

Polyostotic Fibrous Dysplasia of Humerus and Radius – A Rare Case Report



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Abstract

Introduction: Fibrous dysplasia (FD) is a fibro-osseous benign lesion characterized by replacement of osseous tissue with fibrous tissues. FD is due to mutation of Gsα gene. FD has equimodal sex distribution and spans in the age group from 1st to 7th decade. The various forms of FD are monostotic, polyostotic and panostotic FD. Malignant transformation in fibrous dysplasia is about 0.4-4%. Treatment aspect involves use of bisphosphonates or prophylactic surgical management. Recurrence of fibrous dysplasia is very rare when the lesion has occurred in adults.

Case Report: 20 years old female patient presented with pain and deformity over right arm and forearm from past 5 years. The patient noticed a visible deformity over right arm which was gradually progressive and associated with increased intensity of pain. On examination, diffuse tenderness and visible deformity were noted over right arm and forearm. There were no abnormal mobility or crepitus in right arm and forearm segments. The range of movements over right shoulder, right elbow and right wrist were near normal with terminal painful movements. Elevation of serum ALP and low levels of vitamin D3 were noticed. Radiography of right arm and forearm shows the evidence polyostotic pattern of fibrous dysplasia of whole length humerus and radius with ulnar sparing. The patient was posted for open biopsy of distal humerus and subjected for histopathological examination which confirmed the diagnosis. The patient has been managed with bisphosphonates, calcium and vitamin D3 supplementation.

Discussion: Fibrous dysplasia is a non-neoplastic fibrous tissue proliferative disorder of bone. Since the patient does not have any symptoms of imminent fracture, she has been managed conservatively with oral bisphosphonates, calcium and vitamin D3 supplementation for 24 weeks. Every month patient is assessed with radiographs and serum vitamin D3, calcium, phosphorus and alkaline phosphate. The patient is followed up for one year which show no recurrence, decreased pain and improved functional quality of life.

Conclusion: Early diagnosis and treatment of fibrous dysplasia must be administered to prevent complications. A long term follow up is needed to evaluate the recurrence, disappearance of deformity and malignant transformation.

Keywords: Polyostotic; Fibrous dysplasia; Bisphosphonates; Vitamin D3

Introduction

Fibrous dysplasia (FD) is a non-neoplastic, benign, fibro-osseous condition characterized by replacement of bone with fibrous tissues [1]. FD represents 5 – 7 % of all benign bone tumours. The pathogenesis involved in development of fibrous dysplasia is unclear but recent studies suggest that genetic factors are responsible for fibrous dysplasia. FD is linked with mutation of Gsα gene located in chromosome 20q13.2-13.3 [2]. FD appears in equimodal distribution in males and females. The most frequent site of disease manifestation is maxilla, proximal femur, tibia > humerus, ribs, radius and iliac bone. The forms of FD are monostotic, polyostotic and panostotic FD. Polyostotic FD is associated with McCune-Albright syndrome and endocrinal disturbances [3]. Fibrous dysplasia is seen in metaphysis of long bones. This article outlines a case of polyostotic fibrous

dysplasia of humerus and radius in a menstrually active female patient without features of McCune Albright syndrome with ulnar sparing. The patient has been subjected for biopsy to confirm the diagnosis and managed conservatively with bisphosphonates, calcium and vitamin D3 supplementation. The patient was followed up for 1 year for recurrence of disease and the functional outcome.

Case Report

Here we report a case of 20 years old female patient came to JJM Medical College with a chief complaint of pain and deformity over right arm and forearm from past 5 years. The onset of pain over right arm and forearm was insidious, dull aching, non-progressive, non-radiating, aggravated on movements and partially relieved by rest and medications. The patient noticed a

visible deformity over right arm which was gradually progressive and associated with increased intensity of pain. The patient had no clinical evidence of thyroid or menstrual disturbances.

On examination, diffuse tenderness was noted over right arm and forearm. An obvious visible deformity of arm was seen. There were no abnormal mobility or crepitus in right arm and forearm segments. The range of movements over right shoulder, right elbow and right wrist were near normal with terminal painful movements. Thyroid and spine were clinically normal.

Investigations

- a) Hemogram
 - Hb – 11.2 gm/dL
 - Total count – 7800 cells/mm³
 - RBC – 3.6 million/mm³
 - Platelets – 2.19 lakh cells/mm³
 - ESR – 19 mm/hour
 - CRP – 6 mg/L
- b) Renal Function Tests – Urea 34 mg/dL and creatinine 0.9 mg/dL
- c) Random blood glucose – 78 mg/dL
- d) HIV and HbsAg – Non reactive
- e) Serum calcium – 5.7 mg%
- f) Serum phosphorus – 4.2 mg%
- g) Serum alkaline phosphatase – 1479 IU/L
- h) Serum Vitamin D3 – 4.9 ng/mL
- i) Radiography of right arm and forearm shows the evidence of expansile, lytic lesion over metaphysis and diaphysis of humerus and radius showing ground glass matrix without any significant periosteal reaction suggestive of polyostotic pattern of fibrous dysplasia with complete sparing of ulna (Figures 1a & 1b).

