Treatment Of Fibrous Dysplasia With Zoledronic Acid Infusion Case Report, Review Of Literature And Future Prospectives

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Abstract

Several studies have shown that bisphosphonates are useful in alleviating chronic pain in patients with fibrous dysplasia, but further studies are necessary to confirm these promising results. Being the most potent bisphosphonate we treated one patient of distal femur fibrous dysplasia with Zoledronic acid and would like to share our experience as a case report. 52 years old male patient presented in out-patient department complaining of pain and swelling of left thigh lower aspect for approximately eight months. An open biopsy was performed and diagnosis of fibrous dysplasia was confirmed. Due to location of lesion and financial restraints patient was treated with intravenous Zoledronic acid. There was significant functional improvement and reduction of alkaline phosphatase level to normal within a period of six months. Hence it was considered to report this case as it may add up to the available data of usage of Zoledronic acid in treating fibrous dysplasia.

Introduction

Fibrous dysplasia is a developmental anomaly of bone-forming mesenchyme that manifests as a defect in osteoblastic differentiation and maturation. The term fibrous dysplasia was suggested by Lichtenstein and Jaffe in 1942. The etiology of this abnormal growth process is related to a mutation in the gene that encodes the subunit of a stimulatory G protein (Gs α) located on chromosome 20. Mechanical quality of bones is decreased. As a consequence, bones are fragile and patients have an increased risk of developing deformities, pain and pathological fractures. Abnormalities may involve 1 bone in the monostotic form (70% of cases) or many bones in the polyostotic form (30% of cases). The polyostotic form is occasionally associated with precocious puberty and cafe-au-lait skin lesions (McCune-Albright syndrome) or with myxomas of skeletal muscle (Mazabraud syndrome). Fibrous dysplasia can occur anywhere but is usually found in the proximal femur, tibia, humerus, ribs, and craniofacial bones in decreasing order of incidence. Usually, fibrous dysplasia presents clinically in children and adolescents, with a median onset age of 8 years. Most cases manifest themselves before the age of 30 years. Monostotic fibrous dysplasia may be completely asymptomatic and is often an incidental finding on x-ray. Patients usually seek medical care because of either painful swelling and deformity or a pathologic fracture through a weakened bone. Asymptomatic patients do not need treatment. Surgical treatment of fibrous dysplasia is indicated in the prevention or treatment of fractures or major deformity. Several studies have shown that bisphosphonates are useful in alleviating chronic pain in patients with fibrous dysplasia. Zoledronic acid is the most potent bisphosphonate that has been studied in clinical trials to date. Being the most potent bisphosphonate we treated one patient of distal femur fibrous dysplasia with Zoledronic acid and would like to share our experience as a case report.

Case Report(s)

52 years old male patient presented with complaints of pain and swelling of left thigh lower aspect for approximately eight months. Patient noted progressive swelling which was of insidious onset and gradually increased in size. Patient also developed dull aching continuous pain, aggravated by activities and relieved by rest and analgesics. Patient a tailor by occupation had significant restriction of day to day activities like sitting cross legged, squatting, etc. There was no history of trauma or fever. No other co-morbidities like diabetes, hypertension present.

On examination general physical profile was normal with no relevant findings. Local examination revealed a diffuse, ill-defined, hard, globular swelling involving entire left distal femur. Surface was smooth, hard in consistency with ill-defined borders. Skin over the swelling was normal. There was no localized lymphadenopathy and distal neuro-vascular deficit. Laboratory investigations revealed significant elevation of alkaline phosphatase. Clinically parosteal osteosarcoma and chondrosarcoma were the
differential diagnosis. Radiography, CT scan and MRI were done and both reports suggested fibrous dysplasia. So an open biopsy was performed to confirm the diagnosis. The report came out to be fibrous dysplasia. No evidence of malignancy was noted. Routine haematological and biochemical investigations and oral examination were done. Pre-existing hypocalcaemia and altered renal function were ruled out.

