Teriparatide treatment for an atypical femoral fracture in a patient with calcinosis cutis associated with juvenile dermatomyositis: a case report

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Summary

Calcinosis cutis is a late and an unresolved complication of juvenile dermatomyositis. It sometimes causes significant debility with severe pain, joint contracture, skin ulcers. There are several reports that bisphosphonates therapy may affect calcinosis cutis. However long-term use of bisphosphonates is associated with an increased risk of an atypical femoral fracture. We present a case of atypical femoral fracture in a 27-year-old male due to long-term bisphosphonate therapy and adjunctive denosumab for calcinosis cutis associated with juvenile dermatomyositis. Our knowledge, there were no other reports of atypical femoral fractures with calcinosis cutis associated with juvenile dermatomyositis. Our patient was treated with surgery and teriparatide although two case reports documenting the worsening of calcinosis cutis with teriparatide exist. Short-term teriparatide use did not worsen the calcinosis cutis in terms of clinical symptoms and radiological signs, and the atypical femoral fracture healed; however, an increase in bone alkaline phosphatase and tartrate-resistant acid phosphatase Sb was detected.

KEY WORDS: atypical femoral fracture; bisphosphonate; juvenile dermatomyositis; teriparatide.

Introduction

Juvenile dermatomyositis (JDM) is a rare childhood systemic autoimmune disease of unknown etiology characterized by weakness in proximal muscles and pathognomonic skin rashes (1). Calcinosis cutis is a late complication of JDM, present in 25-70% of cases in the juvenile form (2). It sometimes causes significant debility with severe pain, joint contracture, skin ulcers, and muscle atrophy (1, 2). There are several reports that drug therapy may affect calcinosis cutis, for example bisphosphonates (BPs) (3, 4), intravenous immunoglobulin (IVIG) (4, 5), and others. Alendronate is the first-choice drug for patients taking glucocorticoids in order to reduce the risk of fragility fractures (6). BPs are also known to improve quality of life in patients with osteoporosis (7) and reduce mortality in those who have sustained hip fractures (8). However, long-term use of BPs is associated with an increased risk of an atypical femoral fracture (AFF) (9). Elderly postmenopausal women taking a bisphosphate over a long period of time may acquire an AFF, whereas in young men that pathology is rare. As a result of suppressed bone turnover, the healing of BP-associated AFF is also usually delayed (10). Teriparatide, a recombinant form of parathyroid hormone (PTH), enhances bone healing in patients with delayed healing or non-union (11). Two case reports of teriparatide treatment for patients with calcinosis cutis are known, and teriparatide has been shown to worsen calcinosis cutis (12). In these case reports (12), teriparatide was used to treat severe osteoporosis. Here we present the first case of AFF in a young male who was diagnosed with JDM and symptomatic calcinosis cutis and who was treated with surgery and teriparatide.

Case report

A 27-year-old Japanese male was diagnosed with JDM at 11 years of age. He had been treated with high-dose prednisolone (PSL), high-dose intravenous immunoglobulin, rituximab and immunosuppressive drugs including cyclosporine, azathioprine, mycophenolate mofetil, tacrolimus and methotrexate, however, symptoms relapsed with PSL weaning. Subsequently, prednisolone monotherapy, 16 mg daily, was continued. The patient’s medical history included calcinosis cutis which had been exacerbated; he had bilateral pain in his buttocks, elbows and humeri (Figure 1 a). The patient underwent calcinosis cutis excisions on four occasions. He was treated with the BP alendronate 35 mg per two weeks, as well as denosumab 60 mg per a half year for the pain associated with calcinosis cutis. At 25 years of age, the patient sustained a left metatarsal base fracture without trauma. After conservative treatment, he still experienced pain in the absence of bone union. His lumbar spine (L2-L4) bone mineral density (BMD) as measured by dual X-ray absorptiometry (Lunar Prodigy Advance; GE healthcare, Inc., USA) was 0.793 g cm⁻², which was equivalent to 67% of the young adult mean (YAM) in the Japanese male population. Serum bone-specific alkaline phosphatase (BAP) was 6.9 U L⁻¹, which was within normal limits (BAP: 5.7–20.9 U L⁻¹) and the

Clinical Cases in Mineral and Bone Metabolism 2018; 15(3):385-388
active isoform 5b of tartrate-resistant acid phosphatase (TRACP-5b) was 231 (170–590) mU dL⁻¹ at age 26, indicating that bone turnover was severely suppressed. The process in BAP and TRACP-5b are shown in Figure 1 c. At age 27, the patient fell from a standing position and as a result was unable to walk and was admitted to our hospital. He had experienced intermittent pain in his right thigh before the injury. Plain radiographs showed a right femoral subtrochanteric fracture of the reverse oblique type (Figure 2 a). An AFF was diagnosed based on the 2013 American Society for Bone and Mineral Research Task Force definition (9).

