^{68}Ga-DOTATATE PET/CT Findings in Suspected Tumor-Induced Osteomalacia: A Prospective Descriptive Study

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Abstract

Objective. To describe ^{68}Ga-DOTATATE PET/CT findings and their relationship to available histopathology in patients referred for suspected tumor-induced osteomalacia.

Methods. This prospective descriptive study included 18 patients evaluated at a referral center in Argentina.

Results. The median age was 47.5 years and 13 of 18 patients were women. The reported median SUVmax was 17.2 (interquartile range 6.27–30.6). Lesions were most frequently reported in the appendicular skeleton. Eight patients had histologically confirmed phosphaturic mesenchymal tumors (PMTs). Two of these eight patients had lesions with ill-defined margins and involvement of soft tissue and facial bones. Median SUVmax was numerically higher in the PMT group. The difference was not statistically significant as reported.

Conclusion. In this referral cohort, ^{68}Ga-DOTATATE PET/CT helped localize and characterize lesions in patients with suspected tumor-induced osteomalacia. Confirmed PMTs showed variable morphology. The findings support descriptive interpretation in conjunction with histopathology and clinical assessment.

Keywords: Tumor-induced osteomalacia, phosphaturic mesenchymal tumors, ^{68}Ga-DOTATATE, positron emission tomography, computed tomography

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Introduction

Tumor-induced osteomalacia (TIO) is a paraneoplastic syndrome commonly associated with phosphaturic mesenchymal tumors (PMTs) and excess fibroblast growth factor 23 (FGF23). FGF23 reduces renal phosphate reabsorption and inhibits 1-alpha-hydroxylase [1,2,3,4]. Complete resection of the causative tumor can normalize biochemical abnormalities and support remineralization [5]. Somatostatin receptor expression provides a target for molecular imaging [6]. This study describes ^{68}Ga-DOTATATE PET/CT findings and their correlation with available histopathology in an Argentine referral cohort.

Materials and Methods

This prospective descriptive study was conducted at Hospital Universitario CEMIC, Buenos Aires, from December 2019 to July 2023 on behalf of the Argentine TIO working group. Adults referred with clinical or biochemical suspicion of TIO were included. No specific exclusion criteria were applied. Demographic, clinical and biochemical data were collected before imaging.

Imaging Technique

Whole-body PET/CT was performed using a Philips Gemini 64 ToF scanner 60 minutes after intravenous administration of 106.6 ± 22.2 MBq of ^{68}Ga-DOTATATE. Low-dose CT provided anatomical characterization and attenuation correction. PET acquisition lasted three minutes per bed position. Coronal, transverse and sagittal slices were assessed visually and semiquantitatively using SUVmax. Two nuclear medicine specialists and two diagnostic imaging specialists reviewed the scans and resolved disagreements by discussion.

Statistical Analysis

Anonymized data were tabulated in Microsoft Excel. Continuous variables were assessed with the Shapiro–Wilk test and summarized as mean ± standard deviation or median and interquartile range, as appropriate. Categorical variables were summarized with frequencies and percentages. Missing data were not imputed. Exploratory group comparisons used chi-square tests for categorical variables and unpaired t-tests or Mann–Whitney U tests for continuous variables. The reported significance level was $p < 0.05$. Analyses used SPSS Statistics 20.0.0.

Ethics

Written informed consent was obtained from all participants. The CEMIC institutional research committee and the independent CEIINAPsi ethics committee approved the study. The authors report compliance with Argentine regulations and the Declaration of Helsinki.

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Results

The study included 18 patients, of whom 13 were women. Median age was 47.5 years. Fractures were reported in 78.6% of participants and 43.8% were not self-sufficient at imaging. Median FGF23 was 47.5 pg/mL (IQR 42–54).

Median SUVmax was 17.2 (IQR 6.27–30.6). In the distribution shown in Figure 1, 46.7% of cases were assigned to the appendicular skeleton and 40% to the head and neck. Of the 15 cases in Figure 2, 86.7% had one identifiable lesion. Focal, well-defined lesions were reported in 66.7% of cases. Intravenous contrast was used in 12 of 18 patients. Three of the six patients examined without intravenous contrast had negative PET/CT findings.

