DOI: 10.7860/JCDR/2022/55478.16181

Case Series

Pathology Section

Utility of p63 in Giant Cell Lesions of Bone- A Case Series

SHIMA KANNADAS[1], SILY SREEDHARAN[2], CHRIS THOMAS[3], MK RAVINDRAN[4], MM ANEESH[5]

ABSTRACT

Giant cell lesions of bone include a relatively large group of biologically and morphologically diverse bone lesions which shows presence of numerous multinucleate osteoclast like giant cells. Recently, p63 has been found to be a sensitive marker in the diagnosis of giant cell tumour. The aim of this case series is to assess the role of p63 in diagnostically difficult giant cell lesions of bone. The authors here present four cases with giant cell rich lesions of bone as seen in Hematoxylin and Eosin (H&E) staining, in which an accurate diagnosis was not possible with the available clinical and radiological data were included in this study. The tissue was stained with hematoxylin and eosin and Immunohistochemical staining (IHC) with p63 was done. Though the specificity of the marker was found to be less, it was concluded that, p63 can be used as an ancillary aid along with histomorphological and radiological data in arriving at a diagnosis.

Keywords: Aneurysmal bone cysts, Immunohistochemistry, Non neoplastic lesions

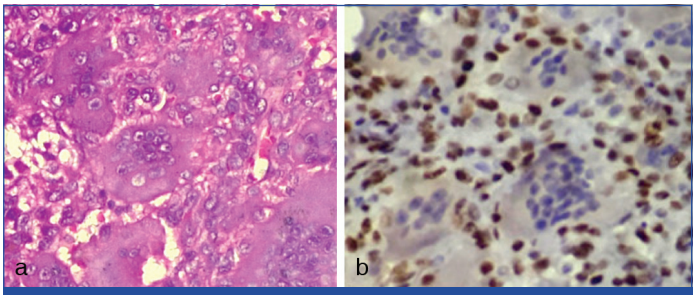
INTRODUCTION

Giant cell-rich lesions of bone show numerous multinucleated osteoclast-like giant cells and the presence of mononuclear stromal cells [1]. The list includes giant cell tumour of bone, aneurysmal bone cysts, chondroblastomas, brown tumour, tenosynovial giant cell tumours, non ossifying fibromas, giant cell reparative granulomas, pigmented villonodular synovitis and osteosarcomas [2]. The diagnosis of these giant cell-rich lesions is often challenging even for an experienced pathologist. As there are no well-established immunohistochemical and molecular markers in differentiating these giant cell lesions, the use of immunohistochemical marker p63 has been studied in some centres outside India and was found to express in the stromal cells of giant cell tumour and negative in non neoplastic lesions [3-5]. As a first study of its kind from our country, easy availability and cost effectiveness p63 was chosen to be used as an aid in differentiating various giant cell-rich lesions [3]. Four such cases are included in this case series which was conducted in a tertiary care centre in North Kerala, India.

CASE SERIES

Case 1

A 35-year-old male presented to the Department of Orthopaedics with pain and swelling of right index finger since two months. On examination, a well-defined mass of size 4×4 cm was palpable on the proximal phalanx of right index finger. Clinical diagnosis were osteosarcoma and aggressive giant cell tumour of small bone. X-Ray showed lytic lesion in the proximal phalanx of the right index finger with sclerotic margins. Magnetic Resonance Imaging (MRI) also showed the same features and suggested the possibilities of chondrosarcoma and enchondroma. Curettage of the mass showed [Table/Fig-1a] a neoplasm composed of uniformly arranged osteoclast like multinucleate giant cells surrounded by stromal cells. Stromal cells are oval cells with vesicular nucleus and prominent nucleoli. Provisional histological diagnosis of giant cell tumour of small bone was made. Immunohistochemistry with p63 showed diffuse strong nuclear positivity in the stromal cells [Table/Fig-1b] Osteoclastic giant cells were negative for p63. Final diagnosis was confirmed as giant cell tumour of small bone. After curettage, patient was asymptomatic without recurrence till the last visit.



