Bangladesh Medical Res Counc Bull 2024; 50: 111-115 DOI: 10.3329/bmrcb.v50i2.75574

CASE REPORT

Giant Cell Tumour of the Skull Bone in a Patient with Paget's Disease of the Skull Bone- A Case Report

Kaisar Haroon[1*], Md. Shafiul Alam[2], Md. Nowfel Islam[3]

[1]Department of Neurosurgery, National Institute of Neurosciences and Hospital, Agargaon Dhaka, Bangladesh, [2]Department of Gamma Knife, National Institute of Neurosciences and Hospital, Agargaon Dhaka, Bangladesh, [3]Department of Neuropathology, National Institute of Neurosciences and Hospital, Agargaon Dhaka, Bangladesh.

Abstract:

Background: Paget's disease of bone (PDB) is a localized disorder of bone remodeling resulting in abnormal bone architecture. It is a chronic and slowly progressive disorder. The disease was first described in England, in 1877, by Sir James Paget who defined it with the name of "osteitis deformans".

Objectives: This patient underwent craniotomy for excision of the swelling. The bony destruction was reconstructed using titanium mesh.

Methods: A forty seven years old lady suffering from Paget's disease, presented to us with a progressive firm swelling in the front of the left frontal bone including the orbit. She was operated upon and her swelling was diagnosed as Giant cell tumour.

Results: After surgery she became well and orbital swelling had subsided and she had a good cosmetic appearance.

Conclusion: surgery is the main options for GCT. Patients with Paget's disease have a tendency to have GCT, and this should be kept in the mind during diagnosis.

Keywords: Giant cell tumour, Paget's disease, Titanium mesh, Alkaline phosphatase, Bangladesh.

Introduction

Paget's disease of bone (PDB) is a localized disorder of bone remodeling resulting in abnormal bone architecture. It is a chronic and slowly progressive disorder involving a single bone location (monostotic) or more than one site (polyostotic)[1]. The disease was first described in England, in 1877, by Sir James Paget who defined it with the name of "osteitis deformans"[2].

In Asian countries including Japan, PDB is an extremely rare disease. The Japan National Survey conducted in 2003 identified only 169 cases of PDB. The incidence of PDB in Japan is 0.15 cases per 100,000 general population, and 0.41 cases per 100,000 population over 55 years old[3]. No similar data is available for our country.

The main risk factors for PDB include increasing age, male sex, and ethnic background[4]. The new results indicated that GCT/PDB is caused globally by the P937R mutation in the ZNF687 gene[5]. Giant cell tumor (GCT) of bone is an uncommon, primary neoplasm that occurs chiefly in the ends of the long bones. GCT is rarely encountered in the skull[6].

There is a general agreement that the primary cell abnormality in Paget's bone disease involves the osteoclasts. Pagetic osteoclasts are markedly increased in number and size, can have as much as 100 nuclei per cell, and contain paramyxoviral like nuclear and cytoplasmatic inclusion[7].

Paget's disease increases the risk of various malignant tumors such as osteosarcoma, fibrosarcoma, chondrosarcoma, malignant fibrous histiocytoma, and very rarely locally aggressive tumor-like giant cell tumor (GCT). The reported cases of GCT complicating Paget's occur mainly in polyostotic disease[8].

GCTs associated with PDB have features distinct from conventional GCTs. GCTs complicating PDB occur in the regions affected by PDB, such as the skull and facial bones, while conventional GCTs arise most

***Correspondence:** Kaisar Haroon, Department of Neurosurgery, National Institute of Neurosciences and Hospital, Agargaon Dhaka, Bangladesh.*
e-mail address: kaisar298@gmail.com
ORCID ID: 0000-0002-3065-7877

commonly in long bones, especially in the area of the knee joint[3]. Rendina et al also in their comparative study of large European studies have concluded that GCT-PDB occurs in the axial skeleton[9].

Alterations in certain laboratory parameters, such as levels of osteocalcin (OC), serum alkaline phosphatase (ALP) and serum parathyroid hormone (PTH), can be used as markers of aberrant bone metabolism in this disease[10].

