RHEUMATOLOGY

Letter to the Editor (Case report)

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Intravenous neridronate is effective in regional migratory osteoporosis

Rheumatology key message

- Intravenous neridronate is effective and safe in regional migratory osteoporosis.

Dear Editor, Regional migratory osteoporosis (RMO) is a rare form of primary bone marrow oedema (BME) syndrome with usually self-limiting features, characterized by migrating arthralgia of weight-bearing joints of the lower limbs and BME, detected trough MRI [1, 2]. Despite its self-limiting nature, treatment with oral and i.v. bisphosphonates could be effective in leading to a faster resolution of RMO [3, 4].

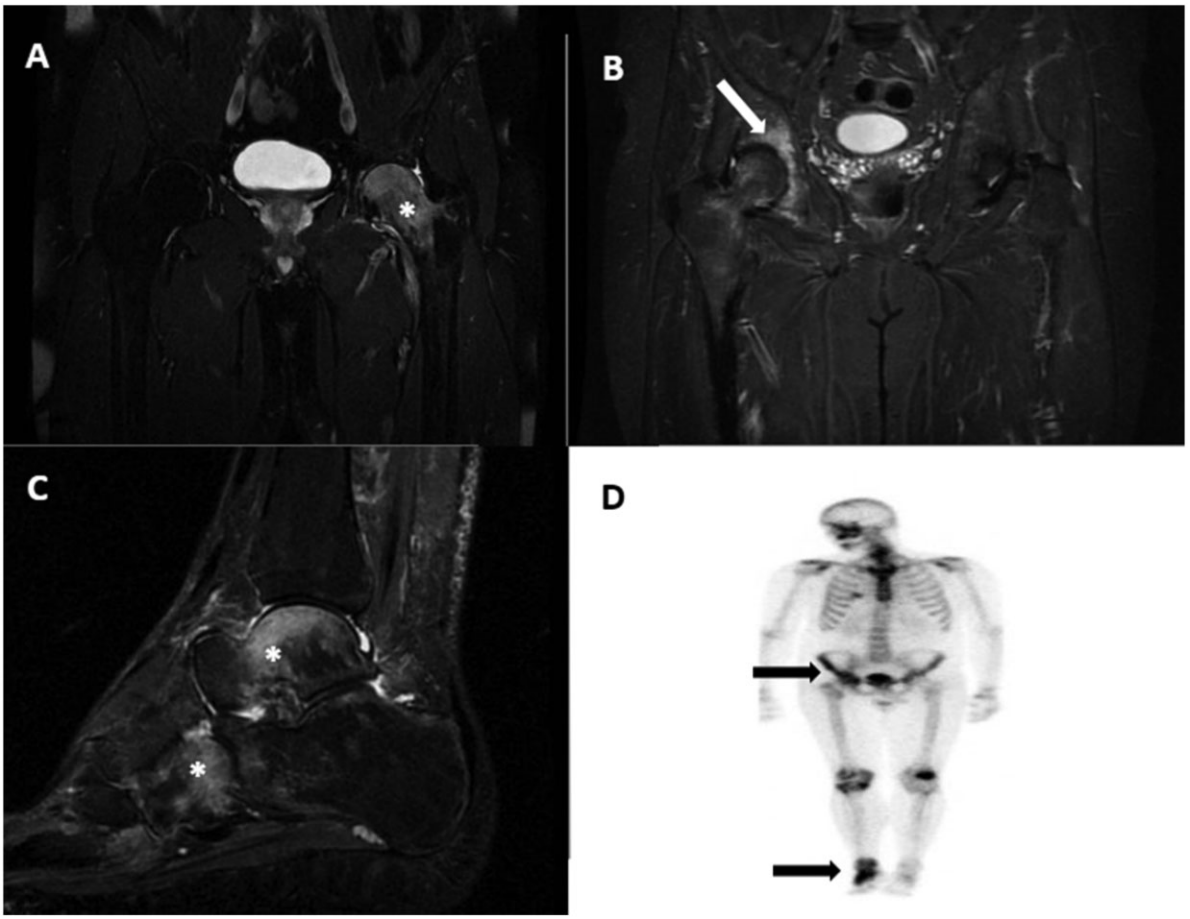
We herein report the case of a 37-year-old male with unremarkable medical history, presenting with left coxalgia associated with limited range of motion in May 2013. In the clinical suspicion of a hip disease, the patient performed a pelvis MRI which showed diffuse BME of the left femoral head and neck (Fig. 1A). On this basis, despite the normality of laboratory tests, an initial diagnosis of seronegative arthritis was made and treatment with analgesics, physical activity and conventional synthetic DMARDs was started. Three months later hip pain disappeared, but a new pain started in his left ankle. As earlier, ankle pain solved within 3 months, while pain and limited range of motion migrated to his right ankle and hip. Eighteen months after the initial presentation, the patient was referred to our centre because of the unresponsiveness to the treatment. Considering the persistent right ankle and hip pain, we decided to perform MRI, which showed diffuse BME of right ankle and acetabulum (Fig. 1B and C). In the suspicion of a bone metabolic disease a skeletal scintigraphy was performed showing uptake of the right ankle and right acetabulum (Fig. 1D). After an accurate re-evaluation of the former MRIs, clinical history and after excluding arthritis, neoplasm or avascular necrosis the diagnosis of RMO was made.

