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Detection of recurrent phosphaturic mesenchymal tumors by using Ga-68 DOTATATE PET/CT

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ABSTRACT

Phosphaturic mesenchymal tumor is a rare clinical condition and often causes osteomalaciadue to tumor. Its diagnosis is often significantly delayed due to its rare occurrence in addition to the generalized and vague symptoms of their presentation. A 19-year-old female with a history of left facial nerve palsy, generalized weakness and hoarseness of voice revealed a dense mass in her brain. In this case, we reported successful application of a Ga-68 labeled DOTATATE PET/CT scan to identify the primary site and distant metastases of phosphaturic mesenchymal tumors and show the diagnostic value of Ga-68 labeled DOTATATE PET/CT imaging for the rare tumors.

Keywords: Phosphaturic mesenchymal tumor, Ga-68 labeled DOTATATE PET/CT scan, osteomalacia

Osteomalacia induced by tumor (OIT) is most often caused by a rare, benign, mesenchymal neoplasm - phosphaturic mesenchymal tumor (PMT) with overexpression of fibroblast growth factor-23 (FGF-23) [1]. PMT causes hypophosphatemia, hyperphosphaturia, bone pain, muscle weakness, and pathological bone fractures. Not more than 1000 cases are described in the literature [2]. The peak incidence is during the forties and fifties. The most frequent site of involvement is bone followed by soft tissue [3, 4]. The development of metastasis is remote possibility with PMT [5, 6] and surgical removal is the curative treatment. Commonly recommended diagnostic modalities including magnetic resonance imaging (MRI) and 18F fluorodeoxyglucose positron emission tomography / computed tomography (18F-FDG PET/CT) prove useful in the evaluation of PMT. 18F-FDG PET-CT has been associated with false-positive results [7]. The discovery of overexpression of the type 2 somatostatin receptor (SSTR) receptor by PMT cells prompted use of more specific imaging with Gallium-68, labelled DOTA-octreotate, oxodotreotide, DOTA-(Tyr3)-octreotate (Ga-68 labeled DOTATATE) [3]. Ga-68 DOTATATE PET/CT is considered more accurate technique for identifying primary tumors and distant metastases, permitting shorter image acquisition interval with reduction in radiation dose to the patient. Additionally, it provides information about the density of SSTR receptors exhibited by the tumor cells, which is a decisive factor in planning targeted radionuclide therapy [7, 8].

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CASE PRESENTATION

A 19-year-old female with a history of left facial nerve palsy and hoarseness of voice underwent a Brain CT scan. She was revealed to have a dense mass (4.0 × 3.5 cm) in the left cerebellopontine angle and cerebellum involving left mastoid air cells, eroding and destroying petrous temporal and occipital bone. In addition, the MRI revealed extra-axial abnormal signal intensity mass in the left jugular foramen region. It also indicated medial widening (4.2 × 2.7 cm) with intracranial extradural extension into cerebellopontine cistern indenting brainstem. Furthermore, ipsilateral superior and middle cerebellar peduncle were associated with perilesional edema resulting in effacement of adjacent cerebellar folia. The middle ear cavity is also compressed laterally, resulting in occlusion of the eustachian tube-posteroinferiorly, causing destruction of basiocciput along the lateral aspect of the foramen magnum. The patient underwent radiotherapy and was prescribed steroids; she remained symptom-free for one year but was readmitted with severe headache and vomiting. The CT Brain revealed obstructive hydrocephalus with cerebral edema and underwent ventriculoperitoneal shunting.

The immunohistochemistry analysis was positive for STAT6 and SATB2, tumor markers frequently reported in PMT cases [9]. MRI Brain showed an aggressive enhancing mass with infiltration into the left cerebellar hemisphere. Compared to previous scans, there was an interval progression of the disease. The Ga-68 DOTATATE PET/CT revealed a moderately avid left intracranial lesion in the left cerebellum (Maximum Standardized uptake value [SUV max] 4.9, 50 × 49 mm) involving basiocciput, occipital and temporal bone (Fig. 1).