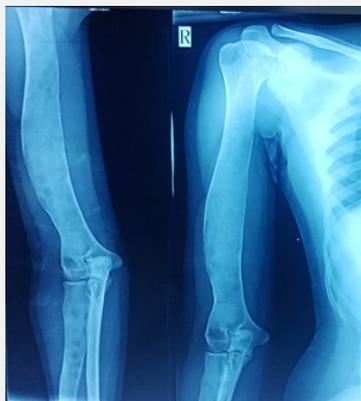


Figure 1a: X ray of humerus – AP & Lateral views.



Figure 1b: X ray of forearm – AP & Lateral views.

j) CT scan of right arm and forearm shows polyostotic pattern of fibrous dysplasia of right humerus and radius with ulnar sparing (Figures 2a-2d)



Figure 2a: CT 3D reconstruction of right humerus and radius & ulna.



Figure 2b: Plain CT right humerus with fibrous dysplasia.



Figure 2c: Plain CT right radius with fibrous dysplasia.

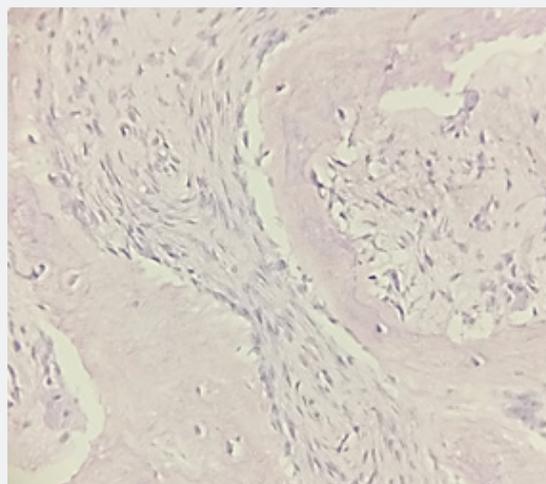


Figure 3b: (40x).



Figure 2d: Plain CT right ulna (deformity spared).

After taking informed and written consent, patient was subjected for biopsy of the lesion. Open biopsy of the lesion was performed under GA over distal end of right humerus. The biopsy report shows trabeculae of woven bone which lacks osteoblastic rimming in a Chinese letter pattern surrounded by fibroblastic proliferation admixed with few osteoclast-like giant cells (Figures 3a & 3b).

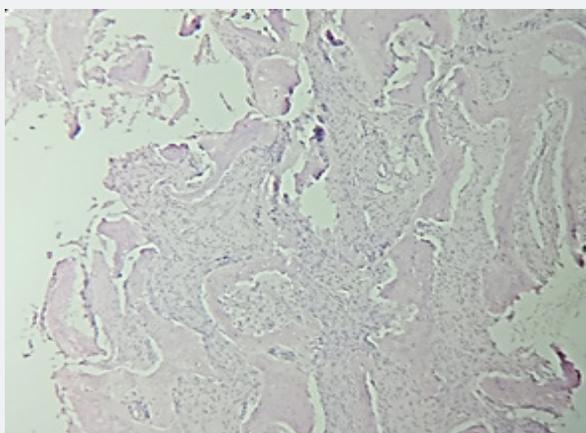


Figure 3a: (10x).

Then the patient was treated with oral risedronate 35 mg once weekly for 24 weeks, calcium and vitamin D3 combination tablets once daily for 6 months. The patient was reviewed every month with serial X rays (Figures 4a-4d) and serum calcium, phosphorus, alkaline phosphatase and vitamin D3 levels to monitor the response to treatment. The patient has been explained about the natural course, outcome and prognosis of the disease. Reassurance was given and the patient was discharged with the advice to retard heavy weight lifting and to perform daily routine activities with caution which will improve the functional quality of life.



Figure 4a: 1 month follow up X ray of humerus – AP and Lateral views.



Figure 4b: 1 month follow up X ray of forearm – AP and Lateral views.



Figure 4c: 6 months follow up X ray of humerus – AP and Lateral views.



Figure 4d: 6 months follow up X ray of forearm – AP and Lateral views.

Discussion

Fibrous dysplasia is a developmental anomaly of the bone characterized by replacement of normal bone and bone marrow by a fibrous tissue. It is a benign fibro-osseous intramedullary lesion, usually involving the long bones [1]. Fibrous dysplasia is caused by mutation in the *GNAS1* (guanine nucleotide binding protein, alpha stimulating activity polypeptide) gene (20q13.2-13.3) and this gene encodes a G-protein which results in overproduction of cAMP in the affected tissues. Furthermore, there is increased the proliferation of melanocytes thus results in cafe-au-lait spots. The cAMP has effect on the differentiation of osteoblasts [2].

