A comprehensive evaluation exercise was conducted to enable review and reflection on all aspects of the course and curriculum with the goal of providing summative evaluation data as to the effectiveness of the educational programme.

Level 2 evaluation results revealed a mean precourse test score of 41% (s.d. 11.6; range 18–66%) and post-test score 64% (s.d. 10.4; range 38–78%). The mean change in score was +22% (s.d. 12.8; range +4 to +48%) ($P$ < 0.001).

This multidimensional evaluation of our pilot educational programme has yielded promising results and provides a preliminary endorsement of our approach. Our learning and teaching strategies appear to be well received by the target audience and have resulted in a demonstrable increase in knowledge and skills. This indicates an efficient and effective programme and provides good evidence for a potential model for future training. We intend to make minor adjustments to our curriculum in response to these data and perform a longitudinal evaluation in order to establish any future change in practice amongst delegates, to assess the long-term impact of our educational interventions. We hope that our experience provides helpful information that will facilitate future informed and constructive educational development in this expanding rheumatology discipline.

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as well. He had become less active and was noted to walk very cautiously. There was a history of weight loss of 1 kg over the previous 4 months. There was no history of joint swelling. He had been previously well with no relevant past medical history. The child was the older of two boys born to consanguineous parents of Pakistani origin. He was developmentally appropriate and fully immunized.

Clinical examination revealed the child to be pale, lethargic and to have a waddling gait. There was evidence of proximal muscle weakness in his lower limbs and brisk lower limb reflexes. The remainder of the musculoskeletal, neurological and systemic examinations were normal and there was no evidence of arthritis.

Initial investigations revealed a haemoglobin level of 8.1 g/dl [normal range (N) 11.5–14.5 g/dl], white cell count 15.5×10^9/l [N (4.5–13.5)×10^9/l], platelets 658×10^9/l [N (150–400)×10^9/l], mean corpuscular volume 61.0 fl (N 77–91 fl) and zinc protoporphyrin 168 μmol/mol haem (N 30–80 μmol/mol haem). Erythrocyte sedimentation rate was 79 mm/h (N 1–7 mm/h) and C-reactive protein was 53 mg/l (N <6 mg/l). Renal and liver function tests, bone biochemistry and muscle enzyme levels were within the normal ranges. His immunoglobulin and complement levels were raised: IgG 19.4 g/l (N 6.7–11 g/l), IgA 4.08 g/l (N 0.6–1.2 g/l), IgM 2.01 g/l (N 0.3–0.7 g/l), C3 1.93 g/l (N 0.83–1.46 g/l), C4 0.55 g/l (N 0.2–0.52 g/l). Autoantibodies, viral serology and Mantoux testing were negative. Urinalysis was normal.

To exclude malignancy a bone marrow aspirate was performed revealing normal marrow. Muscle biopsy excluded active inflammation. The abdominal ultrasound was normal. A skeletal survey demonstrated widespread patchy sclerosis throughout the skeleton, predominately affecting the diaphyses of the long bones and the skull. There was some widening and cortical thickening in the left distal femoral diaphysis and marked periarticular osteopenia in the left distal femur and proximal tibia (Figs 1 and 2). Bone scintigraphy revealed symmetrical increased uptake in the ribs and the metaphyses of the distal femora, proximal tibia, forearms and proximal humeri.

The clinical findings and characteristic radiological appearances led to the diagnosis of Camurati–Engelmann disease. Genetic screening for the known mutations was negative (courtesy of Dr W. Van Hul, Belgium).

The child was managed conservatively with non-steroidal anti-inflammatory drugs (NSAIDs) and his symptoms improved over the next few months. Follow-up over the last year has not shown any deterioration in symptoms, although he continues to experience leg pains which are alleviated by ibuprofen. There is no evidence of muscle weakness currently. He has normal growth velocity and his inflammatory markers are currently normal.

Camurati–Engelmann disease (CED) (also known as progressive diaphyseal dysplasia) is a rare genetic disorder characterized by progressive expansion and sclerosis predominately affecting the diaphyses of the long bones and associated with cranial sclerosis. CED typically presents in childhood with generalized muscle weakness, lower limb pains and a waddling gait [1, 2]. Other manifestations such as anaemia, hepatosplenomegaly and cranial nerve compression due to involvement of the base of the skull are less common [3]. The gene responsible for CED has been identified on chromosome 19q13 [4]. This encodes the latency-associated peptide of transforming growth factor-B1 (TGF-β1), an important mediator of bone remodelling [4]. Biochemical parameters of bone and mineral metabolism are usually normal but the erythrocyte sedimentation rate may be elevated [2, 3, 5–7]. The classical radiological changes include both endosteal and subperiosteal cortical thickening affecting the diaphyses, which may extend to the metaphyses but consistently spare the epiphyses [1, 2]. Typically the long bones, especially the femora and tibiae, are affected but skull, mandible and vertebral involvement is recognized [1, 2]. It is thought, based on cases in the literature, that the clinical and radiological features of CED progress with age [1].

Corticosteroids have been reported to provide effective symptomatic improvement and reduction of the erythrocyte sedimentation rate.
There are conflicting reports as to whether they produce radiological improvements [5, 6]. The use of pamidronate in Camurati–Engelmann disease has been reported with both improvement and exacerbation in clinical symptoms [9, 10].

