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Panniculitis in an 11-year-old girl – symptom of cat scratch disease or systemic lupus erythematosus onset?

Zapalenie tkanki podskórnej u 11-letniej dziewczynki – choroba kociego pazura, a może początek tocznia rumieniowatego układowego?

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Key words: systemic lupus erythematosus, panniculitis, cat scratch disease.

Słowa kluczowe: toczeń rumieniowaty układowy, zapalenie tkanki podskórnej, choroba kociego pazura.

Summary

Panniculitis is defined as an inflammation of the subcutaneous tissue of varying aetiology. It may appear in many systemic diseases, and often occurs in patients suffering from systemic inflammatory connective tissue diseases. It is observed mainly in the course of lupus erythematosus discoides (2–3% of patients), but it may be an early symptom of developing the systemic form of lupus erythematosus. In this paper we present a case of a patient with a severe course of panniculitis manifested as a painful, tough and warm skin lesion on the side of the thigh. It was accompanied by systemic symptoms, such as hectic fever, splenomegaly, and lymphadenopathy. In addition, tuberculosis, Lyme disease, salmonellosis and cat scratch disease antibodies were found positive. Despite aggressive antibiotic and anti-inflammatory therapy, there were no satisfactory results. Steroid therapy was attempted (pulses, followed by oral doses of methylprednisolone), which resulted in an effective clinical outcome.

Streszczenie

Panniculitis, czyli zapalenie tkanki podskórnej, obejmuje zmiany zapalne tkanki podskórnej o różnej etiologii. Może towarzyszyć wielu schorzeniom ogólnoustrojowym, pojawia się często u pacjentów z układowymi zapalnymi chorobami tkanki łącznej. Najczęściej obserwuje się je w przebiegu tocznia rumieniowatego krążkowego (2–3% pacjentów), rzadziej w postaci układowej tocznia. Zapalenie tkanki podskórnej może być jednak pierwszym objawem poprzedzającym rozwój choroby. W pracy przedstawiono przypadek pacjentki z ciężkim przebiegiem zapalenia tkanki podskórnej. U chorej obserwowano bolesną, zlokalizowaną na bocznej powierzchni uda zmianę skórną. Występowały uogólnione objawy, takie jak hektyczna gorączka, splenomegalia, limfadenopatia. Dodatkowo w badaniach laboratoryjnych stwierdzono dodatnie miano przeciwciał diagnostycznych dla wielu chorób infekcyjnych, w tym choroby kociego pazura. Pomimo agresywnej antybiotykoterapii oraz terapii przeciwzapalnej nie obserwowano zadowalających efektów. Z uwagi na całość obrazu oraz dodatni wywiad rodzinny w kierunku tocznia rumieniowatego podjęto próbę steroidoterapii, co przyniosło efekt kliniczny.

Introduction

Panniculitis, or inflammation of the subcutaneous tissue, encompasses inflammatory changes in subcutaneous tissue of various aetiology. Irrespectively of the underlying cause, the condition presents as characteristic skin lesions – red or purplish nodules located mainly on the lower extremities. Some of these lesions may ulcerate, leaving residual scarring or brownish discolouration [1, 2]. Possible initiating causes include mechanical trauma, chemical injury, increased pancreatic enzyme activity, and infections. Subcutaneous tissue inflammation may be observed in a large number of systemic diseases; it is often present in patients with systemic inflammatory connective tissue disorders. Panniculitis is most often observed in the course of lupus erythematosus discoides (in approx. 2–3% of patients) and less often in the systemic form of lupus. However, it may also be the first sign of

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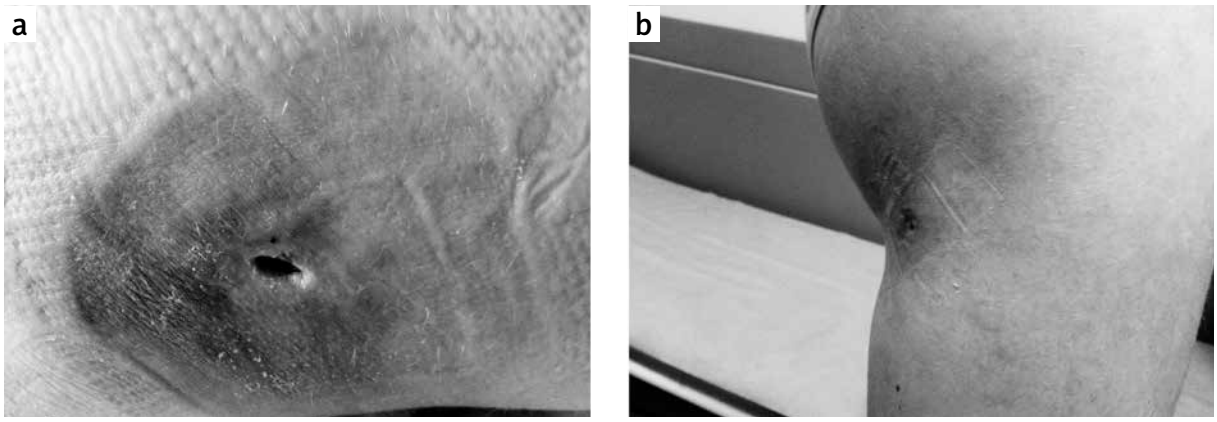