DISCUSSION

PMTs are uncommon, benign, neoplasms of mesenchymal origin and the most frequent etiology of OIT. High amounts of the peptide hormone FGF-23 is produced and secreted by these tumors [1]. FGF-23 is a physiological phosphate regulator that minimizes the phosphate reabsorption in the proximal tubule and inhibits 1-α-hydroxylase, which causes 1-α, 25-dihydroxyvitamin D3 deficiency and hypophosphatemia [1]. There is consequent decrease in mineral density of bones leading to non-specific bone pains, pathological bone fractures, progressive functional weakness and asthenia. Most of the causative tumors for osteomalacia arise from mesenchymal cells; therefore, their usual localization is the layers of bones or soft tissues [3,4]. ~95% of PMT originate in the appendicular skeleton while only 5% occurs in the head and neck regions [10, 11]. The majority of PMTs (more than 80%) are found in the nose and paranasal sinuses [3], and origin in the jaws is exceptionally rare [11]. The diagnosis is usually based on the finding of chronic hypophosphatemia due to isolated renal phosphate depletion. This findings in combination with concomitant elevated or disproportionately normal blood levels of FGF-23 along reduced or disproportionately normal

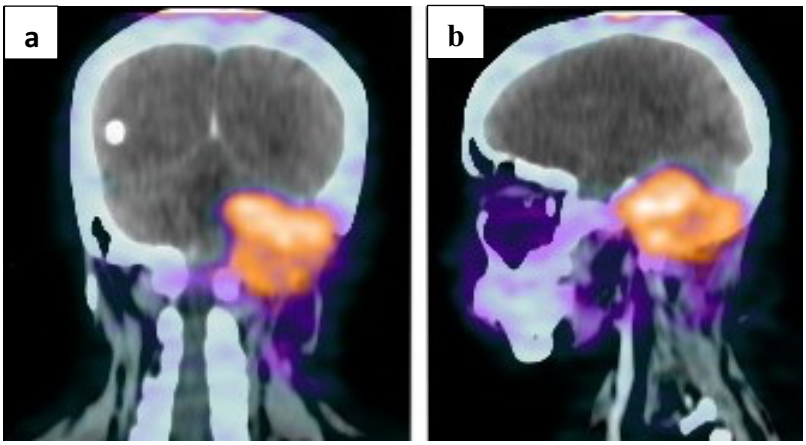

Fig. 1. Ga-68 labeled DOTATATE PET/CT scan (a) Fused coronal image shows avid mass. Occupying the left cerebellar hemisphere and infiltrating basiocciput (b) Fused sagittal image shows avidity in the same area.

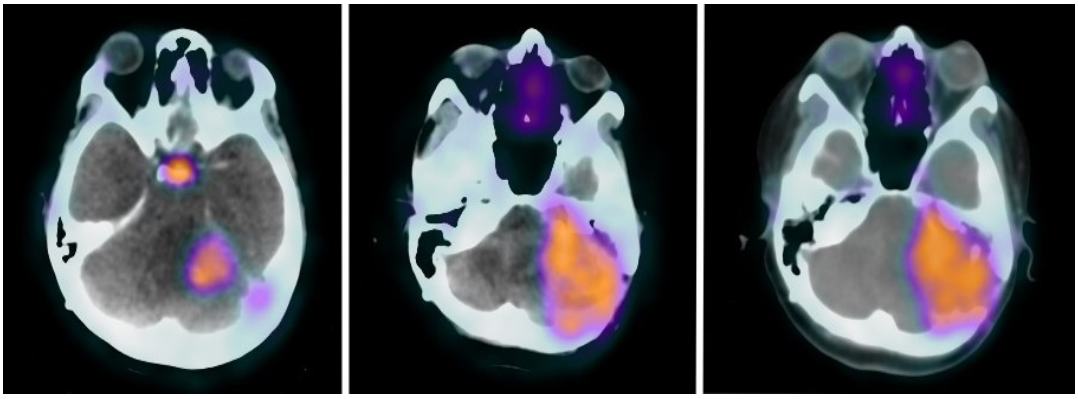

Fig. 2. Ga-68 labeled DOTATATE PET/CT scan shows uptake in the area of the left cerebellar hemisphere.

1,25-OH2-vitamin D (1,25(OH)2D) is hallmark of the diagnostic criteria [11].