The Case presentation

Patient Information: A forty seven years old non diabetic, normotensive, right handed woman presented to us with the complaints of progressive swelling on the left side of the forehead for two years. She said that at first the swelling was small. Then slowly it was growing in size and now it has become quite large and covering her left forehead and causing drooping of her eyelid. It was painless and it hindered her ability to look up. She had no history of trauma or fever associated with it.

Clinical findings: On examination there was a three by four centimeters swelling over the left fronto- orbital area. it was non tender and non-pulsatile. The surface temperature was as the surrounding skin. It was partly firm and partly soft in consistency. There was irregular bony margin palpable around the swelling. The overlying skin was free, but the tumour was fixed with underlying structure. there were no engorged veins on the swelling. Transillumination test was negative. There was no palpable cough impulse, it was neither compressible nor reducible. The swelling had grown out in to the left orbit and as such the left eye lid was partially closed. But her vision in the left eye as well as movement of the left eye was intact. Her neurological examination was normal. All other system examination was normal.

Diagnostic assessment: Her routine blood count was normal. Her CT scan was suggestive of PDB or fibrous dysplasia with outer table erosion in the left side of frontal bone (supraorbital) with adjacent soft tissue swelling (figure 2).

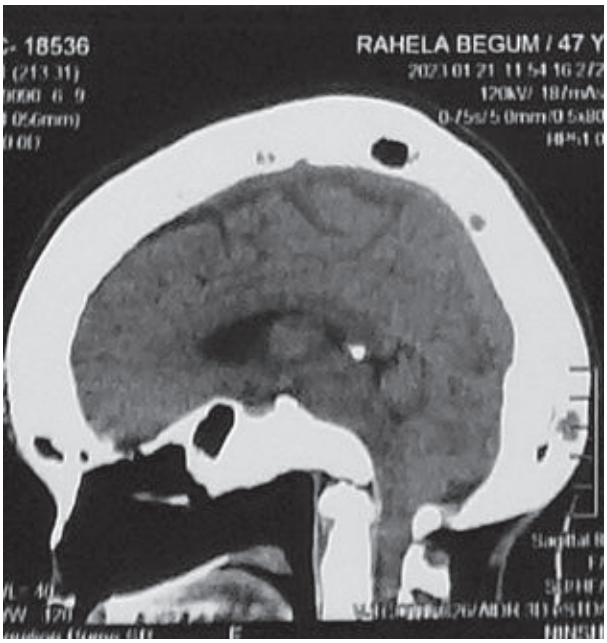

Figure 2: CT scan of head, sagittal section, showing thickening of the skull bone with platybasia.

MRI scan report was suggestive of diffuse infiltrating lesion in the calvaria with superior aspect of orbit (figure 1).

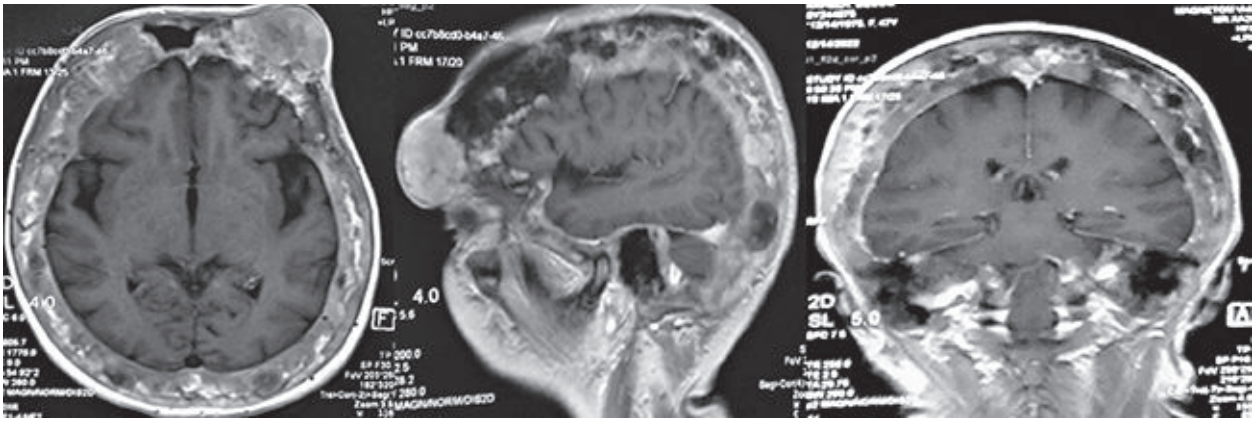

Figure 1: Pre-operative contrast enhanced MRI Showing the thickened skull bone and GCT at the left frontal region.

