Fibrous dysplasia-recent concepts

N. Anitha, S. Leena Sankari, L. Malathi, R. Karthick

Department of Oral Pathology, Sree Balaji Dental College and Hospital, Bharath University, Chennai, Tamil Nadu, India

Address for correspondence:
Dr. N. Anitha,
E-mail: dranitha.nnr@gmail.com

Received : 31-10-14
Review completed : 31-10-14
Accepted : 09-11-14

ABSTRACT

Fibrous dysplasia (FD) is a benign intramedullary fibro-osseous lesion. FD is a bone developmental anomaly characterized by replacement of normal bone and marrow bone by fibrous tissue. It involves any of the bones as single lesion (monostotic) or in multiple bone lesions (polyostotic) or all of the skeletal system (panostotic). Long bones are most commonly involved, which mostly identified incidentally and clinically appears asymptomatic. Clinical, radiographical and histopathological findings will help in confirming the lesion. There are many treatment option available, but still management of FD remains challenging.

KEY WORDS: Bone, fibro-osseous lesions, fibrous dysplasia

Fibro-osseous lesions are a diverse group of processes that characterized by replacement of normal bone by fibrous tissue containing a newly formed mineralized product. The commonly included fibro-osseous lesions are fibrous dysplasia (FD), cemento-osseous dysplasia and ossifying fibroma. FD is a developmental tumor like a condition characterized by replacement of normal bone by an excessive proliferation of cellular fibrous connective tissue intermixed with irregular trabeculae.[1]

Etiology

Fibrous dysplasia is not hereditary in nature and it caused by mutation in the GNAS1 (guanine nucleotide binding protein, alpha stimulating activity polypeptide) gene (20q13.2) 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 have effect on the differentiation of osteoblasts.[2]

Access this article online

Quick Response Code:

Website: www.jpbsonline.org

DOI: 10.4103/0975-7406.155892

Clinical Features

Fibrous dysplasia has three clinical patterns namely monostotic, polyostotic, craniofacial form. About 3% of lesions associated are with skin pigmentation and hyperfunctioning endocrine disorders known as the McCune–Albright syndrome.[3] FD in infancy is rare and heralds severe widespread disease with multiorgan involvement. Pain, fracture and deformity are common clinical features. The pain complaint is less in children and more in adults. The skull base and proximal metaphysic of femora are two sites most commonly involved. In the skull FD involves skull bases and facial bones. In childhood FD presents as facial asymmetry or a bump, but symmetric expansion of malar prominences and/or frontal bosses may be seen. Due to abnormal growth and deformity of craniofacial bones may result in encroachment on cranial nerves.[4] Female patients experience increased pain level during pregnancy and during the menstrual cycle because of estrogen receptors found in FD.[5]

Pathophysiology

Bianco *et al.* demonstrated that FD is a disease of bone marrow stromal cells (BMSC).[6,7] The BMSCs form structural framework upon which hematopoiesis occurs in the bone marrow and a subset of BMSC are multipotent stem cells capable of differentiating into multiple cells including osteoblasts, osteocytes, chondrocytes, bone marrow adipocytes and other cells.[8] In FD BMSC differentiate along osteogenic lineage, but differentiation is arrested and instead undergo

How to cite this article: Anitha N, Sankari SL, Malathi L, Karthick R. Fibrous dysplasia-recent concepts. J Pharm Bioall Sci 2015;7:S171-2.

proliferation giving rise to fibro-osseous masses of tissue.[9] Arrest in differentiation is by mutation in GNAs gene. GNAs codes alpha subunit of signaling G-protein.[10,11] G-protein is central in cell originating pathway leads to the generation of intracellular second messenger, cAMP/protein kinase A signaling. All mutation in Gs alpha identified in association with FD is the 201^{Arg} position. 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.[9]

Gs alpha mutation increased intracellular cAMP and interleukin-6 secretion. Interleukin-6 is responsible for increased numbers of osteoclasts and bone resorption seen in FD. Gene amplification techniques such as polymerase chain reaction is now possible to test for genetic mutation in peripheral blood samples.[5]