Fig. 1. Skin lesion on the side of the thigh (a) before treatment and (b) after steroid treatment.

a developing systemic disorder, often preceding onset of the disease by a period of several years [3].

Case study

An 11-year-old girl was referred to the Department of Paediatric Cardiology and Rheumatology of the Medical University of Lodz with suspicion of systemic inflammatory connective tissue disease. According to her medical history, the child had developed a painful skin lesion on the lateral side of her right thigh three months after the trauma (a fall from a bicycle). Due to conjecture of an inflammatory process and also worsening of the symptoms (lesion increased in size), antibiotic treatment was induced. There was no therapeutic effect. The patient was referred to the Department of Paediatric Surgery for further treatment.

Basic laboratory investigations revealed progressively worsening leukopenia with neutropenia; inflammatory parameters were in normal range. This raised the suspicion of an abscess and the decision was taken to incise the lesion; only serous fluid was obtained. Since that time, the patient has had hectic fever with significant enlargement of the inguinal lymph nodes on the same side as the lesion. In addition, ultrasonography revealed evidence of thrombosis in the right saphenous vein. Antibiotic therapy (metronidazole, a third-generation cephalosporin, clindamycin) was given without any clinical improvement. The clinical features and positive family history for autoimmune disorders (the patient's grandmother has a cutaneous form of lupus erythematosus) raised the suspicion of possible systemic lupus erythematosus associated with antiphospholipid syndrome and the patient was referred to the Department of Paediatric Cardiology and Rheumatology. In addition to a tender purplish skin lesion measuring approximately 15 cm in diameter (Fig. 1a), enlarged lymph nodes on the side of the lesion were observed.

Laboratory investigations revealed progressive leukopenia with a shift to the left and decreased erythrocyte parameters. Inflammatory parameters were in normal range, but test results showed abnormal coagulation parameters (prolonged APTT and elevated D-dimer concentration), and elevated liver enzyme and lactic dehydrogenase activity. The patient continued to have a hectic fever (Fig. 2), and splenomegaly was also observed. Echocardiography and chest X-ray examination revealed the presence of pericardial and pleural exudate. A bone marrow aspiration biopsy did not provide any evidence of a bone marrow proliferative disorder. Various imaging studies of the affected area were carried out. The ultrasound image was dominated by extensive subcutaneous tissue oedema (Fig. 3) and reactive inguinal lymphadenopathy (Fig. 4). Magnetic resonance was performed because of the ambiguousness of the results and confirmed the presence of subcutaneous tissue infiltration without any muscle changes; in addition, the study revealed signs of liquefactive necrosis in lymph nodes (Fig. 5).

Numerous laboratory investigations were performed to identify causative infectious agents; the results were indeterminate for *Mycobacterium tuberculosis* (interfer-

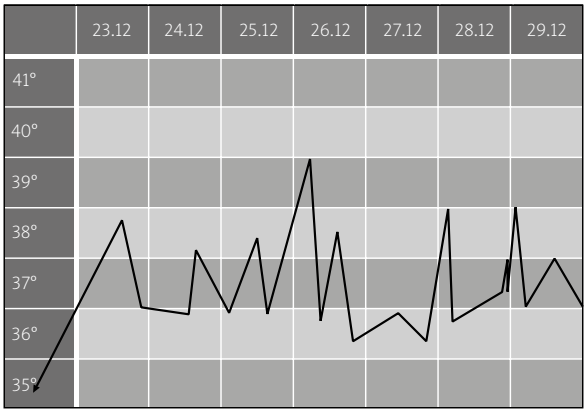

Fig. 2. Course of fever during hospitalization.

