Case Report

A child with panniculitis and microhaematuria/proteinuria—an unusual presentation of p-ANCA-positive vasculitis

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Introduction

Panniculitis is defined as inflammation of the subcutaneous fat. It may be primary (without an identifiable cause) or secondary [1]. The secondary causes of panniculitis include those associated with infection, pancreatitis, immunodeficiency, haematological malignancies, and connective tissue diseases. Erythema nodosa is probably the commonest and best-known form of panniculitis [1]. Other forms are less often seen and recognized, usually leading to a considerable delay in establishing the precise underlying diagnosis. An adequate skin biopsy (wedge rather than punch) is essential in order to define fully the important histopathological features. These include the exact nature of the cellular infiltrate, the presence of vasculitis, and the predominant location of the inflammation, either septal or lobular.

In this report, we present a 12.5-year-old girl who developed rapidly progressive glomerulonephritis (RPGN), secondary to pANCA-positive vasculitis. Among her initial manifestations the most prominent was a panniculitis presenting in a distinctly unusual manner, namely, that of a mass on the inner aspect of the left thigh. As a result, the patient was originally investigated for a possible malignancy. Definitive diagnosis was delayed until the demonstration of a panniculitis with vasculitis on a skin biopsy and a crescentic glomerulonephritis on a renal biopsy. Immunosuppressive treatment led to a rapid and complete disappearance of the panniculitic process. Renal function, however, after an initial partial response, is gradually deteriorating.

Case report

This 12-year-old girl was first referred to the paediatric nephrological outpatient clinic in January 1994, for the investigation of acute renal failure. The patient is the older child (she has a younger healthy brother) of non-consanguineous parents of Iraqi origin. Her maternal grandmother is on maintenance haemodialysis due to end-stage renal disease of unknown aetiology.

In August 1992 the patient was treated by her local paediatrician for what was diagnosed as cellulitis of an ear lobe. During this episode, she was discovered to have haematuria and proteinuria (on a dipstick examination). An ultrasound of the kidneys and intravenous pyelogram were performed, showing normal appearance.

In September 1993, the patient was diagnosed as suffering from ‘erysipelas’ of the left leg, which, however, did not respond to methicillin. Laboratory data at the time showed an erythrocyte sedimentation rate (ESR) of 12 mm in the first hour (Westergren), serum haemoglobin 12.3 g/dl and a blood sugar level of 90 mg/dl. Rheumatoid factor, C-reactive protein and antinuclear factor were negative. Antistreptolysin O titre was 1:400 Todd units. In December 1993, she was admitted to the orthopaedic department upon presenting with a non-tender subcutaneous mass (3 × 4 × 6 cm) of hard consistency located on the medial aspect of her left thigh. There was associated weight loss and fever. No regional or generalized lymphadenopathy was evident. The patient’s ESR had increased to 90 mm/h. Serum haemoglobin was 10.1 g/dl, leucocytes 10 300/μl with a normal differential count, platelets 363 000/μl, urea 40 mg/dl, creatinine 1.2 mg/dl, albumin 3.6 g/dl, and cholesterol 172 mg/dl. Urinanalysis revealed persistent haematuria and proteinuria (not quantitated at this stage). An X-ray of the thigh showed normal bone architecture. Ultrasound examination of the upper abdomen was without pathology.

Computerized tomography of the chest showed increased interstitial lung markings. A surgical biopsy
was performed. The histological specimen consisted of adipose tissue within which there were large foci of a chronic inflammatory (round cell) infiltrate and a number of epitheloid granulomata with multinucleated giant cells. The inflammation involved the fat lobules extending into the septa (Figure 1). Plasma cells were seen surrounding and within the walls of blood vessels, in some of which fibrinoid necrosis was demonstrated (Figure 2).

In January 1994, the patient was referred to us because of a serum creatinine of 2.1 mg/dl. On examination, she appeared ill with a body temperature of 38°C. Her height was 1.63 m, weight 70 kg with well-developed secondary sex characteristics. Blood pressure was 110/70 mmHg with moderate ankle oedema. The spleen was palpable 2 cm below the costal margin. The mass on her left thigh had increased in size to 10 × 8 cm. ESR was 130 mm/h, serum haemoglobin 8.3 g/dl, urea 81 mg/dl, albumin 2.9 g/dl. The urinary sediment contained numerous RBC/HPF with erythrocyte casts. Quantitative proteinuria was 9.1 g/day. Serum C₃ was 130 mg/dl, C₄ 35 mg/dl. ANF, HBsAg and cryoglobulins were negative. IgA was 352, IgG 1478, and IgM 120 mg/dl. A Mantoux test was negative. pANCA was found to be positive. On percutaneous renal biopsy there were 19 glomeruli of which nine were completely hyalinized. All the glomeruli had associated crescents at various stages of maturation, some fibrotic and others as yet cellular (Figure 3). Non-hyalinized glomeruli showed mesangial cell proliferation with thickening of the basement membrane and in some capillaries fibrinoid necrosis. Fibrinoid necrosis was also demonstrated in one medium-sized blood vessel. Immunofluorescence revealed granular deposition of IgM and C₃ along the glomerular basement membrane.