This case describes the application of Ga-68 labeled DOTATATE scan that uniquely identified the primary site of PMT and excluded remotely located metastases. Localization of the site of the primary tumor is essential in the treatment of these tumors, as surgical removal of the primary tumors is often curative. Recent advances in SSTR-based functional imaging have supported the benefits of Ga-68-labeled DOTATATE scanning in tumors that over express somatostatin analogs. PMTs are known to express somatostatin receptor 2A and can therefore be visualized using radiolabeled somatostatin analogs such as In-111 pentetreotide and Ga-68 labeled DOTATATE. Ga-68-labeled DOTATATE images selectively identify SSTR2-avid tissue and are approved forclinical use. The In-111 pentetreotide scan is difficult to interpret unless SPECT-CT is performed to anatomically localize the uptake area, thus labeled Ga-68 is superior to this as tomography is inherent part of PET-CT and provides better resolution and sensitivity.

The somatostatin analogue, tyrosine 3-octreotate is combined with positron emitter (Gallium-68) using DOTATATE as a coupling agent. This Ga-68-labeled DOTATATE conjugate is administered intravenously, complexes with SSTR2, emits positrons detected by a PET scanner, and provides accurate and precise anatomical localization of the tumor. Ga-68-labeled DOTATATE scans are superior to other somatostatin receptor-based studies because they are highly sensitive, specific, accurately localize these tumors, have better spatial resolution, higher affinity for SSTR2, greater accuracy and shorter scan time, and less radiation exposure. However, a full body scan is required instead of the oncology standard body protocol used

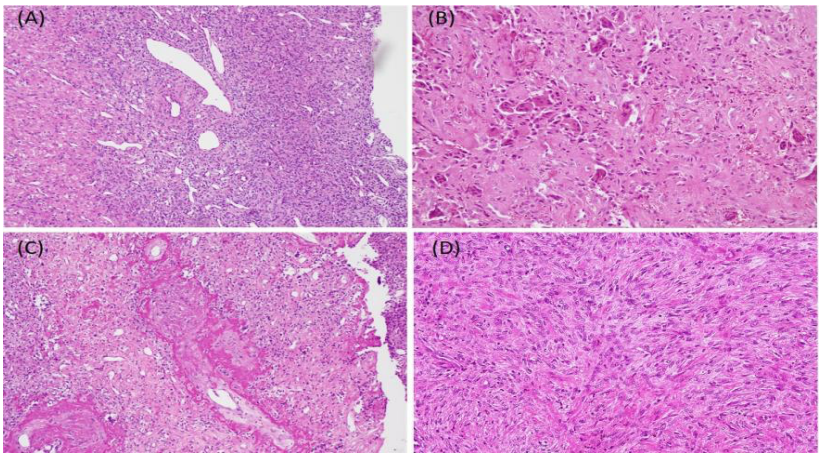

Fig. 3. (A) spindled, fusiform, hemangiopericytoma-like areas and (B) osteoclastic giant cells arranged in sheets. (C) There were also identifiable areas of calcific deposits and (D) sheets of bland spindle cells.

in most cases because PMTs can appear anywhere from head to toe.

Determining the exact location of the tumor is very challenging using conventional X-ray and nuclear medicine images, including MRI and PET/CT. False positive findings have been reported using 18F-FDG PET/CT imaging [7]. Hence use of 18F-FDG PET/CT has not gained wide acceptance in the evaluation of suspected PMT. The fact that SSTR is over expressed in mesenchymal tumors, favors use of Ga-68-labeled DOTATATE targeting SSTRs in these tumors [3]. In this report, we successfully identified a PMT (Fig.2)) using a Ga-68-labeled DOTATATE scan, which revealed a left intracranial mass avidity (SUVmax 4.9, 50×48 mm).

The accuracy of the Ga-68 labeled DOTATATE scan was also confirmed by histopathological analysis with benign features of a PMT. Microscopic findings revealed spindle-shaped, fusiform, hemangiopericytoma-like areas and osteoclastic giant cells arranged in sheets. There were also identifiable areas of calcium deposits and layers of bland spindle cells (Fig. 3), which are particularly characteristic of PMT [12]. In addition, immunohistochemical analysis was positive for STAT6 and SATB2, which are tumor markers frequently reported in PMT cases [9]. In our case, we used a Ga-68 DOTATATE scan to detect the exact anatomical location of the disease and metastatic workup. A primary site of disease was demonstrated and no metastases were detected, consistent with the patient's follow-up to date after disease-free surgical removal.