Table 1. Imaging characteristics as reported

Characteristic	Value
Cohort, n	18
Transverse diameter, median (IQR)	14 mm (11–23.5)
Long axis, median (IQR)	17 mm (10–18)
Intravenous contrast enhancement	66.67%
Tissue involvement (data available for 14 patients)	
Bone only	35.7%
Soft tissue only	35.7%
Mixed	21.4%
Visceral	7.2%
Bone erosion	50%
CT suggesting osteopenia	83.3%

Histopathology

Eight patients had histologically confirmed PMTs. Four had lesions in the limbs, two in the head and neck and two in the axial skeleton. Table 2 and Figure 3 summarize 13 cases with histological data. The narrative analysis reports 12 after exclusion of a thyroid finding considered false positive. Two of the eight PMT cases had ill-defined margins with soft tissue and facial bone involvement. Bone erosion is reported separately in Table 2.

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Histological Group Comparison

Table 2. Characteristics by histological group as reported

Characteristic	PMT	Other histological findings
n/N	8/13 (61.5%)	5/13 (38.5%)
Female sex	75%	60%
Age, median (IQR)	45 years (41–51)	47 years (41–55)
SUVmax, median (IQR)	20.85 (12.4–25.7)	8.3 (4.6–42.5)
Appendicular skeleton	50%	60%
Head and neck	25%	40%
Axial skeleton	25%	0%
Transverse diameter, median (IQR)	15 mm (12–21)	13.5 mm (11–18)
Long axis, median (IQR)	17 mm (11.5–17.5)	17 mm (13–17.5)
Contrast enhancement	62.5%	80%
Bone erosion	37.5%	80%
CT suggesting osteopenia	75%	80%
Bone fractures	83.7%	50%
Soft tissue involvement only	71.4%	0%

The original table includes a note that data were available for six subjects, without a clearly marked row. Percentages are reproduced as reported.

Discussion

The PMT group had a numerically higher median SUVmax, with no statistically significant difference reported. The comparison of isolated soft tissue involvement yielded p = 0.06 using the reported Yates-corrected chi-square test. These exploratory comparisons do not establish a diagnostic threshold.

PMTs showed variable morphology, including ill-defined margins and involvement of adjacent structures [7,8]. TIO can affect physical function, quality of life and skeletal integrity [9,10]. Receptor imaging can help localize candidate lesions and define their anatomical extent [6,11]. Treatment planning depends on lesion localization, extent, resectability and the clinical assessment [12,13,14]. The small single-center referral sample and incomplete histological assessment limit generalization. FGF23 values should be interpreted in the biochemical context [16].

Conclusion

In this referral cohort, ^{68}Ga-DOTATATE PET/CT helped localize and characterize lesions in patients with suspected tumor-induced osteomalacia. Confirmed PMTs showed variable morphology. Findings should be interpreted with histopathology and clinical assessment.

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Lesion Distribution and Number