In bone Scan, there were multiple osteoblastic lesions which was suggestive of multiple skeletal metastasis (figure 3).

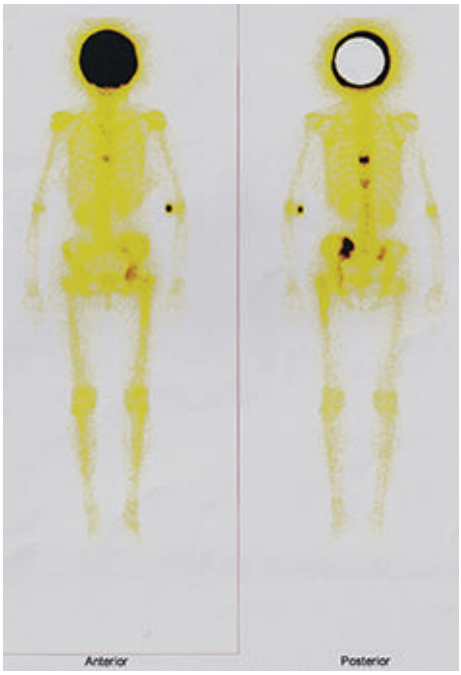

Figure 3: Bone scan (anterior and posterior aspect) showing multiple hotspots, mostly in the skull bone.

Her x-ray skull showed woolly appearance (figure 4).

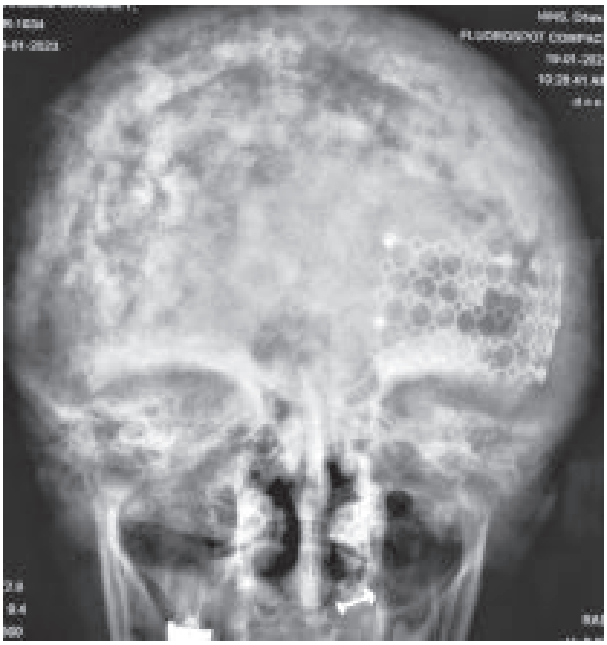

Figure 4: *Post operative skull x-ray A/P view. "Woolly" appearance of the skull bone. Titanium mesh is seen on the left frontal bone.*

Her S. ALP was 2025U/L and S. IPTH was 115.8 pg/mL and 108.3 pg/ml after two weeks. Her serum calcium was normal. Ultrasonogram of the thyroid and parathyroid gland was normal, serum electrophoresis was normal.

Differentials diagnosis: Initially it was thought as a benign scalp swelling, probably a lipoma, osteoid osteoma or extracranial extension of intracranial tumours. These were excluded by CT scan and MRI examination.

Therapeutic intervention: She had undergone tumour excision under general anaesthesia. She was placed on the operation table in supine position with head in the midline. The tumour was approached by left eye brow incision. The tumour was firm, well circumscribed, greyish in colour, moderately vascular and had eroded the left frontal bone in the orbit and attached to the dura. It was totally removed, surrounding bones were drilled out and the hydrogen peroxide toileting was done in the tumour bed. After achieving hemostasis the bony defect was covered with titanium mesh to maintain cosmesis (figure 5).

