Case Report

Aseptic necrosis of both tali in a child with steroid-dependent nephrotic syndrome

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Introduction

Avascular or aseptic necrosis of the talus is rarely seen in paediatric clinical practice. This is a rare finding in the absence of steroid use or significant trauma to the foot [1]. Aseptic necrosis is seen with increasing incidence in patients receiving long-term steroid treatment as in systemic lupus erythematosus or after kidney transplantation [2–5]. We report a patient, who developed aseptic necrosis of both tali during the course of treatment of nephrotic syndrome (NS).

Case report

A 5-year-old female presented with moderate edema, nephrotic range proteinuria, hypoproteinaemia (46 g/l), hypoalbuminaemia (19 g/l) and hypercholesterolaemia (8.6 mmol/l). There was no haematuria; her blood pressure, creatinine clearance, and complement C3 and C4 levels were normal. She was HBs negative. A 4-week trial of corticosteroid treatment (prednisone 2 mg/kg; 40 mg/day) did not result in remission. She was given three intravenous bolus injections of methylprednisolone (500 mg/day) without effect. A percutaneous renal biopsy was performed. Light microscopy showed normal histology and there were no deposits on immunofluorescent study. The electronmicroscopy revealed foot process fusion consistent with a diagnosis of minimal change nephropathy. The prednisone dose was gradually decreased and cyclophosphamide 2.0 mg/kg/day was prescribed for 8 weeks. Complete clinical and biochemical remission ensued and she remained in remission for 1 month followed by relapse. This time corticosteroid treatment induced a remission (prednisone 40 mg/day for 10 days followed by 25 mg on alternate days and then tapered). Her subsequent clinical course was characterized by steroid dependency and a requirement of high doses of prednisone. Attempts to reduce the dose to less than 15 mg on alternate days resulted in the appearance of a relapse of the NS.

One year after the onset of NS, the girl complained of pains and swelling in both the ankles and developed an abnormal gait. Investigations were non-contributory i.e. erythrocyte sedimentation rate, full blood count, C-reactive protein, fibrinogen, ASO titre, complement C3 and C4 level, antinuclear antibodies, Waaler Rose test and latex-rheumatoid factor. One month after the onset of clinical symptoms, the X-ray of both the ankles showed bilateral osteonecrosis of both tali with more extensive bone lesion on the right side (Figure 1). This finding was confirmed by the NMR scanning of both ankles (Figure 2a). The whole skeleton was evaluated by bone scintigraphy, but no other areas of necrosis were detected. At that time the girl had already experienced four relapses of the NS. She had mild cushingoid stigmata and hypertrichosis. The cumulative steroid dose was 4730 mg prednisone and 1500 mg methylprednisolone. After establishing the diagnosis of talar necrosis, steroid therapy was withdrawn and cyclosporine A (Neoral®) was introduced as monotherapy at the dose of 5 mg/kg/day. She has been in remission for 1 year and no adverse effects have been observed. Orthopaedic management of her talar necrosis was conservative and symptoms gradually improved. Plain radiographs and NMR of the ankles (Figure 2b) showed healing of the talar lesions resulting in loss of the bone volume and scarring. The girl was fully rehabilitated with conservative treatment and symptom-free on the last control 6 years after diagnosis of aseptic osteonecrosis. Her NS remains in remission.

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Many systemic diseases and clinical conditions are associated with non-traumatic osteonecrosis. The list includes autoimmune rheumatic diseases, systemic lupus erythematosus, vasculitides, inflammatory bowel diseases, pancreatitis, Gaucher’s disease, sickle-cell anaemia, haemophilia, thrombophilia, alcoholism, pregnancy, use of cytotoxic drugs and corticosteroids [2–8]. Talar localization of atraumatic osteonecrosis is rarely reported in children. Persistent pain in the ankles and an abnormal gait in a child receiving long-term steroid therapy alerted us to the possibility of aseptic necrosis of both tali. Although long-term steroid treatment is responsible for osteonecrosis, there are literature reports in which even short steroid courses for 3 weeks or less might be implicated [9,10].

It is believed that vascular thrombotic changes induced by corticosteroids are responsible for aseptic necrosis. Eberhardt et al. [11] analyzed bone changes in animals treated with methylprednisolone acetate for 4 weeks. Vascular thrombotic changes were not seen. Regional cell death consistent with apoptosis
and changes in matrix permeability were evident as an early event in glucocorticoid-induced bone damage.

Stern and Watts [5] reported that nine of 36 children developed aseptic necrosis after renal transplantation. The most common sites were distal femoral condyle and the femoral head. The latter was the most symptomatic and required hip replacement in three of five patients. Haajanen et al. [4] found that in their series of 546 renal transplant recipients, 29 (5.3%) developed aseptic necrosis of the femoral head. There was no difference in the cumulative dose of steroids between the patients with and without necrosis. A significant difference was found in respect to the number of methylprednisolone boli administered to both the groups.

Since corticosteroids were contraindicated for further treatment of the NS in our patient, we decided to administer monotherapy with cyclosporine A. Hayashi et al. [12] reported a 21-year-old male with NS due to focal segmental glomerulosclerosis who developed aseptic necrosis of the hip. Monotherapy with cyclosporine A was also effective in maintaining remission of NS in their patient.

In conclusion, we reported a child with steroid dependent NS and a rare (talar) localization of aseptic necrosis, which ensued during the management of the disease. Children with NS receiving methylprednisolone boli and long-term steroids should be regularly monitored for osteoarticular symptoms, which may suggest development of osteonecrosis. Early diagnosis is essential in order to modify the treatment of the NS and to prevent the development of osteonecrosis at other locations. In patients with diagnosed aseptic necrosis, monotherapy with cyclosporine is a valuable alternative for maintaining remission of the NS.

Conflict of interest statement. None declared.

References


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