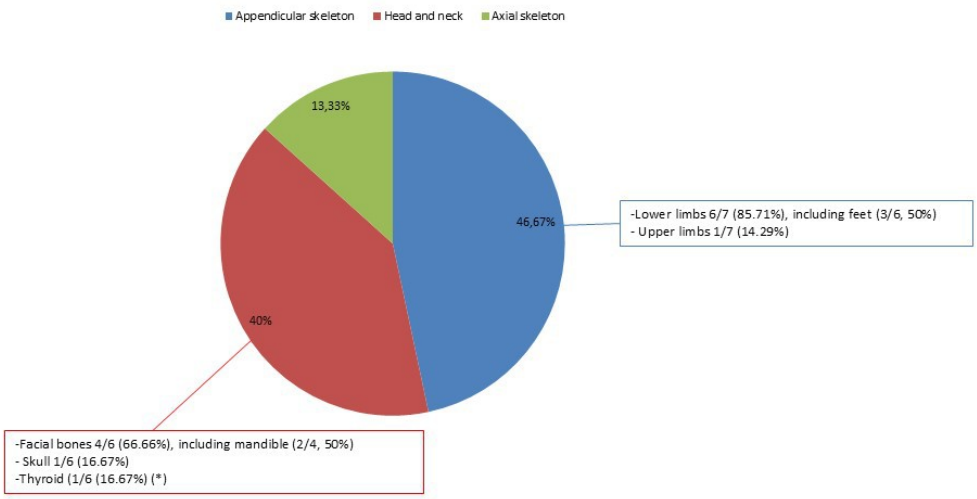


Figure 1. Distribution of lesions (n = 15 with available, confirmed data). (*) The finding was considered false positive after histological examination.

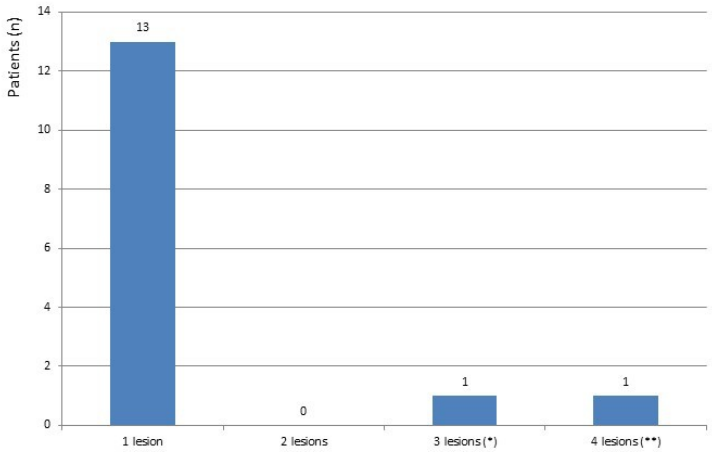


Figure 2. Number of identified lesions (n = 15 with available, confirmed data). (*) Left ischiopubic ramus. (**) Facial bones and skull.

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Histological Diagnoses

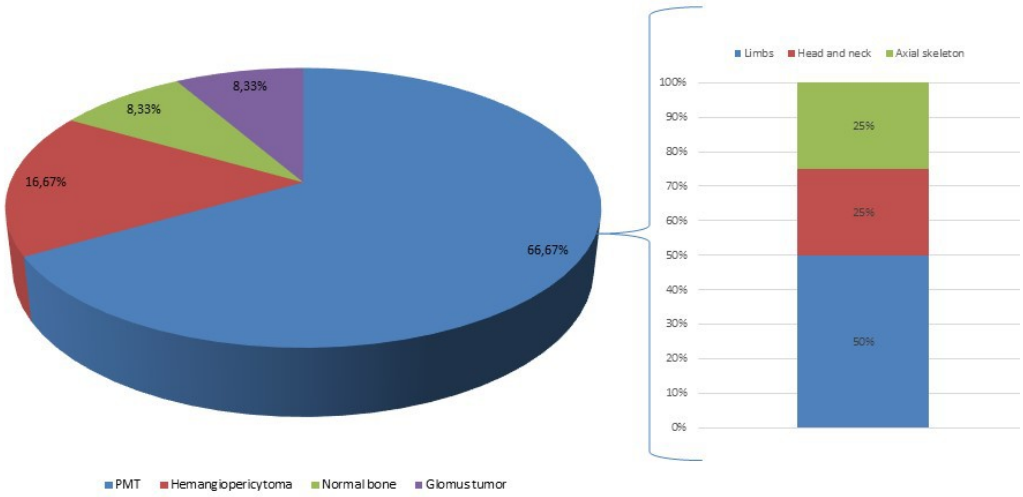


Figure 3. Histological diagnoses in patients with available data (n = 13). PMT: phosphaturic mesenchymal tumor.

Declarations

The authors report written informed consent and preservation of patient anonymity. Ethics approval was obtained. No competing interests or funding were reported. The datasets are available from the corresponding author on reasonable request.

Author Contributions

MB conceived and designed the study. MB, RC and MC prepared materials and analyzed data. MB and BZ collected data. MB drafted the manuscript, and all authors reviewed and approved the final version.

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