Alendronate Therapy in Polyostotic Fibrous Dysplasia Presenting With Pathologic Fracture

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Abstract

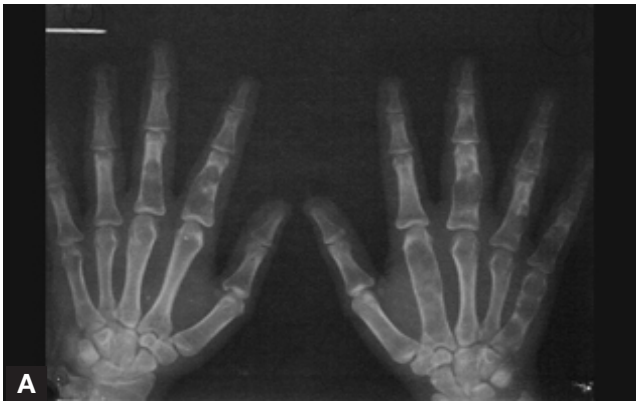
Polyostotic fibrous dysplasia (PFD) is characterized by developmental failure in the remodeling of primitive bone to mature lamellar bone. PFD presents with bone pain, increased bone fragility, deformities, and fractures. Bisphosphonates are the only agents available for medical management.[1,2] Intravenous (IV) pamidronate is the established treatment for symptomatic bone involvement in PFD.[3,4] Oral alendronate holds promise because of its comparable outcomes, lower cost, and ease of administration.[5]

The patient described in this case report provided written informed consent for its print and electronic publication after reviewing the complete manuscript and skeletal radiographic images.

Case Report

An 18-year-old woman presented with history of pain and swelling in the right middle finger after a trivial trauma. She reported occasional vague bone pains that subsided with use of analgesics. There was no past history of proximal muscle weakness, skeletal deformities, renal stones, or fractures. There were no pigmented skin lesions. Menarche had occurred at age 13 years, and the patient had had regular menstrual cycles since then. There was no family history of bone disease or fragility fractures. On physical examination, there were no skeletal deformities, café au lait spots, or proximal myopathy.

A plain radiograph of the right hand showed a closed fracture of the proximal phalanx of the middle finger. There were multiple expansile lesions with inner translucency and thinned-out cortex involving the metacarpals and phalanges. There was a similar lesion in the right superior pubic ramus (Figures 1A, 1B). The rest of the skeletal survey showed normal skull, spine, and long bones. Levels of serum calcium (8.8 mg/dL; corrected, 9.1 mg/dL; normal range, 8.8-10.5 mg/dL), phosphorus (3.6 mg/dL; normal range, 2.5-4.5 mg/dl), alkaline phosphatase (ALP; 58 IU/L; range, 60-120 IU/L), and parathyroid hormone (34 pg/mL; range, 10-65 pg/mL) were within normal limits. Serum 25-hydroxyvitamin D level was 28 ng/mL (normal, >20 ng/mL). Technetium-99 methylene diphosphonate bone scan showed increased focal uptake in the fracture site and in the areas corresponding to the lesions seen on plain radiographs. Uptake in the other bones was normal and kidneys were normal on visualization.



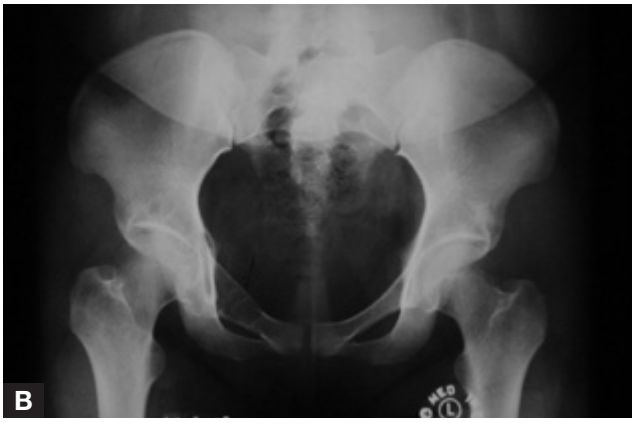


Figure 1. (A) Anteroposterior radiograph of both hands shows expansile lesions with inner translucency and thinned-out cortices of metacarpals and phalanges characteristic of polyostotic fibrous dysplasia (PFD). (B) Anteroposterior radiograph of pelvis shows expansile lesion with inner translucency and thin cortex in superior ramus of pubis on right side, characteristic of PFD.