Diagnosis

The radionuclide bone scintigraphy is useful to demonstrate the extent of disease. Actively formed lesions in adolescents have greatly increased isotope update that corresponds closely to radiographic extent of the lesion. Some characteristic feature is bar-shaped pattern, whole-bone involvement and close match between the size of the lesion on radiograph and the size of the area of uptake. The extent of the lesion is visible clearly on computed tomography, and cortical boundary is depicted more clearly than radiograph. The thickness of cortex, endosteal scalloping and periosteal new bone reaction and homogeneity of the poorly mineralized lesional tissue are well demonstrated.

Delicate trabeculae of immature bone with no osteoblastic rimming enmeshed within a bland fibrous stroma of dysplastic spindle-shaped cells without any cellular features of malignancy. Variable number of immature, nonstress oriented, disconnected dysplastic trabeculae floating in a sea of immature mesenchymal cells that have little or no collagen about them.[5]

Malignant Transformation

Malignant transformation in FD occurs very rarely, about 0.4–4%.[12] Change is noticed. The malignant transformation rate is unknown, but it is likely to be not >1%. Cancer is more likely to occur in polyostotic disease, and most common histological types were osteosarcoma, fibrosarcoma and chondrosarcoma. There are also reports suggesting that the malignant transformation may be more common in Mazabraud's syndrome (FD in association with intramuscular myxomas).[9]

Treatment

Bisphosphonates were postulated to inhibit osteoclastic resorption. The findings in various studies showed that high dose intravenous pamidronate decreases pain and the markers of bone metabolism.[9]

References

1. Neville BW, Damm DD, Allen CM, Bouquot J. Textbook of Oral and Maxillofacial Pathology. 3rd Edition, Elsevier; 2008. p. 553.
2. Shafer WG, Hine MK, Levy BM. Textbook of Oral Pathology. 7th edition, Elsevier; 2012. p. 710.
3. McCarthy EF. Fibro-osseous lesions of the maxillofacial bones. Head Neck Pathol 2013;7:5-10.
4. Collins MT, Bianco P. American Society for Bone and Mineral Research. Ch. 76. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 8th Edition;2003. p. 467.
5. DiCaprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, evaluation, and treatment. J Bone Joint Surg Am 2005;87:1848-64.
6. Bianco P, Kuznetsov SA, Riminucci M, Fisher LW, Spiegel AM, Robey PG. Reproduction of human fibrous dysplasia of bone in immunocompromised mice by transplanted mosaics of normal and Gsalpha-mutated skeletal progenitor cells. J Clin Invest 1998;101:1737-44.
7. Bianco P, Robey Pg. Diseases of bone and the stromal cell lineage. J Bone Miner Res 1999;14:336-41.
8. Bianco P, Riminucci M, Gronthos S, Robey PG. Bone marrow stromal stem cells: Nature, biology, and potential applications. Stem Cells 2001;19:180-92.
9. Leet Al, Collins MT. Current approach to fibrous dysplasia of bone and McCune-Albright syndrome. J Child Orthop 2007;1:3-17.
10. Weinstein LS, Shenker A, Gejman PV, Merino MJ, Friedman E, Spiegel AM. Activating mutations of the stimulatory G protein in the McCune-Albright syndrome. N Engl J Med 1991;325:1688-95.
11. Schwindinger WF, Francomano CA, Levine MA. Identification of a mutation in the gene encoding the alpha subunit of the stimulatory G protein of adenylyl cyclase in McCune-Albright syndrome. Proc Natl Acad Sci USA 1992;89:5152-6.
12. Harris WH, Dudley HR, Barry RJ. The natural history of fibrous dysplasia, an orthopaedic, pathological and roentgenographic study. Am J Orthop 1962;44:207-33.

Source of Support: Nil, **Conflict of Interest:** None declared.