The child in our report presented with the typical clinical features of leg pains and a waddling gait. The plain radiographs, in conjunction with the normal biochemical parameters and the clinical presentation, led to the diagnosis. The child was managed symptomatically with NSAIDs with good clinical improvement such that corticosteroids were not required. We believe that this case highlights the need to consider skeletal dysplasias in the differential diagnosis of non-specific limb pains in addition to arthropathy, neuromuscular disorders, malignancy and non-organic causes.

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FIG. 1. Continued.

FIG. 2. Lateral X-ray of the skull shows osteosclerosis of the skull base especially prominent in the perisellar area and the petromastoid region.


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Positive clinical and biochemical responses to anakinra in a 3-yr-old patient with cryopyrin-associated periodic syndrome (CAPS)

Sir, Cryopyrin-associated periodic syndromes (CAPS) consist of a subgroup among hereditary periodic fever syndromes that includes familial cold-induced autoinflammatory syndrome (FCAS; MIM no. 120100), Muckle–Wells syndrome (MWS; MIM no. 191900) and chronic infantile neurological, cutaneous, articular (CINCA) syndrome (MIM no. 670115), also known as neonatal-onset multisystem inflammatory disease (NOMID), representing different degrees of disease severity. All of them have been recently associated with heterozygous mutations in the \textit{CIAS1}/\textit{PYPAF1}/\textit{NALP3} gene, which encodes the cryopyrin protein [1, 2]. This protein was found to be a constituent of inflammasome, an intracellular multiprotein complex involved in the cleavage and activation of proinflammatory cytokines IL-1\& and IL-18 [3].

Here we present the case of a 3-yr-old male patient, without a familial history of periodic fever, diagnosed with possible MWS. His symptoms began when he was 9 months old, and consisted of long inflammatory episodes, recurring every 4–6 weeks, characterized by high fever, urticarial rash, abdominal pain, headache and irritability secondary to mild chronic aseptic meningitis, conjunctivitis, arthralgia, arthritis and occasionally diarrhoea. Neither reactive AA-type amyloidosis nor sensorineural deafness were present. A strong acute-phase response, with important elevation of C-reactive protein (CRP) and serum amyloid (SAA-1) protein, was detected in all these episodes (Fig. 1).

The diagnosis of CAPS was confirmed by the detection of the \textit{de novo} heterozygous T348M mutation in the \textit{CIAS1}/\textit{PYPAF1}/\textit{NALP3} gene, as has been previously reported [4].

Non-steroidal anti-inflammatory drugs and corticosteroid treatment administered before CAPS diagnosis gave a negative response. Therefore, taking in account previous experience of treatment in adult patients with MWS and CINCA/NOMID syndrome [5–7], we started a therapeutic approach with anakinra, the human recombinant interleukin (IL)-1 receptor antagonist (Kineret; Amgen), that inhibits the pro-inflammatory IL-1 signalling pathway. This treatment was initiated during an inflammatory episode by means of subcutaneous injections, in doses of 1 mg/kg/day. The patient was hospitalized for the first week to detect any of the possible side-effects, and afterwards we maintained an ambulatory routine for 4 weeks, monitoring the clinical and biochemical responses weekly. Eventually, we established periodical controls every 2 weeks. A positive clinical response was detected, with a complete disappearance of skin rash, irritability, periodic fever, conjunctivitis and abdominal pain at 24 h after the first injection, and joint involvement at 48 h. The strong acute-phase response resolved during the first week of treatment, decreasing noticeably the plasma levels of acute-phase reactants. These positive clinical and biochemical responses have persisted during 9 months of follow-up (Fig. 1). No side-effects have been identified. An attempt to reduce the anakinra dose to 0.75 mg/kg/day was unsuccessful, due to the appearance of low fever (37.5°C), headache and discomfort. When the initial dosage was reinstated these symptoms disappeared.

The most severe complications that have been described in patients with MWS are reactive AA-type amyloidosis and progressive bilateral sensorineural hearing loss. The strong decrease and normalization of plasma levels of acute-phase reactants detected in this paediatric patient during continuous treatment with anakinra suggests to us a hopeful decrease in his risk of developing reactive AA-type amyloidosis, due to its relationship with the plasma levels of SAA-1 protein [8]. Longer clinical and biochemical follow-up would be necessary to establish this risk accurately. However, we are not able to state that these positive clinical and biochemical responses to anakinra might prevent the development of sensorineural deafness in the future.

Diezelhuis et al. [9] have recently suggested that intermittent administration of anakinra during acute episodes instead of continuous treatment could be a therapeutic approach in some recurrent autoinflammatory disorders. However, the appearance of some clinical symptoms during an attempt to reduce the anakinra dose in this patient, and the advisability of maintaining his plasma levels of acute-phase reactants at normal values, led us to think that continuous treatment is most convenient in this patient.

We think that it is worthwhile publishing this positive experience with anakinra, because other children with CAPS could benefit from this treatment. As Hawkins et al. [7] suggested, early and prolonged therapeutic trials with anakinra are warranted in patients with CAPS to establish its efficacy and possible side-effects during long-term treatments, and to known if the most severe complications of CAPS—CNS involvement, papilloedema, sensorineural deafness and deforming arthropathy—could be prevented.

**Key messages**

- There was a positive response to continuous anakinra therapy in a paediatric CAPS patient.

![Graph](https://example.com/graph.png)

**Fig. 1.** Serial measurements of plasma levels of CRP and SAA-1. The vertical arrow indicates when treatment with anakinra began. The horizontal discontinuous line marks the upper value of the normal (N) range of CRP (N<5 mg/l) and SAA-1 (N<10 mg/l).