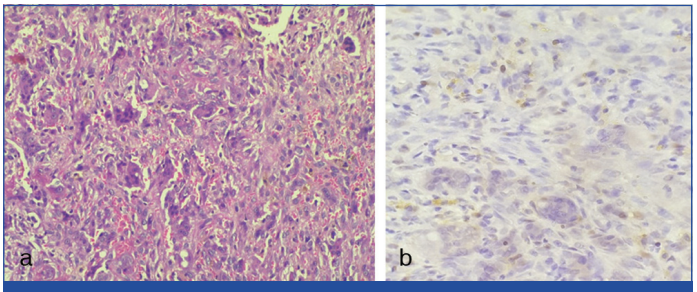
[Table/Fig-1]: a) Showing plenty of giant cells (H&E, 40X) ;b) IHC with p63 positive in stromal cells (40X).

Case 2

A 77-year-old male presented to the Outpatient Department with pain and swelling over upper third of left leg for the last one month. He was diabetic, hypertensive and on dialysis for chronic renal failure. On examination he had an ill-defined swelling over the left upper tibia. X-ray showed a lytic lesion over the anterior aspect of left upper tibia suggesting possibilities of chondrosarcoma, fibrosarcoma and multiple myeloma.

Tru-cut biopsy of the mass showed [Table/Fig-2a] a lesion composed of numerous osteoclast-like multinucleate giant cells which are randomly distributed in the stroma. As there were areas of hemorrhage and hemosiderin laden macrophages, serum parathormone, calcium and phosphorus levels were advised. His serum parathormone levels were found to be elevated (1809 pg/mL), calcium levels were low normal (8.5 mg/dL) and phosphate was high (7 mg/dL). Thus, a diagnosis of Brown tumour due to secondary hyperparathyroidism was made.

Immunohistochemistry with p63 showed absence of staining in stromal cells suggestive of non neoplastic etiology [Table/Fig-2b].



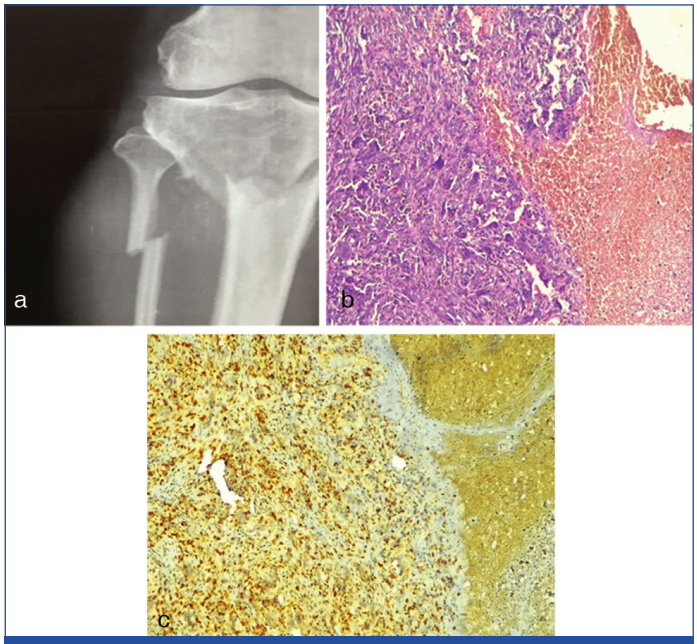
[Table/Fig-2]: a) Section with Giant cells and hemorrhage (H&E, 10X); b) IHC with p63 absent in stromal cells and giant cells (10X).

Final diagnosis was confirmed as Brown tumour. After surgical removal of parathyroid glands, his laboratory values became normal and was symptom-free.

Case 3

A 47-year-old male presented to the Emergency Department with displaced bone fracture proximal third of right leg. On examination there was swelling and deformity in the infrapatellar region of right leg. X-ray showed displaced both bone fracture proximal third of right leg and a lytic lesion involving upper tibia [Table/Fig-3a] suggestive of simple bone cyst, aneurysmal bone cyst and giant cell tumour.

Bone curettings showed [Table/Fig-3b] a lesion composed of blood-filled cystic spaces lined by fibroblasts, reactive osteiod and scattered multinucleate giant cells. Provisional diagnosis was aneurysmal bone cyst. The p63 staining showed nuclear positivity in the stromal cells [Table/Fig-3c]. Final diagnosis was confirmed as giant cell tumour with secondary aneurysmal bone cyst. After complete curettage no recurrence was reported in this case.



