Pathological fracture due to prolonged steroid use in a child with transverse myelitis

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ARTICLE INFO

Keywords:
Transverse myelitis
Corticosteroid
Fracture

ABSTRACT

Introduction: Transverse myelitis (TM), a rare inflammatory disease of the spinal cord, is treated with corticosteroids that could result in other complications. Case report: We present the case of a 4-year-old boy with a closed left femoral fracture after he hit the floor. He was diagnosed with TM 1 year ago and was treated with oral methylprednisolone for 8 months. Discussion: In children, the prolonged use of corticosteroid enhances the osteoclast activity but reduces the osteoblast activity; this imbalance bone turnover causes osteoporosis that increases the fracture risk, which depends on the corticosteroid dose and treatment duration. Of note, the risk of fracture might last for years. Conclusion: The increased risk of fracture because of the prolonged use of corticosteroids might not impede the corticosteroid treatment if indicated. Hence, bone health status and nutritional monitoring must be performed at the beginning of treatment in children who need corticosteroid therapy with a cumulative dose > 1 g/year.

1. Introduction

Transverse myelitis (TM), a rare focal inflammatory disorder of the spinal cord, presents as sensory, motor and autonomic dysfunction; about 20%–30% of TM cases are reported in children aged < 18 years. Two peaks of TM incidence in children are < 3 years and 5–17 years of age. However, the TM onset in children aged < 3 years exhibits worse prognosis. Although no family or gender predisposition exists, most patients are females. Typically, TM is related to multiple sclerosis (MS) or neuromyelitis optica; other aetiologies are post-infection, post-vaccination, systemic inflammatory disease, autoimmune disease and paraneoplastic syndrome [1–4].

TM is suspected when the onset of neurological dysfunction is acute or subacute, which developed to the maximum deficit within 4 h–21 days. The dysfunction involves several spinal cord segments, without the evidence of spinal cord compression. Thus, imaging or laboratory test is needed for confirmation (Table 1). The first-line treatment is high-dose intravenous methylprednisolone for 3–7 days; the treatment may be continued with oral corticosteroids [1,5].

In several online databases, we found no reports of TM-related fractures. However, long-term use of corticosteroids has been reported to cause a fracture. Here, we report the case of a 4-year-old boy with a pathological femur fracture due to prolonged methylprednisolone treatment for TM. This work is constructed according to the SCARE criteria [6].

2. Presentation of case

A 4-year-old boy (weight, 14 kg) was referred from the physiotherapy department to our emergency department because of a closed femoral fracture suspicion. His left thigh hit the floor while playing at his house. Although the exact mechanism of injury was not known, it was attributed to a low-energy trauma. The physical examination revealed swelling of the left thigh without deformity or wound. In addition, distal sensory perception and capillary refill time were normal. The pain score using the Face, Legs, Activity, Cry, Consolability scale was 2–4. Moreover, the hip and knee range of movement was limited due to pain. The extension of the ankle and great toe was normal. Furthermore, we noted no leg length discrepancy between both legs. Fig. 1a and b showed the clinical picture and femoral x-ray of the patient.

One year ago, the patient was diagnosed with TM; at that time, the patient could not walk. He was hospitalised and received intravenous methylprednisolone (125 mg) twice daily for 1 week. Since 7 months...
The prolonged use of corticosteroids interrupts the bone turnover cycle and causes osteoporosis, which results in pathological fracture. In addition, corticosteroids decrease osteoprotegerin (OPG) and increase the receptor activator of nuclear factor κB ligand (RANKL) expression, which stimulates the osteoclast production. Moreover, corticosteroids affect the stimulation of the osteoclast activity, which, in turn, elevates bone resorption. Reportedly, corticosteroids might prolong the lifespan of mature osteoclasts, which aggravate their deleterious effects.

Corticosteroids decrease the calcium absorption in the intestine and increase the calcium excretion in the kidneys. A low calcium level increases the parathyroid hormone secretion, subsequently inducing the bone resorption. Furthermore, corticosteroids decrease the androgen and oestrogen production, which, in turn, increases the bone resorption.