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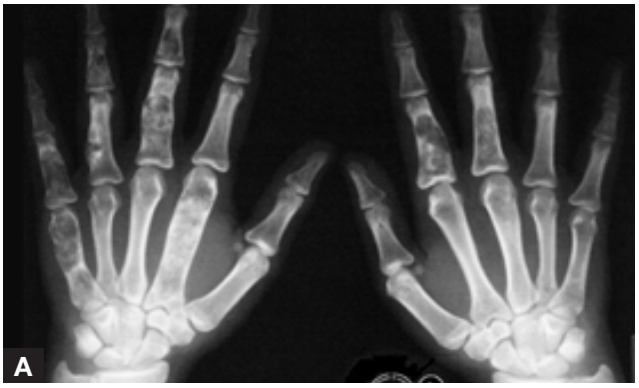


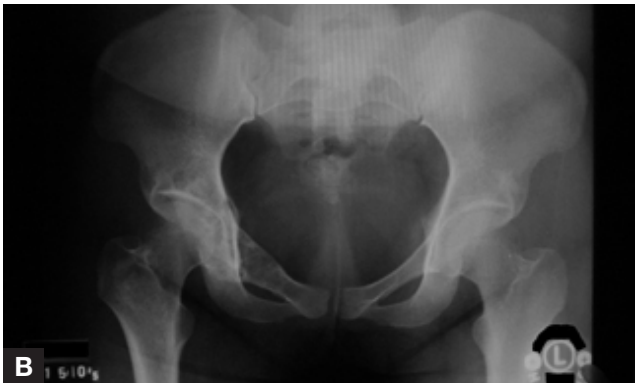
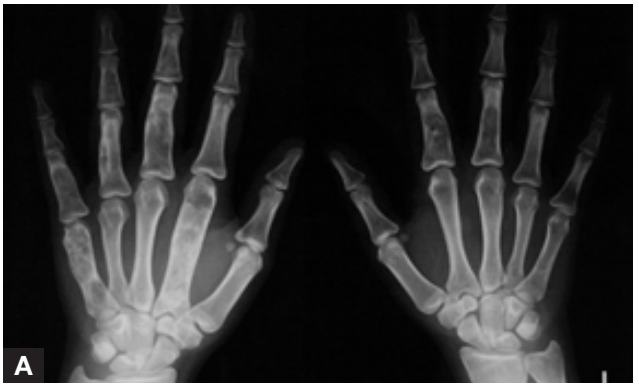


Figure 2. (A) Follow-up radiograph of both hands after 1 year of alendronate therapy shows appearance of small foci of calcification within bone lesions, thickening of cortices, and reduction in size of bone lesions. (B) Follow-up radiograph of pelvis after 1 year of alendronate therapy shows reduction in size of bone lesions, thickening of cortex, and appearance of small foci of calcification within bone lesion.



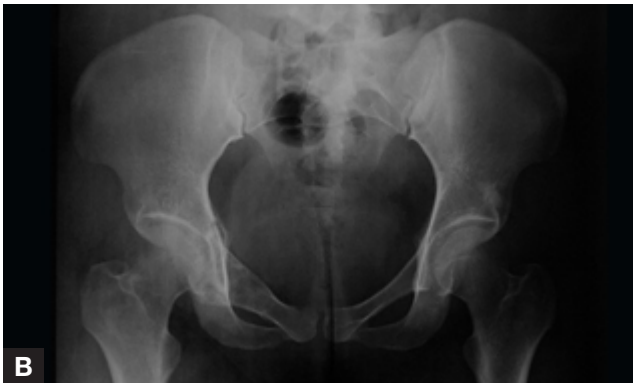


Figure 3. (A) Follow-up radiograph of both hands after 6 years of alendronate therapy shows calcification within bone lesions, thickening of cortices, marked reduction in size of bone lesions, and apparent improvement in bone density. (B) Follow-up radiograph of pelvis after 6 years of alendronate therapy shows apparent improvement in bone density, reduction in size of bone lesion, thickening of cortex, and calcification within lesion.

In view of the symptomatic lesions of PFD with a fragility fracture, the patient was treated with oral alendronate 70 mg weekly, calcium carbonate 1000 mg daily, and vitamin D (cholecalciferol) 400 IU daily. The fracture site was immobilized by strapping. Over the next 3 months, the fracture healed well, and the patient's bone pains subsided. Annual follow-up radiographs showed reductions in lesion size, partial refilling, and ossification within the lesions with an increase in cortical thickness. Overall improvement in apparent bone density was noted on plain radiographs (Figures 2A, 2B).

During follow-up, a single, progressively enlarging euthyroid cystic nodule was detected in the right lobe of the thyroid (thyroid simulating hormone, 2.3 mIU/L). Fine-needle aspiration cytology results were indeterminate. A right hemithyroidectomy was performed; the histopathology of the nodule was benign.