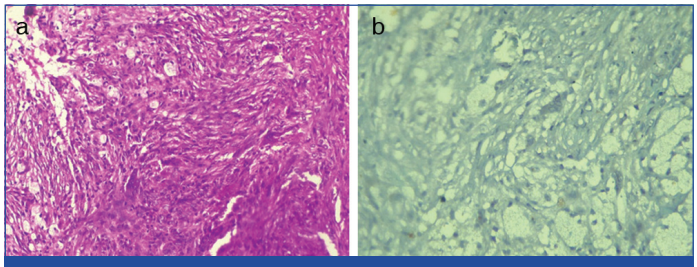
[Table/Fig-3]: a) X-ray depicting pathological fracture and lytic lesion tibia; b) Section with plenty of giant cells lining hemorrhagic areas (H&E,4X); c) IHC with p63 positivity in stromal cells (4X).

Case 4

A 14-year-old boy presented to the Orthopaedic Outpatient Department with swelling and deformity of right leg for six months duration. On examination there was a hard swelling with fixity to the underlying left tibia. The MRI showed a well defined cortical based lesion with sclerotic margins in the lower metadiaphyseal region of tibia suggestive of a benign bone tumour.

Therapeutic excision of the tumour showed [Table/Fig-4a] spindle cells arranged in storiform pattern with scattered osteoclast like giant cells and foam cells suggestive of non ossifying fibroma.

The p63 staining showed absent staining in the stromal cells and osteoclastic giant cells [Table/Fig-4b]. Final diagnosis was confirmed as non ossifying fibroma. Patient was asymptomatic till the last follow-up.



[Table/Fig-4]: a) Showing spindle cells, foamy macrophages and giant cells (H&E,10X); b) IHC with p63 absent in stromal cells (40X).

DISCUSSION

The p63 belongs to the family of transcription factors and plays a role in skeletal development as mutations in p63 in humans lead to limb abnormalities and null p63 mice exhibit skeletal defects [4]. Based on its function in the cell, p63 could contribute to tumorigenesis by inactivating p53 (tumour suppressor gene) [6] and regulate apoptosis [7] and cell-cycle [8]. The expression of p63 in various bone lesions is shown in [Table/Fig-5] [9].

Lesions	Expression of p63 in stromal cells
Giant cell tumour	Positive
Aneurysmal bone cyst	Variable/Negative
Brown tumour	Negative
Non ossifying fibroma	Variable

[Table/Fig-5]: Pattern of p63 staining in various giant cell lesions [9].

Among the giant cell lesions, Giant cell tumour of bone is the most frequently reported, locally aggressive, and has a propensity to recur locally which mandate the use of markers in its prompt diagnosis [10-12].

In the first case of the present series, even though the clinical presentation was favoring an aggressive giant cell tumour, radiological features were suggestive of a chondroid neoplasm. Histological findings and immunohistochemistry confirm the diagnosis as giant cell tumour. In a study reported by Lee CH et al., [5], p63 overexpression was seen in significant number of giant cell tumours with a strong staining confined to the stromal component [3-5]. As mutations in the H3F3A gene (encodes Histone H3.3) is involved in the pathogenesis of Giant cell tumour of bone, immunohistochemical staining using a monoclonal antibody directed against H3F3A is positive in 95-100% of giant cell tumour [13]. But the specificity and availability of this marker is very less [14].

In the case of brown tumour, the initial clinicoradiological features were suggestive of a neoplastic etiology. Absence of p63 supported by lab values, suggested a nonneoplastic etiology [5]. The rate of p63 expression in aneurysmal bone cyst in Dickson BC et al., and Lee's CH et al., [4,5] studies is lower when compared to giant cell tumour of bone. De la Roza et al., [3] and Linden MD [14] found higher results. If some cases of aneurysmal bone cyst are p63 positive, there would be a component of a giant cell tumour of bone. Hence in third case of present case series possibility of giant cell tumour with secondary aneurysmal bone cyst was considered.