The patient was given an infusion of 5mg of intravenous Zoledronic acid as an infusion after adequate hydration. After 24 hours he developed myalgia, polyarthralgia and mild fever which persisted for 72 hours and then subsided. The patient was put on regular 3 month follow up and was also restricted from activities that can stress distal femur significantly like running, jumping, sitting cross legged, squatting etc. He was advised to use a walking stick in the opposite hand for three month period. After 6 month and after one year evaluation there was significant functional improvement and reduction in pain. The alkaline phosphatase value normalized and is maintained in normal range till now. He was given another dose of 5mg of intravenous Zoledronic acid as an infusion one year later and now after an approximate two year follow-up he is having significant reduction in pain, better functional abilities and a normal alkaline phosphatase level. There is no increase in size of lesion as noted by limb girth measurements. There is neither a decrease in size of lesion. A CT scan performed at the end of one and a half years showed no significant filling of the lytic lesion. At the time of the latest follow up evaluation, no lesion had been resorbed with persistence of the lesion. At the time of the latest follow up evaluation, no lesion had been eradicatd or had decreased in size. The other treatment options had limitations like affordability, availability of allograft or prosthesis, morbidity associated with the procedure as well as the active lifestyle of the patient which may lead onto early failure.

The surgical treatment options available are curettage and bone grafting and if more radical procedure is required, resection and reconstruction with custom made prosthesis or osteo-allografts. Curettage and Cancellous or cortical bone grafting did not appear to have any advantage in the treatment of symptomatic lesions. All grafts resorbed with persistence of the lesion. At the time of the latest follow up evaluation, no lesion had been eradicatd or had decreased in size. The other treatment options had limitations like affordability, availability of allograft or prosthesis, morbidity associated with the procedure as well as the active lifestyle of the patient which may lead onto early failure.

Response to therapy was monitored by serial measurements of alkaline phosphatase levels and assessment of Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36), which assesses eight aspects of health status: general and mental health, physical and social functioning, physical and emotional roles, pain and vitality; scores on each scale can range from 0 (worst) to 100 (best). Alkaline phosphatase level normalized within 6 months of treatment and the physical component summary score of the Medical Outcomes Study 36-item Short-Form
General Health Survey, a measure of quality of life, increased significantly from baseline at 6 months. Pain score also improved significantly. Alkaline phosphatase level remained normal in these two years as well as the SF – 36 remained significantly improved.

It is encouraging that the marked biochemical effects of Zoledronic acid appeared to be accompanied by significant improvements in indexes of quality of life, physical functioning, pain, general health, vitality and emotional well being. Despite previous reports of limitation or reduction in size of fibrous dysplasia lesions, it is our experience that bisphosphonate treatment of fibrous dysplasia does not arrest the expanding nature of these lesions whilst apparently safe and providing continuing pain control. Our findings confirm the efficacy of Zoledronic acid in patients with fibrous dysplasia and add substantially to the available data by demonstrating that prolonged remission can be achieved, accompanied by improvements in quality of life. Although early results are encouraging, many questions remain about optimizing their use for fibrous dysplasia therapy. Management of FD has previously consisted of either conservative follow-up or surgery depending on disease activity and localization. Bisphosphonates may be suitable especially for lesions in which surgical treatment is particularly challenging.

Despite these promising results, FDA reports have surfaced about serious adverse effects associated with bisphosphonates which include jaw osteonecrosis, atrial fibrillation and medication-induced fractures. For suspected adverse events, including atrial fibrillation and medication-induced fractures, more data is needed before final recommendations can be made. We need to move from smaller, retrospective series to long-term studies with well-controlled data collection before indications and contraindications for bisphosphonate use can be better defined.

Abbreviations(s)

FD: Fibrous Dysplasia

References

Illustrations

Illustration 1

LATERAL RADIOGRAPH

Illustration 2

ANTEROPOSTERIOR RADIOGRAPH
Illustration 3

CT SCAN IMAGES
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