function. Denosumab, a fully human neutralizing antibody directed against RANKL, has been demonstrated to increase bone mass at both axial and peripheral skeletal sites, as well as in trabecular and cortical areas of bone [8]. It can probably prevent not only the generalized bone loss in RA, but also the joint destruction inhibiting the bone erosion [9]. On the other hand, zoledronic acid is a potent third-generation aminobisphosphonate that is thought to act by inhibiting the osteoclast lifespan. It has been suggested that, added to MTX, it reduces the number of bone erosions in RA [10].

It seems clear that the new challenge in the treatment of RA should be not only to arrest the structural damage, but also to repair the previous erosions. Anti-TNF-α therapy, zoledronic acid and denosumab, alone or in combined therapy, are among the potential candidates to achieve that ambitious but, we think, realistic goal.

**Rheumatology key message**

- Repair of erosions in RA is a realistic goal.

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**Fig. 1. Evolution of joint erosions in the left first MCP joint of a patient with severe RA, from 1987 to 2007. Therapy with etanercept was initiated in 2004, with excellent control of the inflammatory activity of the disease.**

**Sarcoidosis and inclusion body myositis**

Sir, Sarcoidosis, a multisystem disease of unknown etiology, is pathologically characterized by the presence of non-caseating granuloma in the affected organs [1, 2]. Muscle involvement is quite frequent; however the association of a sarcoid myopathy with IBM, a chronic inflammatory myopathy of the adults, has been reported only in six cases [1–5]. We report two more patients...
with muscle biopsies harbouring the pathological hallmarks of both sarcoidosis and IBM.

A 54-yr-old man had 1-yr history of myalgia on climbing stairs and difficulty in lifting heavy weights. On examination he had proximal muscle weakness at four limbs and atrophy of the third distal segment of thighs and brachial biceps. Tendon reflexes were lost and sensation was normal. Blood test results were normal and serum Creatine Kinase (CK) was 2-fold the normal value. Chest CT showed bilateral hilar lymphoadenopathy without infiltration (Stage 1). Electromyography (EMG) recorded myopathic and neurogenic changes. Biopsy of brachial biceps muscle showed numerous non-caseating granulomas in the connective tissue and within the muscle bundles (Fig. 1A); no cellular necrosis was observed. Muscle fibre membranes did not express MHC class I (MHCI) and no amyloid deposits were detected within the myofibres. A diagnosis of sarcoid myopathy with pulmonary involvement was made. The patient was treated with prednisone for 2 yrs without any improvement. At the age of 58 yrs, he noted progressive left foot drop that forced him to use the handrail to climb stairs; he rose from the squatting position with some difficulty and was able to do only three knee bends consecutively. Arm movements were full and muscle strength was unchanged. Blood tests, chest CT and EMG were unchanged. A second biopsy from vastus lateralis muscle showed numerous non-caseating granulomas and the typical features of IBM, i.e. rimmed vacuoles, eosinophilic inclusions and non-necrotic fibres invaded by inflammatory cells (Fig. 1B), amyloid deposits and amyloid-β-immunoreactive inclusions (Fig. 1E and F); the sarcolemma of many fibres expressed MHCI.

The second patient, a 48-yr-old man, had a diagnosis of lung sarcoidosis on the basis of bilateral hilar lymphadenopathy with infiltration by chest radiographs (Stage 2) supported by the histological evidence of non-caseating granulomas by transbronchial biopsy. He did not complain of any muscular symptoms and the neurological examination was normal. The patient responded to treatment with prednisone. At the age of 55 yrs, he developed dysaesthesia followed by progressive muscle weakness. On examination, 5 yrs later, proximal and distal muscles of the four limbs were weak, sensation was reduced distally and tendon reflexes were lost. EMG was consistent with a sensory-motor polyneuropathy. A sural nerve biopsy showed severe loss of myelinated fibres without inflammatory infiltrates or amyloid deposits. Muscle weakness worsened in time. When the patient was 62-yr old, CK was 8-fold the normal value. Biopsy of vastus lateralis muscle showed fibre size variability, small groups of atrophic fibres, few necrotic fibres and endomysial fibrosis. A small non-caseating granuloma and rimmed vacuoles inside many fibres with few eosinophilic inclusions were present (Fig. 1C and D). A few muscle cells expressed MHCI on sarcolemma.

The association of IBM and muscular sarcoidosis is probably casual, nevertheless, our observation, together with previous reports [3–5], raises the likelihood of a link between these two apparently unrelated diseases. From 2952 consecutive muscle biopsies performed in our department, we identified six patients with pulmonary sarcoidosis (0.20%) and 27 patients with IBM who represent 0.91% of our patient population, a frequency that ranges between those reported by other authors (0.4–1.3%) [6]. Among the six patients with pulmonary sarcoidosis, two had muscular sarcoidosis and IBM, two patients had a non-specific myopathy and two a normal muscle. In addition, 7.4% of our IBM patients had sarcoidosis; this is a considerable frequency compared with previous papers reporting the association of IBM with other autoimmune disorders in 1–4% of the cases [7, 8]. It is relevant to underline that IBM and sarcoidosis are mediated by Th1-driven immune reactions [9]. Interestingly, in our first patient the histological features of both sarcoidosis and IBM were clearly demonstrated only at the second muscle biopsy thus suggesting that sarcoid myopathy may have promoted IBM. Also the clinical course supports this hypothesis since the asymmetrical muscle weakness that can be observed in IBM is not usually reported in chronic sarcoid myopathy. Even though we cannot exclude that the discrepancy observed between the first and the second muscle biopsy may be due to the different muscles chosen for the pathological examination, we consider it unlikely since IBM features are usually present at the four limbs [10]. Another possibility is that the presentation of the two diseases occurs at different times, as it frequently happens in autoimmune disorders; alternatively IBM could represent a common phenotypic endpoint of muscular sarcoidosis [11].

