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Sarcoidosis or scleroderma? An unusual case of sarcoidosis

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Sarcoidosis or scleroderma? An unusual case of sarcoidosis in a 3-year-old Caucasian girl

Sin, A 3-year-old girl presented with generalized pain, stiffness and tightness of skin over 4 months. She was stiff, unable to walk or open and close her hands fully, became anorexic and her growth dropped significantly. She had no difficulties with swallowing or breathing, no RP or symptoms to suggest Mycobacterium infection.

On examination, her skin was shiny and indurated. She had sclerodactyly, livedo reticularis and her range of movement was significantly reduced particularly in the MCP and IP joints of hands. Her blood pressure was at the 95th percentile. Ophthalmological examination revealed bilateral Meibomian gland dysfunction and punctate epithelial erosions. Nail-fold capillaries and other examinations were unremarkable.

Table 1 shows the laboratory investigations. She was anaemic with high acute-phase reactants. Renal function was impaired (creatinine 80 μmol/l) and serum calcium was grossly elevated (3.6 mmol/l) with suppressed PTH. The 1,25 dihydroxycholecalciferol was at the high end of normal. Skeletal survey showed generalized osteopenia and she was given 25-OH vitamin D supplementation before assessment. Despite ceasing the supplement and hyperhydration, the hypercalcaemia persisted. Antibody screen found negative ANAs and ENAs (anti-Scl 70, ACAs, anti-Ro, -La and anti-RNP). RF was positive (66 IU/ml, range 0–90) and her angiotensin-converting enzyme (ACE) level was elevated at 238 U/l (0–90). Urine albumin creatinine ratio was normal.

MRI of thighs showed mildly increased signal from muscle and fascia on T2- and STIR-weighted sequences. These were consistent with myositis. Echo found no cardiac involvement or pulmonary hypertension. Chest X-ray and high-resolution CT scan showed no evidence of lymphadenopathy or parenchymal lung disease. Barium meal was normal.

Skin biopsy taken from thigh showed focally prominent perivascular collections of epithelioid cells but not fibrosis. Renal biopsy showed a multinucleated giant cell reaction in the interstitium. Both pointed to the diagnosis of sarcoidosis. No granuloma was demonstrated histologically. There was no clinical or histological evidence of mycobacterium infection. Bone marrow examination was negative.

A diagnosis of sarcoidosis alone or overlap with deSSc was made. Due to the hypercalcaemia and severe skin disease, she was treated with pulsed intravenous methylprednisolone, followed by reducing doses of oral prednisolone. Serum calcium and renal function normalized and her skin became less inflamed allowing improved mobility. Meibomian gland dysfunction also resolved. She commenced subcutaneous MTX 15 mg/m² as maintenance. She remained well with no recurrence of symptoms at follow-up 5 months later.

Sarcoidosis can co-exist with various CTDs including SSc in adults [1–4]. Enzeniauer and West [2] reported that 6 out of 569 adult patients with CTDs developed sarcoidosis over 10 years. Sarcoidosis was usually diagnosed due to the presence of hilar lymphadenopathy, systemic or respiratory symptoms and proven on biopsy. Renal failure due to sarcoidosis on first presentation was also rare [5].

Hypercalcaemia is reported in ~10% of the adult patients with sarcoidosis [5] and as high as 30% in children [6]. The mechanism is thought to be an increased 1α-hydroxylase activity of macrophages in granuloma, especially in patients with pulmonary involvement. However, it was also demonstrated in those without lung granuloma [7]. A normal 1,25 dihydroxyvitamin D does not exclude sarcoidosis as the cause of hypercalcaemia [8]. Furthermore, Bell et al [9] demonstrated that addition of small amount of vitamin D caused hypercalcaemia in sarcoidosis patients but not in normal subjects.

In our case, sarcoidosis was diagnosed based on histology, hypercalcaemia and persistently elevated ACE, though pulmonary disease and lymphadenopathy were absent and skin involvement was clinically atypical for sarcoidosis.

It is possible to speculate that this case represents sarcoidosis mimicking SSc rather than an overlap. However, the current classification for childhood SSc does not require exclusion of sarcoidosis [10]. While we cannot be certain that the muscle and eye involvement seen in this case was due to sarcoidosis as we have no histological specimens, sarcoidosis could definitely be the cause of the inflammatory myositis in this case. In fact, sarcoidosis can

<table>
<thead>
<tr>
<th>TABLE 1. Blood results</th>
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<tr>
<td>Laboratory test</td>
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<tr>
<td>Hemoglobin, g/l, range 11.5–14.5</td>
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<tr>
<td>White cell count, x10⁹/l, range 5–15</td>
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<tr>
<td>Platelet, x10⁹/l, range 150–450</td>
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<tr>
<td>ESR, mm/h, &lt;10</td>
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<tr>
<td>Sodium, mmol/l, range 133–146</td>
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<tr>
<td>Potassium, mmol/l, range 3.5–5.5</td>
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<tr>
<td>Urea, mmol/l, range 2.5–6</td>
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<tr>
<td>Creatinine, μmol/l, range 20–50</td>
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<tr>
<td>Calcium, mmol/l, range 2.22–2.51</td>
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<tr>
<td>Phosphate, mmol/l, range 1.2–1.8</td>
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<tr>
<td>Albumin, g/l, range 35–52</td>
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<tr>
<td>ALT, U/l, range 10–25</td>
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<tr>
<td>ALP, U/l, range 150–380</td>
</tr>
<tr>
<td>1,25 dihydroxyvitamin D, pmol/l, range 40–150</td>
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<tr>
<td>ACE, U/l, range 0–90</td>
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*Signifies abnormal result.


