is a chronic systemic disease, which can involve multiple organs. Children usually have a more severe disease at onset, and a more aggressive clinical course than adults.[11,12] Our case initially manifested as marasmus and fatigue without other typical presentations. Her condition then became rapidly aggravated and finally died of severe lung involvement. This may have been pulmonary hemorrhage, which at least 2 roentgenologists considered from a chest radiograph as the classic triad of hemoptysis, an abrupt fall in hemoglobin and new pulmonary infiltrates is not uniformly seen in all cases.[13,14] Therefore, pediatricians should be aware of unclear marasmus and fatigue; SLE should be suspected while excluding malignancy, particularly in children of school age. Early recognition and immediate treatment are the most effective way to save lives. Interestingly, in our case, LEP associated with SLE did not confer a less severe disease course in all cases.

4. Conclusions

Our report highlights an unusual manifestation of LEP associated with SLE in a child. Our results suggest that pediatricians should be aware of unclear marasmus and fatigue in children, because it can be the first and only obvious manifestation in childhood-onset SLE. The monitoring of ANA and anti-dsDNA and a renal biopsy as soon as possible are effective to obtain early recognition and immediate treatment, which could save patients’ lives.

References

[1] Fraga J, García-Diez A. Lupus erythematosus panniculitis. Dermatol Clin 2008;26:453–63.
[2] Ng PP, Tan SH, Tan T. Lupus erythematosus panniculitis: a clinicopathologic study. Int J Dermatol 2002;41:488–90.
[3] Martens PB, Moder KG, Ahmed I. Lupus panniculitis: clinical perspectives from a case series. J Rheumatol 1999;26:68–72.
[4] Bacani A, Uzun S, Ciftcioglu MA, et al. A case of lupus erythematosus profundus with unusual manifestations. Lupus 2003;14:403–5.
[5] Sanchez NP, Peters MS, Winkelmann RK. The histopathology of lupus erythematosus panniculitis. J Am Acad Dermatol 1985;13:673–80.
[6] Wu CY, Chiang CP. Clinicopathologic challenge: multiple tender lesions on both upper extremities and the back. Int J Dermatol 2010;49:380–1.
[7] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.
[8] Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7.
[9] Rakkaloulu A, Lupus nephropathy in children. Nephrol Dial Transplant 2001;16(suppl 6):126–8.
[10] Petri M. SLICC revision of the ACR classification criteria for SLE. Arthritis Rheum 2009;60(suppl 10):895.
[11] Tucker LB. Making the diagnosis of systemic lupus erythematosus in children and adolescents. Lupus 2007;16:546–9.
[12] Jimenez S, Cervera R, Font J, et al. The epidemiology of systemic lupus erythematosus. Clin Rev Allergy Immunol 2003;25:3–12.
[13] Çiftçi E, Yakinçayla F, Ince E, et al. Pulmonary involvement in childhood-onset systemic lupus erythematosus: a report of five cases. Rheumatology (Oxford) 2004;43:587–91.
[14] Stichweh D, Arce E, Pascual V. Update on pediatric systemic lupus erythematosus. Curr Opin Rheumatol 2004;16:577–87.