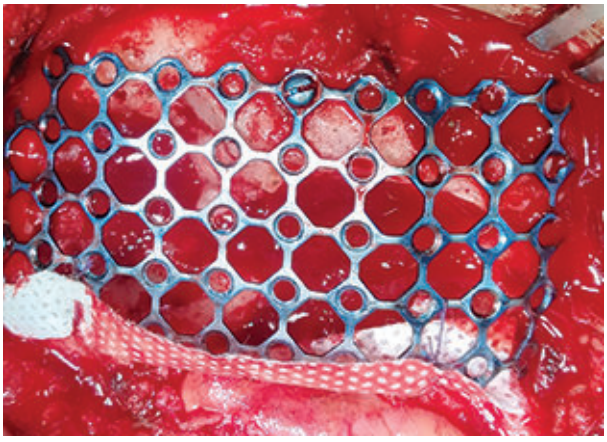

Figure 5: Intraoperative photograph showing the bony defect covered with titanium mesh.

Skin was closed in layers. The tumour was incised, it was very firm and fleshy (figure 6).

Her histopathological study showed background spindle shaped cells and irregularly disposed nuclei containing multinucleated giant cells. There were also sparse osteoid materials (figure 7).

Her post-operative period was uneventful. She was discharged from the hospital on the 10th post–operative day with advice to consult an oncologist.

Follow-up and outcome: the patient was followed up in the out-patient department after surgery at one month and six months. During these follow-ups, she was tumour free and her wound had healed well.

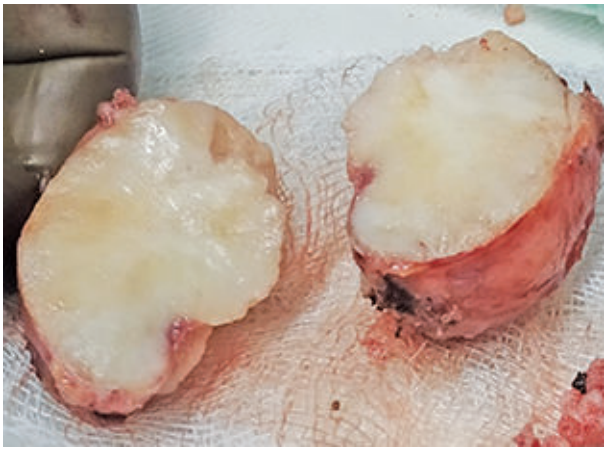

Figure 6: The tumour incised after removal

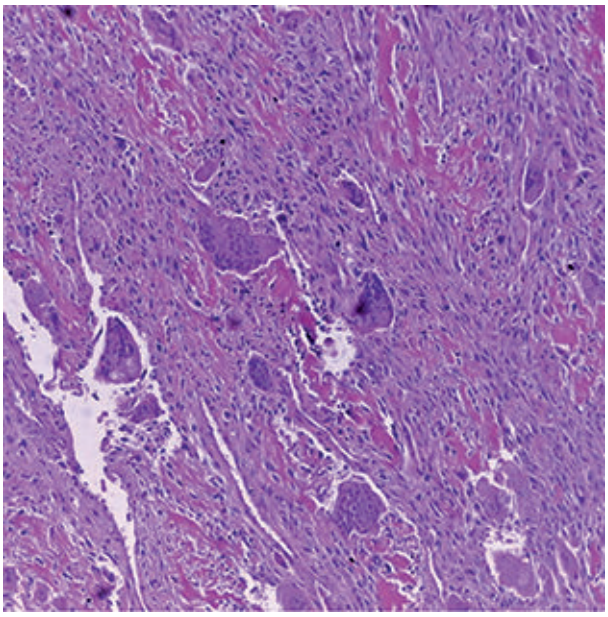

Figure 7: Histopathological picture H&E staining, showing irregularly disposed nuclei, background spindle shaped cells containing multinucleated giant cells. sparse osteoid materials are also seen.