After 6 years of oral alendronate therapy, the patient's bone lesions were markedly improved (Figures 3A, 3B). Levels of corrected serum calcium (9.7 mg/dL), phosphorus (3.6 mg/dL), and ALP (82 IU/L) were within normal limits. We found no fracture recurrence, radiologic evidence of osteopetrosis, or adverse effects of long-term bisphosphonate-like osteonecrosis of the jaw.

Discussion

Our patient, an 18-year-old woman with a fragility fracture of the proximal phalanx, was incidentally found to have PFD. There were no other features of McCune-Albright syndrome in the form of café au lait lesions or endocrinopathy. Six years of weekly treatment with oral alendronate at standard dosage resulted in clinical improvement and no fracture recurrence. Plain radiography showed reductions in lesion size, increased cortical thickness, and ossification within the lesions. There were no adverse effects of long-term bisphosphonate therapy.

Fibrous dysplasia is caused by somatic activating mutations of the gene encoding the α subunit of the stimulatory G protein. There is a developmental failure in the remodeling of primitive bone to mature lamellar bone. Immature isolated trabeculae enmeshed in dysplastic fibrous tissue do not complete the remodeling process and fail to mineralize normally. The combination of a lack of stress alignment and insufficient mineralization results in a weak bone, leading to pain, deformity, and pathologic fractures. The lesions are usually focal and may be monostotic or polyostotic (with or without features of McCune-Albright syndrome). On plain radiography, the lesions have a radiolucent appearance with a grayish "ground-glass" pattern that

is similar to the density of cancellous bone but is homogeneous and has no visible trabeculae.[6]

Decreased bone strength in fibrous dysplasia predisposes to fragility fractures. Fractures have been noted in the long bones of upper and lower limbs.[7] Fractures of short bones, like metacarpals and phalanges, as occurred in our patient, are uncommon.

Although there is no clear evidence of increased osteoclastic activity in PFD, the benefits of using antiresorptives (eg, bisphosphonates) in the treatment of this condition have been significant. Bisphosphonates are safe and effective in reducing bone pain and incidence of fractures in PFD.[1,8,9] In adults, good response to pain and filling up of lesions have been noted.[10] In children, there is significant pain relief with bisphosphonates, but bone lesions may persist.[3,5,9]

Whereas the benefits of intravenous (IV) pamidronate therapy are well documented, only a few studies of oral alendronate have been reported. Those studies, however, have found that oral alendronate has comparable benefits to IV administration, offers the convenience of oral administration, and has a lower cost of therapy.[1,5,8]

The benefits and safety of long-term bisphosphonate therapy (up to 10 years' duration) have been documented.[11] Jaw osteonecrosis and bone fragility, caused by excessive suppression of bone turnover, leading to unusual shaft fractures of long bones, are seldom noted. A drug-free interval is advised after 5 to 6 years of use in postmenopausal women at low risk for fracture.[11] A similar advisory does not exist for PFD, and decisions need to be based on severity of bone lesions and fracture risk.

Bisphosphonate treatment was indicated in our patient's case because of her multiple lesions in hand bones and her pelvis presenting with fracture and bone pains. Alendronate was preferred given the restricted availability and prohibitive costs of IV pamidronate. Over 6 years of treatment, the patient showed marked improvement in bone pain, no fracture recurrence, and no adverse effects of alendronate. Plain radiography showed reductions in lesion size, increased cortical thickness, and ossification within the lesions. Serum calcium, phosphorus, and ALP levels were normal before treatment and at follow-up. Although 25-hydroxyvitamin D levels were normal as per standards at time of therapy initiation, we treated the patient with calcium and cholecalciferol in adequate maintenance dosage. The possible adverse affects of alendronate on the fetus was explained to the patient, and she was advised to inform us regarding any plans for conception in the near future.

Evidence regarding the effect of bisphosphonates on fracture healing is mixed, but most reports suggest that fracture healing occurs unimpeded with bisphosphonates.[12] We proceeded with bisphosphonate therapy for our patient with a minor fracture, kept a close watch on fracture healing, and noted it was adequate.

Monitoring bisphosphonate therapy with bone resorption markers like N-telopeptide to avoid oversuppression of bone turnover is well accepted. Given the nonavailability of this test in our area, however, we had to monitor our patient only with serial radiographs and serum biochemistry. There was no evidence of osteopetrosis or adynamic-bone-disease–like changes on serial skeletal radiographs. We plan to closely watch for these effects during follow-up.

In reporting on this young woman's case of PFD, we have highlighted its unusual involvement of the small bones of the hand and the pelvic bone. We have also highlighted the safe and effective use of long-term oral alendronate therapy in the successful treatment of PFD presenting with a pathologic fracture.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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