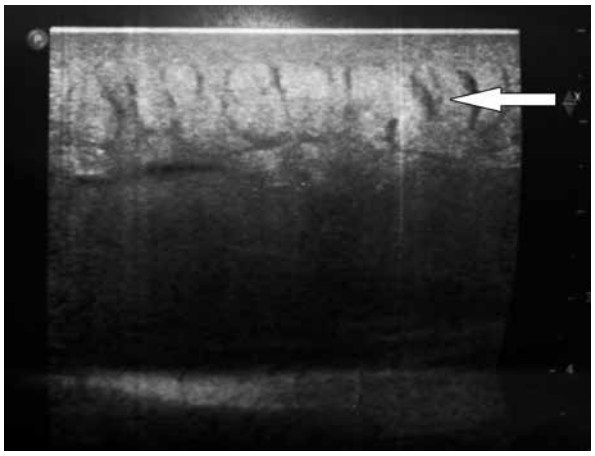

Fig. 3. Extensive subcutaneous oedema in ultrasound examination.

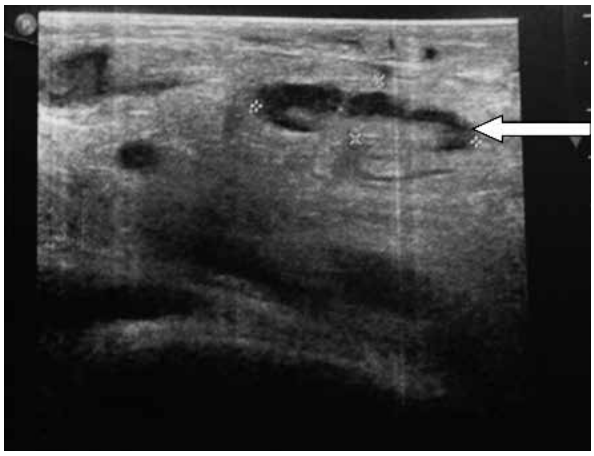

Fig. 4. Reactive enlargement of inguinal lymph nodes.

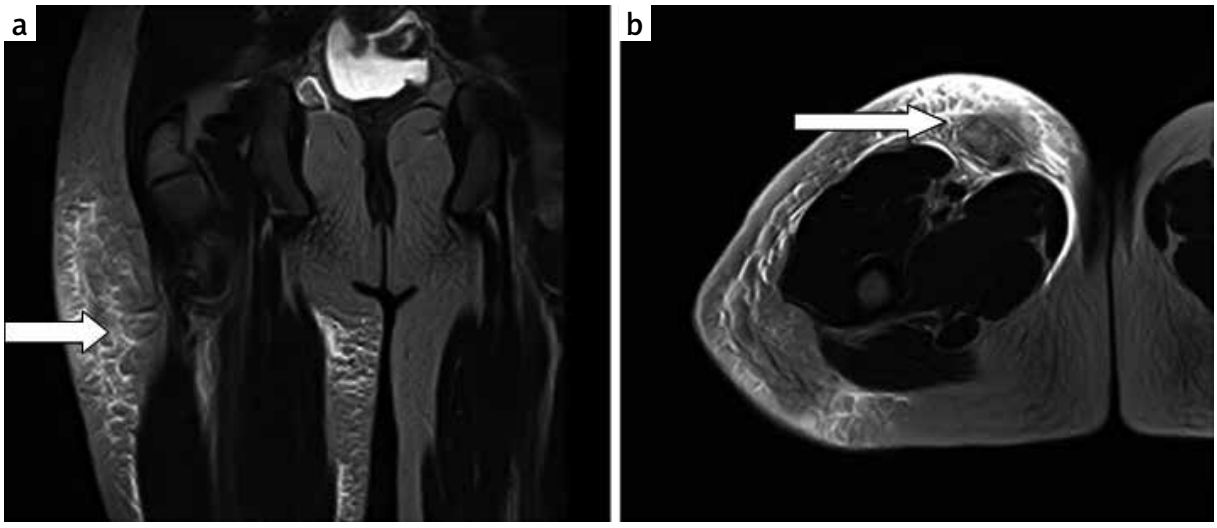

Fig. 5. MRI imaging of the lesion and lymph nodes.

