The specificity of PCR for TB is at least 95–98% when cultures are positive and 95% when there is a negative culture. In the USA, 90% of adult tuberculosis cases were confirmed by culture. In contrast, only 28% of the children with tuberculosis had positive cultures, and here PCR appears to be more reliable [8].

We present the first case of extrapulmonary tuberculosis in a child with severe s-JIA treated with infliximab who also developed a fatal (opportunistic) pulmonary infection. The diagnosis of tuberculosis is difficult to make in an immunocompromised host. One must be alert to alarming symptoms indicating possible tuberculosis, even in children without risk factors. While a patient on immunosuppressive therapy, one must look out for opportunistic infections and the possibility of an atypical presentation.

The authors have declared no conflicts of interest.

Rheumatology

| Key message |
| Infections (including tuberculosis) can occur in children treated with anti-TNF-α. |

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ANCA-associated giant cell arteritis presenting with mononeuritis multiplex and central retinal artery occlusion: a case report

Sir, We report a woman with temporal artery biopsy-proven giant cell arteritis coupled with high activity perinuclear-ANCA (p-ANCA) with specificity against myeloperoxidase (MPO) presenting with small and large vessel vasculitis as foot drop and central retinal artery occlusion, respectively. To the best of our knowledge, this combination of presentations has not been reported previously in the English literature. The initial clinical manifestations, high erythrocyte sedimentation rate (ESR) and high C-reactive protein (CRP), responded well to pulse methylprednisolone and pulse cyclophosphamide.

A 55-yr-old Chinese woman developed gradual weakness of her left foot followed by, 6 weeks later, an acute loss of her left eye vision. She denied jaw claudication, headache, girdle pain, fever or weight loss. Neurological examination showed left foot drop, weakness in the dorsiflexion of the left foot with power grade 1/5, and otherwise normal neurological findings. The visual acuity comprised hand movement in the left eye and 6/12 in the right. Fundoscopy revealed central retinal artery occlusion with generalized retinal and macular oedema, cherry red spot at macula, pale optic disc and sluggish blood flow in retinal arteries (Fig. 1A). Normochromic normocytic anaemia (haemoglobin 9.6 g/dl, mean cell volume 80 fl), creatinine 83 μmol/l, ESR of 130 mm/h and CRP of 202 mg/l were found. Indirect immunofluorescence (IIF)-documented p-ANCA positivity and enzyme-linked immunosorbent assay (ELISA)-based MPO antigen specificity were demonstrated with titres being 160 and >200, respectively. Other autoimmune markers including antinuclear antibody (ANA), anti-dsDNA and rheumatoid factor were negative. Chest radiography was normal. All neuroimaging was unremarkable. Biopsy of the left superficial temporal artery was normal. Subsequent right superficial temporal artery biopsy showed necrobiosis granuloma in the adventitia of the artery, intimal thickening with narrowing of the arterial lumen, accumulation of histiocytes and lymphocytes in the arterial wall and absence of diffuse fibrinoid necrosis as evidenced in panarteritis, strongly favouring giant cell arteritis (Fig. 1B). She was treated with pulse methylprednisolone 1 g intravenously for 3 days followed by oral prednisolone 60 mg daily. In addition, we started pulse cyclophosphamide 750 mg intravenously for 3 days followed by oral prednisolone 60 mg daily. Subsequent right superficial temporal artery biopsy showed necrobiosis granuloma in the adventitia of the artery, intimal thickening with narrowing of the arterial lumen, accumulation of histiocytes and lymphocytes in the arterial wall and absence of diffuse fibrinoid necrosis as evidenced in panarteritis, strongly favouring giant cell arteritis (Fig. 1B). She was treated with pulse methylprednisolone 1 g intravenously for 3 days followed by oral prednisolone 60 mg daily. In addition, we started pulse cyclophosphamide 750 mg intravenously. Three weeks later, left foot dorsiflexion returned to full power while both titres of p-ANCA and anti-MPO showed marked decrement. Her left eye visual acuity reverted to 6/30. Inflammatory markers (ESR 15 mm/h and CRP 7.1 mg/l) were normalized.

The association between giant cell arteritis and ANCA remains obscure despite several published studies [1–5]. Giant cell arteritis is a granulomatous necrotizing vasculitis of large arteries with predilection over cranial arteries, aorta and their branches [2], whereas ANCA is believed to play a key role in pathogenesis in a specific group of patients with small and medium-sized vessel vasculitis like Wegener’s granulomatosis, polyarteritis nodosa and microscopic polyangiitis [1, 6]. Mononeuritis multiplex manifestation such as wrist drop or foot drop is extremely uncommon in giant cell arteritis and the combination of both small and large
vessel vasculitic presentation may obfuscate the primary or coexisting diagnosis [3].