Discussion:

GCT usually does not occur in frontal bone[11]. This patient had this because of PBD. Haibach et al in 1985 had reviewed 82 cases of neoplasms arising in Paget's disease of bone. In their study, there were 77 osteosarcomas, 3 fibrosarcomas, 1 chondrosarcoma, and 1 giant cell tumour[12]. Bertoni et al had reviewed 546 cases of giant cell tumour. Of them, only 15 were in the skull. Only one patient with PDB had GCT in the frontal bone[6]. In another study by Dahlin et al, out of 195 patients only one of the GCT occurred in a patient with Paget's disease of bone[13]. This patient had GCT of the frontal bone also.

Scintigrams are more sensitive than conventional radiography, revealing up to 30% more bone lesions, especially in sites with multiple overlapping radiographic shadows such as the ribs, sternum, and scapula[14]. In this patient there was more uptake in the skull, left hemipelvis, D9 and D11 vertebra, both SI joints and the head and upper end of left femur.

Radiologically, all remnants of osteoporosis circumscripta disappear, being replaced by condensing foci of sclerosis and obscuration of the inner and outer tables combined with considerable bony sclerosis and widening. Sclerotic bone occurs primarily along the inner table. There will be marked thickening of the skull vault and peripheral migration of the outer table correlate with the clinical finding of an enlarged head diameter. Bone softening of the skull in Paget's disease may lead to basilar invagination, "dropping" of the occiput, and platybasia[15]. This patient had such feature in x-ray skull and CT scan. When in the skull, GCT shares anatomical characteristics and imaging features with several other tumors, including chordoma, chondrosarcoma, meningioma, and osteosarcoma, among others[16].

In a cross sectional study by Seton et al, out of 285 patients, lesions in the skull were endorsed in 29% of self-reported data, and were detected in 30% and 19% of bone scan and X-ray data, respectively[17]. This patient was detected by CT scan and MRI of the skull.

Of the biochemical parameters, ALP is raised in PDB and Calcitonin is normal range[10]. In this patient S ALP was 2025 U/L. this was much higher than the normal range. Her S. parathyroid hormone level was 115.8 pg/ml and 108.3 pg/ml after two weeks. Which may be due to pagetic hyperparathyroid syndrome[18].

Intraoperatively, the tumour was extradural and closely attached with dura. It had eroded the frontal bone and the orbital rim and had entered the orbit. In a study, all the GCT of the skull had an extradural location and were closely adherent to the dura mater, with destruction of the regional bones[11]. We had to reconstruct the eroded orbital rim with titanium mesh to maintain cosmetic result.

Pathologically, GCTs consist of three types of cells: round monocytes-resembling cells, spindle-shaped fibroblast-like stromal cells and multinucleated giant cells[11].

Although GCTs are generally benign lesions, they have the potential for locally aggressive behavior and less commonly, malignant differentiation. Surgical excision is the first line of treatment with the subsequent prognosis closely related to the degree of excision[11]. We had excised the total tumour and then reconstructed the defect of the orbital rim with titanium mesh.

Recommendations:

Paget's disease of the bone is a rare entity, in the skull it is even rarer. Giant cell tumour is infrequently seen in patients with PDB. But in the frontal bone is also rare. We must keep this uncommon diagnosis in mind while diagnosing and preparing the patient for surgery.

Conflict of interest: There was no conflict of interest

Funding: Self-funded

Ethical approval: Head of the department, Department of Neurosurgery, NINS&H.

Submit Date: 14 May, 2024

Final Revision Received:

Accepted: 23 February, 2024

Publication: 01 August, 2024

References

1. Ferraz-de-Souza B, Correa PHS. Diagnosis and treatment of Paget's disease of bone: a mini-review. Arquivos Brasileiros de Endocrinologia & Metabologia. 2013;57 DOI: 10.1590/S0004-27302013000800001.
2. Gennari L, Rendina D, Merlotti D, Cavati G, Mingiano C, Cosso R, et al. Update on the pathogenesis and genetics of Paget's disease of bone. New perspectives on osteoclasts in health and disease. 2022;16648714:139. DOI: 10.3389/fcell.2022.932065.
3. Karakida K, Ota Y, Aoki T, Akamatsu T, Kajiwara H, Hirabayashi K. Multiple giant cell tumors in maxilla and skull complicating Paget's disease of bone. Tokai J Exp Clin Med. 2010;35:112-7. PMID: 21319038
4. Ralston SH, Corral Gudino L, Cooper C, Francis RM, Fraser WD, Gennari L, et al. Diagnosis and management of Paget's disease of bone in adults: a clinical guideline. Journal of Bone and Mineral Research. 2019;34:579-604. DOI: 10.1002/jbmr.3657.
5. Scotto di Carlo F, Pazzaglia L, Mumm S, Benassi MS, De Chiara A, Franchi A, et al. ZNF687 Mutations in an Extended Cohort of Neoplastic Transformations in Paget's Disease of Bone: Implications for Clinical Pathology. Journal of Bone and Mineral Research. 2020;35:1974-80. DOI: 10.1002/jbmr.3993.
6. Bertoni F, Unni KK, Beabout JW, Ebersold MJ. Giant cell tumor of the skull. Cancer. 1992;70:1124-32. DOI: 10.1002/1097-0142(19920901)70:5.
7. Rendina D, Mossetti G, Soscia E, Sirignano C, Insabato L, Viceconti R, et al. Giant Cell Tumor and Paget's Disease of Bone in One Family: Geographic Clustering. Clinical Orthopaedics and Related Research®. 2004;421:218-24. DOI:10.1097/00000118702.46373.e3.
8. Verma V, Puri A, Shah S, Rekhi B, Gulia A. Giant Cell Tumor Developing in Paget's Disease of Bone: A Case Report with Review of Literature. J Orthop Case Rep. 2016;6:103-7. DOI:10.13107/jocr.2250-0685.594.
9. Rendina D, De Filippo G, Ralston SH, Merlotti D, Gianfrancesco F, Esposito T, et al. Clinical Characteristics and Evolution of Giant Cell Tumor Occurring in Paget's Disease of Bone. Journal of Bone and Mineral Research. 2015;30:257-63. DOI: 10.1002/jbmr.2349.
10. Donaìth J, Speer G, Pooìr G, Gergely P, Jr, Tabaìk A, Lakatos P. Vitamin D receptor, oestrogen receptor-á and calcium-sensing receptor genotypes, bone mineral density and biochemical markers in Paget's disease of bone. Rheumatology. 2004;43:692-5. DOI:10.1093/rheumatology/keh162.
11. Zhang Z, Xu J, Yao Y, Chu S, Cheng H, Chen D, et al. Giant cell tumors of the skull: a series of 18 cases and review of the literature. J Neurooncol. 2013;115:437-44. DOI:10.1007/s11060-013-1242-z.
12. Haibach H, Farrell C, Dittrich FJ. Neoplasms Arising in Paget's Disease of Bone: A Study of 82 Cases. American Journal of Clinical Pathology. 1985;83:594-600. DOI:10.1093/ajcp/83.5.594.
13. Dahlin DC, Cupps RE, Johnson Jr EW. Giant-cell tumor: A study of 195 cases. Cancer. 1970;25:1061-70. DOI: 10.1002/1097-0142(197005)25:5.
14. Mirra JM, Brien EW, Tehranzadeh J. Paget's disease of bone: review with emphasis on radiologic features, part I. Skeletal Radiology. 1995;24:163-71. DOI:10.1007/BF00228918.
15. Mirra JM, Brien EW, Tehranzadeh J. Paget's disease of bone: review with emphasis on radiologic features, part II. Skeletal Radiology. 1995;24:173-84. DOI:10.1007/BF00228919.
16. di Carlo FS, Whyte MP, Gianfrancesco F. The two faces of giant cell tumor of bone. Cancer Letters. 2020;489:1-8. DOI: 10.1016/j.canlet.2020.05.031.
17. Seton M, Moses AM, Bode RK, Schwartz C. Paget's disease of bone: The skeletal distribution, complications and quality of life as perceived by patients. Bone. 2011;48:281-5. DOI:10.1016/j.bone.2010.09.021.
18. Brandi ML, Falchetti A. What Is the Relationship Between Paget's Disease of Bone and Hyperparathyroidism? Journal of Bone and Mineral Research. 2006;21:P69-P74. DOI:10.1359/jbmr.06s213.