CONCLUSION

PMT is characteristically benign, extremely rare neoplasm and is known to be one of the most common causes of OIT. Identifying the location of the tumor is often very challenging using conventional radiologic techniques. This study reported the successful application of Ga-68 DOTATATE scan for identifying the primary site and exclude distant metastases of PMT that was further confirmed by histopathological analysis. The case shows the diagnostic value of Ga-68 labeled DOTATATE PET/CT imaging for rare tumors.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images or data.

Authors' Contribution

Study Conception: MNY; Study Design:MNY, WA, MF; Supervision: MNY, SF; Funding: N/A; Materials: SF, II, MK; Data Collection and/or Processing: WA, MK, MF; Statistical Analysis and/or Data Interpretation: WA, MK, MF; Literature Review: MK, MF, II; Manuscript Preparation: II, WA and Critical Review: SF, MNY.

Conflict of interest

The author disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

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REFERENCES

1. Ghorbani-Aghbolaghi A, Darrow MA, Wang T. Phosphaturic mesenchymal tumor (PMT): exceptionally rare disease, yet crucial not to miss. Autops Case Rep. 2017;7(3):32-37. doi: 10.4322/acr.2017.031.
2. Brandi ML, Clunie GPR, Houillier P, et al. Challenges in the management of tumor-induced osteomalacia (TIO). Bone. 2021;152:116064. doi: 10.1016/j.bone.2021.116064.
3. Lee DY, Lee SH, Kim BJ, et al. Usefulness of 68Ga-DOTATOC PET/CT to localize the culprit tumor inducing osteomalacia. Sci Rep. 2021;11(1):1819. doi: 10.1038/s41598-021-81491-2.
4. Moreno Romero M, Pérez Muñoz I, González Lizán F, Gallego Rivera JI, Valdivielso Cañas L. The phosphaturic mesenchymal tumor as a cause of oncogenic osteomalacia. Three cases and review of the literature. Rev Esp Cir Ortop Traumatol (Engl Ed). 2021:S1888-4415(21)00050-3. doi: 10.1016/j.recot.2020.12.004.
5. Qiu S, Cao LL, Qiu Y, et al . Malignant phosphaturic mesenchymal tumor with pulmonary metastasis: a case report. Medicine (Baltimore). 2017;96(17):e6750. doi: 10.1097/MD.0000000000006750.

6. Oyama N, Kojima-Ishii K, Toda N, et al. Malignant transformation of phosphaturic mesenchymal tumor: a case report and literature review. Clin Pediatr Endocrinol. 2020;29(2):69-75. doi: 10.1297/cpe.29.69.
7. El-Maouche D, Sadowski SM, Papadakis GZ, et al. 68Ga-DOTATATE for tumor localization in tumor-induced osteomalacia. J Clin Endocrinol Metab. 2016;101(10):3575-3581. doi: 10.1210/jc.2016-2052.
8. Fallahi B, Manafi-Farid R, Eftekhari M, et al. Diagnostic efficiency of 68Ga-DOTATATE PET/CT as compared to 99mTc-Octreotide SPECT/CT and conventional morphologic modalities in euroendocrine tumors. Asia Ocean J Nucl Med Biol. 2019;7(2):129-140. doi: 10.22038/AOJNMB.2019.39392.1263.
9. Chatterjee D, Bardia A, Pal R, Saikia UN, Bhadada SK, Radotra BD. Clinical, morphological and immunohistochemical analysis of 13 cases of phosphaturic mesenchymal tumor - A holistic diagnostic approach. Ann Diagn Pathol. 2021;54:151783. doi: 10.1016/j.anndiagpath.2021.151783.
10. Folpe AL, Fanburg-Smith JC, Billings SD, et al. Most osteomalacia-associated mesenchymal tumors are a single histopathologic entity: an analysis of 32 cases and a comprehensive review of the literature. Am J Surg Pathol. 2004;28(1):1-30. doi: 10.1097/00000478-200401000-00001.
11. Pelo S, Gasparini G, Garagiola U, et al. Phosphaturic mesenchymal tumor, an unusual localization in head and neck. J Surg Case Rep. 2018;2018(5):rjy091. doi: 10.1093/jscr/rjy091.
12. Richardson AL, Richardson OK. Phosphaturic mesenchymal tumor: case report. Radiol Case Rep. 2019;14(12):1518-1524. doi: 10.1016/j.radcr.2019.09.027.