In addition, long-term corticosteroid inhibits the osteoblast differentiation, which causes decreased bone formation. The decreased osteoblast differentiation shifts the normal differentiation pattern of mesenchymal stem cells, which differentiates to other types of cells, including adipocytes that cause obesity. Obesity might impair bone mineralisation by decreasing vitamin D capture. Corticosteroids induce apoptosis of osteocytes, which cause osteonecrosis. Furthermore, corticosteroid suppresses osteogenic factors production of osteoclasts, which decrease the bone formation [7–9].

In children, osteoporosis could occur at any age in both sexes and is usually asymptomatic. The osteoporosis development is also attributable to the corticosteroids use, especially in children with the autoimmune or inflammatory disease who receive long-term corticosteroid therapy. In addition, corticosteroids might impair the bone growth by decreasing the growth hormone secretion, resulting in short stature. Reportedly, growth usually catches up occur after the treatment stops [2,3].

Osteoporosis in children caused by chronic corticosteroid use poses an increased risk of fracture, but, unfortunately, this could be disregarded by clinicians. In a retrospective study of 15 children, Harrington et al. [10] reported decreased trabecular thickness, osteoid thickness, osteoblast surface and increased trabecular separation. In addition, the severity of trabecular abnormality correlated with the corticosteroid dose. Hypermineralisation of trabecular was noted with the heterogeneous pattern, suggesting the decreased bone turnover. Reportedly, bone hypermineralisation contributes to the bone brittleness and fracture tendency [10].

The elevated fracture risk depends on the dose and duration of treatment. The higher risk is in the first 3 months, and then slowly decreases, although it does not return to normal. In addition, intermittent corticosteroid use exerts a cumulative effect on bones, but smaller than the continuous dose [10].

In a large observational study of children aged 4–11 years, van Staa et al. reported an increased risk of fracture in children who received > 4 cycles of corticosteroid therapy. In addition, high-dose prednisolone (> 30 mg daily or equivalent) demonstrated a higher risk of fracture compared with the lower dose [11]. Another observational
study reported that every 0.5 mg/kg increase of daily prednisolone dose (or equivalent) correlated with the doubled fracture risk in children with the corticosteroid treatment due to rheumatic disorder [12]. In a case–control study, Gray et al. reported an increased risk of fracture in asthmatic children treated with a systemic corticosteroid in 1 year (oral or intramuscular), demonstrating that the systemic corticosteroid effect might last long after therapy was ceased [13]. Furthermore, a large cohort with adult subjects reported that the risk of fracture would last until 10 years after ≥ the 1-month period of oral corticosteroid therapy was stopped [13,14].

A pathological fracture due to corticosteroid typically occurs in the vertebrae or ribs. However, osteoporosis as a side effect should not make clinicians hesitate to administer corticosteroids to children who need it. Children who require long-term systemic corticosteroid therapy with a cumulative dose > 1 g/year must be monitored since the treatment initiation. In addition, the nutritional intake should be adequate, but should not excessive to avoid obesity; calcium, vitamin D and protein should be maintained in sufficient levels. Moreover, physical activities, particularly weight-bearing exercises, are recommended to add benefits for the bone and muscle strength, as well as obesity prevention. Of note, activity should be supervised carefully to avoid accidents that might cause a fracture. Furthermore, the bone health status should be monitored, usually with Dual Energy X-ray Absorptiometry (DEXA) examination [8,15].

We searched several online databases, such as PubMed or ScienceDirect, but found no report of fracture in patients with TM. To the best of our knowledge, this is the first case report of a fracture in a patient with TM. Further searching revealed no evidence of fracture as a TM complication. In our case, the prolonged corticosteroid use for TM therapy might be the aetiology of femur fracture. Nevertheless, further research is warranted to establish the correlation between prolonged corticosteroid therapy in patients with TM and fracture.

4. Conclusion

The prolonged use of corticosteroid causes osteoporosis, which increases the risk of fracture that could last up for 10 years after treatment discontinuation. Thus, treating physicians and caretakers must be made aware of the possible side effects on the bone; however, this complication might not impede the corticosteroid treatment if indicated. The bone health status (by serial X-rays or DEXA, for example) and nutritional monitoring may be performed at the beginning of and after treatment in children who need corticosteroid therapy with a cumulative dose > 1 g/year [7].

Patient Consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflict of interest statement

The following authors have no financial disclosures: RAJ, RHT, RPW, TK.

Funding

No funding or grant support.

Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.epsc.2019.02.011.

References