We then decided to treat the patient with i.v. neridronate. Serum creatinine and calcium were within the normal range before the treatment. In particular, the patient received four infusions of neridronate of 100 mg each, for a total of 400 mg over a 10-day time period. Moreover, oral Vitamin D and calcium supplementation was started and abstention from weight bearing was suggested. A partial clinical response, characterized by an improvement of articular range of motion and a reduction of visual analogical scale (VAS) pain (range 0–100 mm) from 70/100 to 40/100, was reached after 1 month. Then, the same therapeutical protocol was repeated 30 days after the last infusion. We observed a clinical healing of RMO defined as a complete restoration of the articular range of motion and pain disappearance (VAS pain 0/100) corresponding to the last neridronate infusion. Furthermore, the BME resolution was assessed at hip MRI re-evaluation 1 year later, in April 2016. The patient did not report any immediate or late adverse event to the treatment. In January 2022, more than 5 years on from the last MRI, the patient did not report any symptoms referring to RMO or avascular necrosis.

Neridronate is an amino bisphosphonate that has been shown to be effective and has been registered for the treatment of PD of bone and osteogenesis imperfecta, and more recently for complex-regional-pain syndrome as well as showing effectiveness in BME and pain due to knee osteoarthritis [5]. Two cycles of neridronate were performed (800 mg in total), leading to a complete clinical and imaging resolution of RMO in our case. In particular, the role of bisphosphonates in the treatment of BME syndrome of the foot and ankle was assessed in a paper of Singh *et al.* [6]. Their efficacy in RMO might be explained by the reactive bone formation and the osteoclastic bone resorption present in many cases, demonstrated on biopsy specimens of RMO patients [7]. Moreover, bisphosphonates might have a crucial role in the treatment of several forms of BME, leading to a reduction of osteoclast activity responsible for an increase of bone turnover, and having a role in reducing bone pain, acting on the acid–bone microenvironment [8]. Despite not being labelled for RMO, i.v. neridronate was chosen, in our case, because of its availability in our hospital, the good risk–benefit ratio according to our clinical experience, as well as its demonstrated clinical efficacy and safety at least in BME syndromes [5]. On the other hand, it must be pointed out that there is a lack of consistent evidence for bisphosphonates in RMO, at least before 2020 [4]. Among the limits of this treatment, the need for several instances of hospital access for the patient (from four to eight) to complete the treatment cycle must be considered, which can, nowadays, be limiting considering the spread of COVID-19 and the consequent limitations according to local health facilities.

In conclusion, i.v. neridronate showed efficacy and safety in RMO even in a long duration disease. More infusions could be needed in refractory cases. To our knowledge this is the first evidence of its use and efficacy in RMO. However, further studies are needed to confirm our evidence.

Fig. 1 Imaging evolution of the regional migratory osteoporosis of the patient



(**A**) Coronal STIR sequence of magnetic resonance (MR) showing diffuse bone marrow edema (BME) of the left femoral head and neck (white star), performed in May 2013. (**B**) Coronal STIR sequence of MR showing diffuse BME of the right acetabulum (white arrow), performed in November 2014. (**C**) Sagittal MR STIR sequence of the right ankle showing diffuse BME of talus, middle foot and metatarsal bones (white stars). (**D**) Bone scintigraphy showing uptake of right ankle and acetabulum (black arrows). Parts (C) and (D) were both performed in November 2014.

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Consent: Consent has been received from the patient.

Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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