In the literature, there have been only a few reported cases of giant cell arteritis associated with small vessel vasculitis as mononeuritis multiplex and they have been attributed to arteritis of the vasa nervosum [5, 7]. The presentation of neuropathy preceding other giant cell arteritis symptoms was however extremely unusual [5, 7]. Among all these cases, ANCA status was either unreported or lacking. Cytoplasmic ANCA (c-ANCA) is considered to have high immunodiagnostic value in Wegener’s granulomatosis whereas p-ANCA is generally believed to be less specific [3]. Central retinal artery occlusion as a complication of ANCA-associated vasculitis or Wegener’s granulomatosis is extremely rare, and only a few cases have been reported [8]. The role of ANCA in giant cell arteritis, in contrast, is unclear and immunofluorescent studies addressing ANCA positivity in 153 patients have demonstrated nine (6%) with p-ANCA pattern. However, p-ANCA immunofluorescence may simulate positive results because of the presence of ANA and validation of ANCA positivity by other methods such as by ELISA is important [6].

Gross et al. [3] demonstrated p-ANCA pattern in 7 of 62 patients with giant cell arteritis. Baranger et al. [1] found no typical ANCA in 23 patients with giant cell arteritis when antigen-specific ELISA methods were used in addition to IIF. Nassberger and Andersson [4] showed p-ANCA in 2 out of 10 patients with biopsy-proven giant cell arteritis, but none of them had antibodies against MPO. All the reported cases had low incidence of ANCA in giant cell arteritis and no specific association was demonstrated upon further validation with more specific ELISA-based antibodies against MPO. ANCA cannot be used as a real marker for giant cell arteritis. In our case, the high activity of p-ANCA was confirmed with the ELISA method and it was unlikely to be an epiphenomenon related to age [4].

The temporal biopsy of our patient was highly suggestive of giant cell arteritis [9], although vasculitis of the temporal artery can also be involved in some other vasculitic syndromes such as Wegener’s granulomatosis [8] and polyarteritis nodosa [10]. In such cases, the histology shows the presence of necrotizing vasculitis and absence of giant cells as the characteristic features. In our patient, the mononeuritis multiplex with unilateral foot drop as small vessel vasculitis was seemingly in agreement with the presence of high serological titres of p-ANCA and anti-MPO. Clinical improvement correlates well with decline of the p-ANCA activity after initiation of immunosuppressants. The subsequent manifestations of central retinal artery occlusion and histology-proven giant cell arteritis are atypical and may signify the coexistence of both small and large vessel diseases.

As a result, in patients presenting with vague peripheral neuropathy and unexplained ANCA positivity, it is important to watch out actively for giant cell arteritis that carries significant ophthalmic and neurological morbidity if left untreated.

Informed consent was obtained from the patient for treatment and publication.

The authors have declared no conflicts of interest.

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**Key message**

Large and small vessel vasculitis can coexist with mixed manifestations.

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**Rheumatology**

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Refractory polymyositis responding to infliximab: extended follow-up

Sir, The management of patients with dermatomyositis (DM) or polymyositis (PM) who fail to respond durably to conventional treatments remains difficult [1, 2]. We report the case of a 63-yr-old woman with refractory PM that dramatically responded to the addition of anti-TNF-α agent infliximab.

A 63-yr-old woman presented in August 2000 with a 3-month history of gradually deteriorating proximal muscle weakness, diffuse muscle tenderness, dyspnoea on exertion and weight loss. Physical examination revealed a symmetrical proximal muscle weakness in the upper and lower extremities, as well as trunk muscle weakness, making her unable to get up from squatting or supine positions. ’Velcro’ crackles were heard in the lung bases but the dermatological manifestations characteristic of DM were not seen. Laboratory studies revealed elevated serum creatine kinase (CK) (6547 IU/l, normal value <190 IU/l) and aldolase of 57 IU/l (normal value <8 IU/l). The erythrocyte sedimentation rate was 80 mm/h. Autoantibody screening yielded negative results.

Electromyographic (EMG) studies and deltoid muscle biopsy revealed abnormalities consistent with PM. Interstitial lung disease was also demonstrated (vital capacity 65%). Additional work-up for underlying neoplasm was unrevealing and a diagnosis of idiopathic PM was made.

The PM was refractory to corticosteroids alone (Fig. 1) but responded to additional treatment with intravenous immunoglobulins (monthly IVIg, 6 courses) allowing the reduction of the prednisone dose to 10 mg daily. However, a severe PM relapse occurred 3 months later. The prednisone dose was therefore increased to 20 mg/day and IVIg (three courses) was resumed, but this time yielded no response. Further addition of methotrexate (Mtx), 30 mg weekly, and later azathioprine (Aza), 150 mg daily, resulted only in partial improvement.

In December 2001 she complained of severe muscle pain. She required assistance to walk and was barely able to sit on her bed without help. After discussion with the patient and obtaining her consent, treatment was commenced with infliximab (Remicade® 10 mg/kg). Infusions were given from January 2002 at weeks 0, 2, 4, 6 and 9, the rest of her treatment being pursued without dose adjustment. Impressive improvement in muscle strength was observed from the first infusion and further improvement was seen during the following 2 months. Similarly, the serum CK level slowly returned to normal. Shortly after the last infusion, EMG studies also showed improvement, with less spontaneous activity and larger compound motor action potential of longer duration. By then, the pulmonary function tests had almost normalized. In June 2003, 15 months after the last infliximab infusion, the patient only takes prednisone 6 mg/day and methotrexate 30 mg every

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**Fig. 1** Patient’s response to treatment, as assessed by serum CK measurements