The patient was administered intravenous pulse methylprednisolone (1.5 g/day) for 3 consecutive days followed by oral prednisone 100 mg/day together with cyclophosphamide 150 mg/day. The panniculitic mass on her left thigh resolved within a few days. Serum creatinine peaked at 3.2 mg/dl, decreasing, thereafter, to 1.6 mg/dl after a month’s therapy. pANCA in March 1994, was negative. Currently (as of May, 1996) the patient’s serum creatinine is stable at 2.5 mg/dl, creatinine clearance of 35 cc/min.

**Discussion**

In its primary form, panniculitis, an inflammation of the subcutaneous fat is usually an isolated abnormality of the skin and subcutis [1]. However, even primary panniculitis (so called Weber–Christian disease or its variant Rothman–Makai) may have associated systemic manifestations. Secondary forms of panniculitis are seen with infection (probably the most common cause), pancreatic diseases, immunodeficiency states, malignancies (lymphoma and leukaemia) and connective tissue diseases. Cutaneous polyarteritis nodosa typically presents as painful red nodules (0.5–3.0 cm)

![Fig. 1. Subcutaneous adipose tissue involved by an inflammatory infiltrate composed of round cells, extending into the septa. (PAS, magnification ×40).](image1)

![Fig. 2. High-power view showing fibrinoid necrosis of small blood vessels. (Masson trichrome, magnification ×250).](image2)

![Fig. 3. Renal biopsy showing a fibrocellular crescent occupying about 50% of Bowman's space and compressing the glomerular tuft—all 19 glomeruli of the biopsy specimen were similarly affected. (H&E, magnification ×100).](image3)
p-ANCA-positive vasculitis in a child with panniculitis particularly on the lower extremities [2]. Its diagnosis is established by the finding of dermal vasculitis with or without panniculitis in the absence of any visceral involvement. It usually follows a chronic, relapsing pattern but is benign. Magilvay et al. [3] have suggested that this entity may simply be the initial manifestation of an evolving systemic vasculitis. This certainly appears to be the case in our patient. Retrospectively, in fact, the episodes diagnosed as cellulitis of an ear lobe and erysipelas of the left leg probably represent a form of cutaneous vasculitis, possibly erythema nodosum.

Although haematuria and proteinuria were already documented at this early stage of the patient’s illness, these findings were only subjected to a cursory evaluation. Upon presenting with a mass on her left inner thigh, suspicion of a malignant tumour was entertained. However, even following biopsy of the mass, definitive diagnosis of the patient’s underlying disease was still delayed, being finally established on renal biopsy and further confirmed by the finding of a positive p-ANCA.

Our patient meets the diagnostic criteria for systemic vasculitis in childhood as proposed by Ozen et al. [4]. Renal and musculoskeletal involvement conjointly or one of these major in addition to four minor criteria (out of 10) correlated with the histopathological diagnosis in 97% of patients (30 of 31). Our patient exhibited renal involvement as the major and panniculitis, constitutional symptoms (fever, weight loss), possible lung involvement and acute phase reactants as the minor criteria. Systemic vasculitis in children has been associated with antecedent streptococcal infection [5,6]. However, in our case, antistreptolysin O titre was only positive at 1:400 Todd units, with no rise in convalescent titres.

In contrast to adults, where it correlates poorly with disease activity, an elevated ESR is prominent in active cases seen in childhood [2,4]. This feature was aptly demonstrated in our patient. Upon therapy, the patient’s panniculitis resolved completely. Her renal function, however, did not revert to normal and she is in advanced chronic renal failure. This is undoubtedly due to the unfortunate delay in diagnosis and institution of appropriate treatment. As shown on renal biopsy, nearly 50% of the glomeruli were hyalinized and fibrotic crescents were seen in some of the remaining glomeruli.

In summary, we have presented a child who developed a rapidly progressive glomerulonephritis presenting as a vasculitis related panniculitis. Due to the unusual mode of presentation, the correct diagnosis was considerably delayed. In cases of panniculitis, prompt diagnosis emphasizing the relevant histological features requires the performance of an adequate skin biopsy. Only thus and with increased physician awareness of the entity and its secondary causes, can we hope for better management.

References


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