Studies on p63 expression in non ossifying fibroma are rare as it is a less common benign fibrohistiocytic tumour of bone. In a study conducted by Hammas N et al., [Table/Fig-5], it was found that only 25% of cases were p63 positive [9]. The absence of p63 staining in fourth case of present case series suggests that staining of p63 is variable in non ossifying fibromas and hence thorough morphological correlation should be done for the confirmation of diagnosis. Similar studies in larger number of cases are required to know utility of p63 in giant cell lesions of bone as an effective diagnostic marker.

CONCLUSION(S)

This case series shows that p63 may serve as an effective surrogate biomarker for differentiating giant cell tumour from other giant cell lesions of bone.

REFERENCES

[1] Zambo I, Pazourek L. Giant cell-rich lesions of bone and their differential diagnosis]. Cesk Patol. 2017 Spring;53(2):61-70.
[2] Rosenberg AE, Nielsen GP. Giant cell containing lesions of bone and their differential diagnosis. Curr Diagn Pathol. 2001;7(4):235-46.
[3] De la Roza G. p63 Expression in Giant Cell-Containing Lesions of Bone and Soft Tissue. Arch Pathol Lab Med. 2011;135(6):776-79.

[4] Dickson BC, Li SQ, Wunder JS, Ferguson PC, Eslami B, Werier JA, et al. Giant cell tumor of bone express p63. Mod Pathol. 2008;21(4):369-75.
[5] Lee CH, Espinosa I, Jensen KC, Subramanian S, Zhu SX, Varma S, et al. Gene expression profiling identifies p63 as a diagnostic marker for giant cell tumor of the bone. Mod Pathol. 2008;21(5):531-39.
[6] Moll UM, Slade N. p63 and p73: Roles in development and tumor formation. Mol Cancer Res. 2004;2:371-86.
[7] Kakizoe M. Apoptosis in giant cell tumors of bone. Kurume Med J. 2000;47:125-34.
[8] Flores ER. The Roles of p63 in cancer. Cell Cycle. 2007;6:300-04.
[9] Hammas N, Laila C, Youssef ALM, Hind EF, Harmouch T, Siham T, et al. Can p63 serve as a biomarker for giant cell tumor of bone? A Moroccan experience. Diagn Pathol. 2012;7:130.
[10] Errani C, Ruggieri P, Asenzio MAN, Toscano A, Colangeli S, Rimondi E, et al. Giant cell tumor of the extremity: A review of 349 cases from a single institution. Cancer Treat Rev. 2010;36(1):01-07.
[11] Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumor of bone. J Bone Joint Surg Am. 1987;69(1):106-14.
[12] McDonald DJ, Sim FH, McLeod RA, Dahlin DC. Giant-cell tumor of bone. J Bone Joint Surg Am. 1986;68(2):235-42.
[13] Lüke J, von Baer A, Schreiber J, Lübbehüsen C, Breining T, Mellert K, et al. H3F3A mutation in giant cell tumour of the bone is detected by immunohistochemistry using a monoclonal antibody against the G34W mutated site of the histone H3.3 variant. Histopathology. 2017;71(1):125-33.
[14] Linden MD. Bone & Soft Tissue. Mod Pathol. 2009;22(S1):11-26.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, Malabar Medical College, Calicut, Kerala, India.
2. Professor, Department of Pathology, Malabar Medical College, Calicut, Kerala, India.
3. Assistant Professor, Department of Pathology, Malabar Medical College, Calicut, Kerala, India.
4. Professor, Department of Orthopaedics, Malabar Medical College, Calicut, Kerala, India.
5. Associate Professor, Department of Radiology, Malabar Medical College Hospital and Research Centre, Modakkalloor, Calicut, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Shima Kannadas,
Assistant Professor, Department of Pathology, Malabar Medical College, Modakkalloor, Calicut-673315, Kerala, India.
E-mail: drkshima@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 10, 2022
- Manual Googling: Feb 21, 2022
- iThenticate Software: Mar 29, 2022 (16%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Feb 08, 2022**
Date of Peer Review: **Mar 04, 2022**
Date of Acceptance: **Mar 16, 2022**
Date of Publishing: **Apr 01, 2022**