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adequately explain all the clinical features. It reflects the need for more specific criteria for diagnosing SSc.

In summary, this case highlights the importance of recognizing the very atypical presentation of sarcoidosis and its ability to mimic SSc in children, which cannot be excluded by the current classification criteria.

**Rheumatology key message**

- Sarcoidosis can mimic scleroderma and is not excluded by the current scleroderma classification criteria.

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**Sudden visual loss in a patient with microscopic polyangiitis**

Sir, A 51-year-old woman with pulmonary–renal syndrome was admitted to our department. She complained of a dry cough, which had been present for 6 months, with intermittent mild haemoptysis. One day before admission, chest CT scan suggested interstitial lung disease. At admission, blood chemistry revealed highly elevated acute phases parameters (CRP 15.6 mg/dl) and renal failure (creatinine 3.2 mg/dl). Autoantibody profiling revealed positive MPO-ANCA. Urine analysis showed granular casts, glomerular hematuria and proteinuria. Renal biopsy revealed pauci-immune crescentic glomerulonephritis. Microscopic polyangiitis (MPA) was diagnosed, and corticosteroids, cyclophosphamide and five courses of plasmapheresis commenced.

Initially, the patient responded rapidly to treatment. Inflammation markers decreased, renal function recovered and haemoptysis ceased. Despite the addition of several anti-hypertensive drugs, blood pressure, however, was rising up to 180/110 mmHg. Twenty days after immunosuppressive treatment was started, the patient suffered from severe headache and a generalized seizure. A cerebral CT scan excluded cerebral haemorrhage. Five hours later, the patient complained of complete visual loss. Cerebrospinal fluid analysis was completely unremarkable but the patient suffered from recurrent seizures necessitating transfer to an intensive care unit. MRI images showed symmetrical subcortical oedema (Fig. 1A and B). Diffusion-weighted sequences suggested cerebral ischaemia. Having excluded CNS infection, sinus vein thrombosis, subarachnoidal haemorrhage and arterial dissection, CNS vasculitis was initially suspected despite remission of pulmonary and renal disease. Methylprednisolone pulse therapy was commenced and anti-convulsant therapy started. The following day, cerebral MR angiography (MRA) showed severe bilateral narrowing of M1 and M2 cerebro-vascular segments (Fig. 1C). Over the next days, seizures subsided and the patient completely regained vision. Repeated cerebral MRA demonstrated full resolution of previously narrowed vessels and subcortical bilateral lesions (Fig. 1D–F) within 6 weeks. The patient remained in complete remission thereafter.

CNS involvement is an infrequent complication of MPA [1]. In our patient, an isolated cerebral vasculitic relapse was initially suspected after exclusion of infectious disease, sinus vein thrombosis and arterial dissection. However, the strict symmetric pattern and the rapid resolution of clinical symptoms and reversibility of arterial lesions as evidenced by MRA argue against our primary hypothesis. Also, large vessel involvement in ANCA-associated vasculitis is extremely rare. Moreover, arterial lesions of cerebral vasculitis do not usually completely resolve after healing [2]. In addition, the patient’s renal and pulmonary disease responded dramatically to immunosuppressive treatment at the time of neurological deterioration. In view of these findings, we considered another diagnosis.

Recently, a group of disorders with similar clinical and angiographic findings have been described and the term reversible cerebral vasoconstriction syndrome (RCVS) has been introduced [3]. The main clinical feature of RCVS is acute onset severe headache associated with or without neurological features. The morphological basis is a prolonged but reversible multifocal cerebral vasoconstriction. Although brain MRI is frequently normal, signs of brain infarction may occur [4]. Cerebrospinal fluid analysis is normal in the majority of the cases [5]. RCVS occurs in a variety of clinical settings: drugs including cyclophosphamide, pregnancy, tumours, trauma and uncontrolled hypertension and many other factors have been reported [3]. In our patient, worsening hypertension, which occurred shortly before the clinical onset of RCVS, most likely was the final trigger, although we cannot formally exclude other causes. The optimal treatment of RCVS is uncertain but calcium-channel blockers, brief courses of corticosteroids and simple observation have been reported (6). The previous diagnosis of systemic vasculitis in our patient complicated a correct diagnosis. To our knowledge, this is the first report of RCVS complicating ANCA-associated vasculitis.

**Rheumatology key message**

- Reversible cerebral vasoconstriction syndrome is an important differential diagnosis of cerebral vasculitis.

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