associated or not, have been evoked to explain SNHL: the presence of autoantibodies, vasculitis and/or a granulomatous process. Various antigenic targets, such as type II collagen and anti-68 kDa had been incriminated [4]. Circulating immune complexes have been found in patients with SNHL, leading to the hypothesis that their deposition in the inner ear and labyrinthic vessels could result in vasculitis and ischaemic injury [5]. Also, in analogy with cases of deafness in granulomatosis with polyangiitis, it has been suggested that granulomatous inflammation could lead to hearing loss [6]. The dramatic improvement with high-dose CSs and anti-TNF suggests, in our patient, a relationship between this symptom and its underlying inflammatory disorder.

The efficacy of anti-TNF in autoimmune SNHL has been reported with controversial results: mostly negative for etanercept [7] and possibly positive for infliximab [8] or adalimumab [9]. Also, a possible induction of SNHL with adalimumab has been suggested [10] in two cases. However, these cases of unilateral deafness could suggest a possible infectious origin. No cases of CD-associated SNHL treated with anti-TNF have been reported, and the possible role of granulomatous inflammation might explain the dramatic improvement observed in our patient. In conclusion, even though it is rare, severe deafness might occur and be inaugural in IBD associated with SpA.

Rheumatology key messages

- Severe deafness might complicate SpA associated with IBD and could improve with anti-TNF.

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Fig. 1 Serial plain radiographs of proximal tibial bone defect.

Site of fracture non-union after bone transport (a) after 12 weeks of teriparatide 20 μg/day; (b) 4 weeks after infusion of 5 mg zoledronic acid; (c) 36 months after initial fracture, with intramedullary nail in situ.

She was referred to the Bone Clinic, Oxford, UK, and treated for both vitamin D deficiency and low BMI (17.0 kg/m²) with oral vitamin D and dietary advice. Since her arthritis was well controlled, treatment with MTX 20 mg/week and LEF 10 mg/day was temporarily stopped to minimize any adverse effects on bone healing. She was not currently using CSs. Given the long history of non-union, alendronic acid was discontinued and she was commenced on teriparatide 20 μg/day.

Over a 12-week period, she developed a firm tissue bridge between the bone ends that was palpable clinically. There was no evidence of calcification radiographically (Fig. 1a). There was concern about continued use of the Ilizarov fixator as she suffered recurrent local pin-site infections and could not bear weight. After extensive discussion regarding potential risks and benefits, she then received a single zoledronic acid infusion (5 mg). Within 4 weeks early radiographic calcification of the tissue bridge was demonstrated (Fig. 1b) and 2 months later her external fixation was exchanged for an intramedullary nail and weight bearing was encouraged. She restarted MTX and LEF and 36 months after the initial fracture she had good arthritis control and bone healing (Fig. 1c).

In this patient, the aetiology of fracture non-union and poor regenerate bone formation was likely to be multi-factorial. Adults with JIA have reduced BMD compared with healthy controls [1]. Pathological changes of bone in JIA might occur for several reasons including malnutrition, medication (long-term CS use), lack of muscle force/inactivity, hormonal dysregulation, cytokine activity and growth retardation [2]. Other contributory factors include her low BMI, indicating suboptimal nutrition [3], low vitamin D [4] and localized infection. Disease-modifying drugs including MTX have not been shown to be detrimental to bone density in JIA [5].

Bone healing following prolonged non-union was induced by combined treatment with teriparatide and a single zoledronic acid infusion; while calcification of the callus could have occurred in the absence of zoledronic acid, the callus should have started to calcify within 12 weeks of teriparatide therapy. Experimentally, PTH enhances fracture healing in both healthy and elderly or malnourished animals, as measured by the size and strength of callus formation [6]. In a study of 112 post-menopausal women with fractures of the distal radius, low-dose teriparatide (20 μg daily for 8 weeks) significantly reduced time to fracture bridging compared with placebo (7.4 weeks vs 9.1, P = 0.006) [7]. The same result was not seen for women receiving 40 μg teriparatide and so the results of this study need to be interpreted with caution. In an open-label study, pelvic fractures in osteoporotic women healed significantly more quickly if they were given 100 μg recombinant PTH 1-84 once daily for 24 months in addition to 100 mg calcium and 800 IU vitamin D3 compared with those given dietary supplementation alone. The mean time for complete cortical bridging of the fracture site, as determined by CT scanning, in the 21 women given PTH was 7.8 weeks compared with 12.6 weeks in the 44 women who were not (P < 0.001) [8].

Clinical use of zoledronic acid and other bisphosphonates to aid fracture healing is not well described, although these drugs are routinely prescribed to increase bone density in osteoporotic patients for fracture prevention. In a rat closed fracture model, bolus treatment with zoledronic acid improved both the strength and size of callus formation compared with both placebo controls and weekly zoledronic acid treatment [9] suggesting that the clinical use of bisphosphonates in fracture healing warrants further investigation.

Evidence regarding the use of teriparatide and zoledronic acid combination therapy in osteoporosis treatment has been investigated; 137 post-menopausal women, given an infusion of 5 mg zoledronic acid as well as daily 20 μg teriparatide experienced significantly faster increases in spinal BMD after 13 and 26 weeks (P < 0.001) compared with receiving either therapy in isolation, suggesting a synergistic mechanism between teriparatide and zoledronic acid [10]. The regulation of bone mineralization is a dynamic and complex process involving endocrine, paracrine and autocrine effects. While the precise mechanism for the synergism between teriparatide and zoledronic acid is not known, in a recent animal model,
synchronous use of zoledronic acid and teriparatide led to an increase in calcified callus size as well as trabecular thickness in part through suppression of receptor activator of nuclear factor-κB (RANKL) and maintenance of osteoprotegerin [11]. Our case report supports the hypothesis that teriparatide and zoledronic acid work synergistically to promote fracture healing and that such dual therapy warrants further investigation in patients with fracture non-union and poorly formed regenerate bone.

Rheumatology key message

- Teriparatide with zoledronic acid is an option for patients with treatment-resistant fracture non-union.

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