In fibrous dysplasia, the differentiation of stromal cells is arrested and undergo proliferation into fibro-osseous mass of tissue. Arrest in this differentiation is due to the mutation of the *GNAS* gene which codes alpha subunit of signalling G- protein. In > 95% cases arginine is replaced by either cysteine or histidine (R201C or R201H). This result in inhibition of intrinsic GTPase activity of Gs alpha protein and it is this aspect that leads to constitutive, ligand-independent generation of intercellular cAMP. IL-6 secretion is responsible for increased osteoclastic activity seen in fibrous dysplasia [2,3].

Fibrous dysplasia has three clinical patterns namely monostotic, polyostotic or panostotic. Monostotic FD (70 – 85%) occurs in single bone and ceases with the onset of menarche. Polyostotic FD (10 – 15%) occurs in multiple bones in a unilateral distribution and tends to continue after skeletal maturity and leads to severe skeletal deformity. 3% of lesions are associated with skin hyperpigmentation and hyper-functioning endocrine disorders which is known as McCune-Albright syndrome [3,4]. Panostotic FD (<1%) is very rare and occurs throughout the body. Pain, fractures and deformity are the common clinical presentation of fibrous dysplasia. Abnormal growth of craniofacial bones will result in entrapment of cranial nerves. Oestrogen receptors are excess in this condition resulting in increased pain level during menstrual cycle and pregnancy [5,6].

Malignant transformation in fibrous dysplasia is about 0.4-4% which is most likely to occur in polyostotic forms [7]. Most common histological types of malignant transformation are osteosarcoma, chondrosarcoma and fibrosarcoma. Treatment aspect involves use of bisphosphonates for inhibiting osteoclastic resorption, various studies shows high dose IV pamidronate for decreasing pain and the markers of bone metabolism [8].

Management of fibrous dysplasia depends on symptoms. Asymptomatic FD patients' needs no surgical management [9]. Symptomatic FD patients require medical management in the form of bisphosphonates and prophylactic management in the form of curettage and bone grafting. If patients present with impending fracture, then prophylactic fixation with load sharing devices [10]. Recurrence of fibrous dysplasia is very rare when the lesion has occurred in adults. The reason behind recurrence

is because of inadequate medical management and unsuccessful removal of lesion. Patients with craniofacial FD have 15% to 20% of recurrence. The hematological marker for recurrence of FD is serum alkaline phosphatase. Park et al confirmed the higher serum ALP levels indicates the progression of tumour [11]. The differential diagnosis for fibrous dysplasia is chondroma, simple bone cyst, non-ossifying fibroma, adamantinoma, chondroblastoma and low-grade intramedullary osteosarcoma [12].

Our patient has presented with pain and deformity over right arm and forearm from past 5 years. She was further evaluated which shows the elevation of serum alkaline phosphatase and

decreased serum vitamin D3 levels. Radiograph of right arm and forearm shows the classical features of polyostotic fibrous dysplasia with ulnar sparing and without any pathological fractures. CT scan of right arm and forearm outlined the delineation between normal and diseased process of the bony architecture. The patient was offered for open biopsy of right distal humerus with GA. Then the histopathological report showed trabeculae of woven bone which lacks osteoblastic rimming in a Chinese letter pattern surrounded by fibroblastic proliferation admixed with few osteoclast-like giant cells which confirmed the diagnosis of polyostotic fibrous dysplasia of humerus and radius with ulnar sparing (Table 1).

Table 1: Serological battery Panel.

Duration	Serum Calcium	Serum Phosphorus	Serum Alkaline Phosphatase	Serum Vitamin D3 Levels
Before the start of treatment	5.7 mg%	4.2 mg%	1479 IU/L	4.9 ng/mL
At the end of 1 st month	6.9 mg%	4.54 mg%	891 IU/L	9.41 ng/mL
At the end of 6 th month	8.1 mg%	5.01 mg%	317 IU/L	14.46 ng/mL
At the end of 12 th month	10.3 mg%	5.43 mg%	91 IU/L	26.91 ng/mL

The patient was offered with medical management with tablet risedronate 35 mg once weekly, tablet calcium aspartate 500 mg once daily and capsule vitamin D3 60,000 U once weekly for a total duration of 24 weeks. The patient was followed up every monthly interval with serial radiographs and serum calcium, phosphorus, alkaline phosphatase and vitamin D3 levels which were normalized at the end of 1 year follow up. The patient was further followed up for 1 year which show no recurrence, malignant transformation over the existing lesion, decreased intensity of pain and improved functional quality of life.

Conclusion

Early diagnosis and treatment of fibrous dysplasia must be administered to prevent complications. A long term follow up is needed to evaluate the recurrence, disappearance of deformity and malignant transformation. The combination of bisphosphonates, calcium and vitamin D3 supplementation forms the gold standard treatment modality of symptomatic cases without the signs of fractures.

Conflict of Interest

Nil.

Acknowledgement

Nil.

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Nil.

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