Two days after his injury, an open reduction and intramedullary nailing was performed to treat the fracture (Figure 2 b). Bisphosphonate treatment was discontinued after the injury and low-intensity pulsed ultrasound was started. The use of teriparatide was discussed with the patient because it has risks and benefits; teriparatide has the potential to worsen calcinosis cutis (12), but can facilitate the healing of an AFF, respectively (13). The patient consented to the use of teriparatide 600 μg per day and the treatment was initiated, although teriparatide use was restricted to the period before callus formation. A month after the operation, partial

Figure 1 a-c - (a) Lateral view of left elbow radiograph revealing calcinosis cutis before teriparatide use and (b) is after teriparatide use. We could not detect the worsening of calcinosis cutis after teriparatide use. (c) It shows process in BAP and TRACP-5b throughout 14 months of treatment. The X axis shows month and injury day, the left Y axis shows the range of TRACP-5b and the right Y axis shows the range of BAP. The period for the administration of each drug shows over the top of the graph as arrows. Blue arrow shows alendronate using over 1 year, yellow allow shows teriparatide (TPTD) using 2 months and gray arrow shows denosumab 60 mg using one time. Blue line shows TRACP-5b process and red line shows BAP process, blue and red dash line shows TRACP-5b and BAP normal range respectively.
weight bearing was permitted, and two months after the operation the patient could support his full weight on his right leg. At that time, callus formation was detected at the fracture site and the teriparatide treatment was discontinued. During the treatment period, the patient's calcinosis cutis did not worsen in terms of clinical symptoms and radiological signs (Figure 1 b), although there was an increase in BAP and TRACP-5b (Figure 1 c). Six months after the operation, his femoral fracture had acquired bone union without complications such as infection and/or delayed healing of the surgical scar (Figure 2 c).

Discussion

Calcinosis is a common and an unresolved complication in JDM which causes suffering in the long-term. Although there are several reports that indicate multiple treatment strategies - including bisphosphonates - may be effective for calcinosis cutis in JDM (3, 4), at present specific medical therapies for this condition are not highly effective (1). Although glucocorticoids are important for dermatomyositis treatment (1); their use in the long-term as a treatment induces osteoporosis. For those reasons, patients with calcinosis cutis associated with dermatomyositis have no other long-term treatment options other than bisphosphonates. Bisphosphonates are the most commonly prescribed drugs to reduce the risk of osteoporosis fracture. However, long-term treatment with bisphosphonates, which can severely suppress bone turnover but is associated with an increased risk for AFF (14). In the current case, long-term bisphosphonate treatment over ten years plus later denosumab treatment resulted in severely suppressed bone turnover and an AFF occurred. Suppressed bone turnover usually delays healing of an AFF (13). The patient in our case experienced pain associated with the delayed union of a metatarsal fracture which was treated conservatively. Teriparatide, a recombinant form of parathyroid hormone (PTH), is an anabolic agent with potent bone-forming effects (15); it can enhance bone healing as has been reported in the case of AFFs (13). Two case reports have shown that when teriparatide was used for patients with calcinosis cutis, increased and extensive calcification in the soft tissues were shown by the X-ray (12). In our case, the patient underwent four surgical treatments for severe calcinosis cutis, making the choice of teriparatide treatment very controversial. After discussing the risks and benefits of teriparatide treatment with the patient, he consented to short-term use of the drug. After two months of treatment with teriparatide, his calcinosis cutis did not worsen and cal- lus formation was evident. However, we detected an associated increase in BAP and TRACP-5b. Therefore, teriparatide administration over the long-term may exacerbate calcinosis, as has been suggested in previous reports.

Conclusion

We report on the first case of an AFF in a patient who was treated with long-term bisphosphonate treatment and adjunctive denosumab for calcinosis cutis associated with JDM. We combined short-term teriparatide administration with surgical therapy for the treatment of an AFF, and we achieved bone
union without worsening of the patient’s calcinosis cutis, although not without an increase in BAP and TRACP-5b.

References