We emphasize the importance of a careful clinical follow-up, eventually with a second muscle biopsy, in patients who present an unusual course of muscular sarcoidosis or an uncommon pattern of muscle weakness.

**Rheumatology key message**

- A close relationship may be present between sarcoidosis and IBM.

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**Fig. 1.** Haematoxylin and eosin stain (A–D). Patient 1 muscle biopsies (A, B). The first specimen from the brachial biceps muscle shows few atrophic fibres in abundant connective tissue and sarcoid-like granulomas (arrows) (A). The second biopsy from vastus lateralis muscle shows increased fibre size variability and rimmed vacuoles in atrophic fibres (arrows); an eosinophilic inclusion within a rimmed vacuole (arrow) and increased connective tissue are also present (B). Patient 2 muscle biopsy (C, D). Fibre size variability and a small granuloma compressing a muscle fibre (arrow) (C). A small group of atrophic fibres and a muscle fibre with a rimmed vacuole and eosinophilic inclusion (arrow) (D). Congo red staining and immunohistochemistry for amyloid-β (E, F). The second muscle biopsy from Patient 1 demonstrates an amyloid deposit within a muscle fibre with Congo red staining (arrow) (E) and an amyloid-β-immunoreactive inclusion with mouse monoclonal antibody 6E10, which recognizes amyloid-β (arrow) (F).
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Castleman’s disease in childhood: a surgically curable mimic of autoimmune disease

Sir, Castleman’s disease (CD) is a rare, non-malignant, lymphoproliferative disorder of uncertain aetiology that is an important, surgically curable mimic of autoimmune disease. CD is classified clinically into two subtypes: unicentric and multicentric CD [1]. Pathologically, two major histological types are recognized: hyaline-vascular CD and plasma cell type. A mixed form, hyaline-vascular plasma cell CD is uncommon [2]. We present a case of unicentric plasma cell CD in a child presenting with a lupus-like phenotype where the lesion and extent of the disease was identified prior to surgery by 18-fluorine-2-fluoro-2-deoxy-D-glucose PET/CT (18F-FDG PET/CT).

A 3.5-year-old boy presented with a 4-month history of pyrexia of unknown origin (PUO), abdominal pain, weight loss and lethargy. Examination revealed a cachectic child with 4 cm hepatomegaly. Investigations revealed a hypocromic microcytic anaemia and thrombocytosis. ESR and CRP were elevated at > 150 mm/h and 144 mg/l, respectively. Extensive investigations for infective causes of the presenting clinical features were negative. Autoantibody screening was initially negative.

Abdominal USS and CT revealed two enlarged lymph nodes close to the pancreas. Biopsies of these at laparotomy revealed reactive hyperplasia only. Liver and gastric biopsies were unremarkable, and bone marrow examination demonstrated reactive inflammatory changes. Upper gastro-intestinal endoscopy revealed minor, non-specific inflammatory changes. A therapeutic trial of corticosteroids resulted in transient improvement of symptoms but no sustained disease control.

Nine months after the first presentation he developed multiple autoantibodies: anti-cardiolipin IgG elevated to 55.5 GPL U/ml (reference range <17 GPL U/ml), lupus anti-coagulant-positive, ANA 1/160 (speckled), positive Coomb’s test and low C3 and low C4. Plasma cytokines revealed elevated IL-6 of 46.6 pg/ml (reference range 0.43–8.9 pg/ml), elevated IL-10 of 17.1 pg/ml (reference range 0–3.8 pg/ml), normal TNF-α of 12.4 pg/ml (reference range 0–15.6 pg/ml), elevated IL-1 receptor antagonist (IL1ra) of 3734 pg/ml (range 48–1168 pg/ml) and elevated TNF-receptor 1 (TNF-R1) of 1435 (reference range 484–1345 pg/ml).

Severe ongoing systemic inflammatory symptoms, with lupus-like features led to empiric sequential trial of treatment with monthly IV cyclophosphamide, rituximab (chimeric anti-CD20 monoclonal antibody) and AZA, but with no improvement. New development of microscopic haematuria and albuminuria of 154 mg/mmol creatinine led to renal biopsy that showed florid membranous nephropathy, deposition of mesangial IgM, IgG and C1q consistent with (but not pathognomonic of) a lupus Class V glomerulonephritis.

In view of ongoing symptomatology, whole body 18F-FDG PET/CT scanning was undertaken. This revealed a single 29-mm FDG avid soft-tissue mass in the left retroperitoneum, anterior to the left kidney and inferior to the tail of the pancreas, which coincided with a lymph node identified on abdominal ultrasound and CT scan (Fig. 1A). A second laparotomy with resection of the lesion was undertaken. Histology confirmed the diagnosis of plasma cell CD (Fig. 1B). Prompt recovery of symptoms and