on-gamma release assay – IGRA) and positive for *Borrelia burgdorferi*, *Salmonella* and *Bartonella henselae* (ELISA) infection. Despite treatment with wide-spectrum antibiotics (amikacin, ciprofloxacin), the patient's clinical condition did not improve. Inflammatory parameters were found to be elevated. Histopathological assessment of a skin biopsy specimen obtained from the site of the lesion revealed the presence of features of subcutaneous tissue inflammation (panniculitis) and blood vessel inflammation (vasculitis). In consideration of the positive family history for lupus erythematosus and the histopathology result, a decision was reached to introduce glucocorticosteroid therapy. Initially, the patient received pulses with methylprednisolone at a dose of 20 mg/kg b.w., followed by oral steroids at a dose of 0.5 mg/kg b.w. per day. This treatment led to gradual reduction of inflammatory infiltration and inguinal lymph nodes and normalization of laboratory test results. Hydroxychloroquine was added to the treatment regimen, at a dose of 200 mg/day. The patient remains under the care of a rheumatology out-patient clinic; substantial clinical improvement has been observed (Fig. 1b), permitting gradual reduction of glucocorticosteroid dosage.

Discussion

Subcutaneous tissue inflammation in the course of lupus erythematosus in childhood is a rare manifestation of the disease. It can be associated with systemic disease (2–5%), but its purely cutaneous form (lupus erythematosus panniculitis) is more common [4]. The clinical presentation is highly variable, leading to difficulties in

establishing a diagnosis. Reaching a diagnosis requires combining clinical presentation with laboratory test results and histopathological analysis. The disease is much rarer in children than in adults and skin lesions may occur but are not limited to the lower extremities, appearing most often on the face and upper extremities [5]. Despite the absence of disease-specific laboratory tests, it is believed that high antinuclear antibody titres in the course of subcutaneous tissue inflammation may signal the development of the systemic form of lupus erythematosus [6]. Fernandes *et al*. [7] described the case of a child who developed classic symptoms of systemic lupus erythematosus a year after presenting with subcutaneous tissue inflammation.

Typical features of panniculitis observed in histopathological studies are lobular or mixed subcutaneous tissue inflammation in association with infiltrating lymphocytes as well as lymphocytic small-vessel inflammation in lobular adipose tissue (vasculitis) [8, 9]. Erythema nodosum, Weber-Christian disease and sarcoidosis as well as T-cell cutaneous lymphoma should all be considered in the differential diagnosis [10]. Reports in the literature indicate that the clinical presentation of T-cell cutaneous lymphoma may suggest an autoimmune process, and reliable verification of the diagnosis can only be obtained through histopathological analysis [11]. Pasqualini *et al.* presented a case in which subcutaneous tissue inflammation was an initial sign of haemophagocytic lymphohistiocytosis [12].

Antimalarial drugs, hydroxychloroquine and chloroquine, are first-line treatment for panniculitis [13]. Glucocorticosteroids are reserved for cases of severe and refractory disease. In addition, good results have been reported using immunosuppressive drugs such as methotrexate, mycophenolate mofetil, and cyclosporine. Beneficial results of treatment using rituximab have also been reported [14].

The case of the 11-year-old girl presented in this article is atypical. Initially, the presence of a skin lesion located on the lower extremity and accompanied by lymph node enlargement suggested bacterial inflammation. Cat scratch disease, a bacterial animal-transmitted disease caused by *Bartonella* sp., was also considered in the differential diagnosis. This disease generally presents as sub-acute local lymphadenopathy; skin lesions typical for panniculitis may also be present, and approximately 10% of cases display systemic symptoms such as high fever, apathy, and weakness [15]. A detailed family history revealed that the patient's parents had a rabbit farm; similarly to cats, rabbits are a reservoir for *Bartonella* sp. *Bartonella sp.* infection was confirmed serologically, but attempts at targeted therapy using wide-spectrum antibiotics did not produce a desired effect. The whole process, including clinical presentation, the presence of venous thrombosis as well as the positive family history, prompted diagnostic testing directed at detecting an autoimmune process. Laboratory findings (which included progressive leukopenia and abnormal coagulation) as well as clinical features – hectic fever, splenomegaly, and pleural and pericardial exudate – supported a diagnosis of connective tissue disorder. Despite many doubts, on obtaining the results of the histopathological examination, the decision was taken to administer steroid therapy, which resulted in a very good clinical response. Although the patient was negative for antinuclear antibodies, a decision was reached to add chloroquine to the treatment regimen. Despite the absence of antinuclear antibodies, the dramatic course of the disease, typical histopathological examination result, positive serological findings of various infectious agents non-responsive to antibiotic therapy and the positive family history necessitate continued observation of this patient for systemic lupus erythematosus.

In summary, subcutaneous tissue inflammation often poses a significant challenge, not only a diagnostic but also a therapeutic challenge. In view of the large number of diseases that may potentially be associated with this type of underlying inflammation, great discernment must be exercised in the course of the diagnostic process.

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