

Phosphaturic Mesenchymal Tumor of the Pelvis: A Multidisciplinary Approach

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ABSTRACT

Phosphaturic mesenchymal tumor (PMT) is an infrequent clinicopathological entity. It presents insidious bone pain and polymyalgia, accompanied by alterations in calcium and phosphorus metabolism that are difficult to resolve clinically. A multidisciplinary approach is a key to success in this pathology. We present the case of a 52-year-old female patient with a 10-year history of PMT in the right hemipelvis with ipsilateral hip extension. From the clinical point of view, she presented oncogenic osteomalacia (hypophosphatemia and hyperphosphaturia) that did not correct despite being administered the latest generation medication, burosumab, an FGF-23 inhibitor that increases renal tubular phosphate reabsorption. Resection with oncological margins was decided by a multidisciplinary committee resolving her clinical condition. Due to the rarity of this pathology, we decided to report the case.

Keywords: Phosphaturic mesenchymal tumor; oncogenic osteomalacia; oncological orthopedics; pelvic surgery.

Level of Evidence: IV

Tumor mesenquimático fosfático de pelvis: abordaje multidisciplinario

RESUMEN

El tumor mesenquimático fosfático es una entidad clinicopatológica sumamente infrecuente. Además de provocar dolor óseo insidioso y polimialgias, se acompaña de alteraciones del metabolismo fosfocálcico de difícil manejo clínico. El abordaje multidisciplinario resulta la clave del éxito en esta enfermedad. Presentamos una paciente de 52 años de edad con antecedente de tumor mesenquimático fosfático en la hemipelvis derecha con extensión a la cadera homolateral de 10 años de evolución. Clínicamente presentaba osteomalacia oncogénica (hipofosfatemia e hiperfosfaturia) que no se corregía, pese a un agente de última generación, el burosumab, un inhibidor del factor de crecimiento fibroblástico 23, que aumenta la reabsorción tubular renal de fosfatos. En un comité multidisciplinario, se decidió la resección con márgenes oncológicos y se logró una mejoría clínica franca. Comunicamos este caso, debido a que es un cuadro infrecuente.

Palabras clave: Tumor mesenquimático fosfático; osteomalacia oncogénica; ortopedia oncológica; cirugía de pelvis.

Nivel de Evidencia: IV

INTRODUCTION

Phosphaturic mesenchymal tumor (PMT) is an extremely rare clinicopathological entity. It is a low-grade tumor that affects both sexes equally, between 40 and 60 years of age. The reason for consultation is usually insidious bone pain, polymyalgia, difficulty walking, and incomplete pathological fractures. Its main clinical characteristic is to induce osteomalacia.

Tumor-induced osteomalacia was first described in 1947 by McCance.¹ Based on the histology of the neoplasm, in 2006, Weidner and Santa Cruz² subdivided them into different categories, where PMT represents 90% of the cases. Since its initial description in 1947, about 500 osteomalacia-inducing tumors have been reported, with only a small proportion causing lytic lesions.³ The characteristic laboratory parameters of PMT are hyperphosphaturia, hypophosphatemia, and elevated alkaline phosphatase levels.

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How to cite this article: Cullari LM, Senes S, Taleb JP, Fita I, Sarmiento PD. Phosphaturic Mesenchymal Tumor of the Pelvis: A Multidisciplinary Approach. *Rev Asoc Argent Ortop Traumatol* 2022;87(3):360-370. <https://doi.org/10.15417/issn.1852-7434.2022.87.3.1371>

Although systemic treatments or minimally invasive therapeutic procedures have been described, tumor resection with wide oncological margins is the definitive treatment. We present the case of a patient with PMT located in the right hemipelvis with extension to the ipsilateral hip.

CLINICAL CASE

A 52-year-old woman with a clinical history of oncogenic osteomalacia (hypophosphatemia and hyperphosphaturia). She had undergone a partial resection of the iliac bone plus cementoplasty eight years earlier, at another Center, with an initial histopathological diagnosis of hemangiopericytoma.

The patient attended our institution in March 2018. On physical examination, a palpable mass was observed on the outer aspect of the right iliac bone associated with pain in the anterior aspect of the ipsilateral thigh. She reported pain during flexion-extension of the right hip and rotations, as well as pain upon weight-bearing on that limb. She wandered only around the home assisted with a walker. A pelvis radiograph (Figure 1) showed an alteration of the structure compatible with an expansive lesion that compromised the right iliac bone, with a heterogeneous appearance and irregular edges, in addition to the presence of cement from the previous cementoplasty.



Figure 1. Panoramic pelvic radiograph. Note the radiopaque image corresponding to the previous cementoplasty, with lytic alteration around the cement and extension to the femoral head (arrowheads).

Magnetic resonance imaging (Figure 2) revealed a formation in the right hemipelvis with altered morphology and signal intensity of the right iliac bone with involvement of the acetabulum, ischium, and iliopubic ramus. In its topography, we recorded a lesion with soft tissue signal intensity, heterogeneous, predominantly hypointense in the T1 sequence.



Figure 2. Magnetic resonance imaging of the pelvis, T1 sequence. A formation in the right hemipelvis with altered morphology and signal intensity of the right iliac bone with involvement of the acetabulum, ischium, and iliopubic ramus. A lesion with soft tissue signal intensity, heterogeneous, predominantly hypointense is observed.

Clinically, the patient suffered from insidious muscle pain and generalized weakness, for which biochemical analyses were requested, which yielded the following results: calcemia 9.1 mg/dl (normal value [NV] 8.5-10.5), phosphatemia 1.1 mg/dl (NV 2.5-4.5), magnesium 2.5 mg/dl (NV 1.9-2.5), parathormone 61 pg/ml (NV 12-72), alkaline phosphatase 368 IU/l (NV 40-100), 25-OH vitamin D 8.4 ng/ml (NV 14-39) and phosphaturia 1871 mg/24 h (NV 350-1000). The association of hyperphosphatemia and hyperphosphaturia is encompassed in a clinical disorder called oncogenic osteomalacia. To confirm the diagnosis, a CT-guided biopsy was performed. The clinical presentation together with the imaging studies and the CT-guided biopsy (Figure 3) led to the diagnosis of phosphaturic mesenchymal tumor.

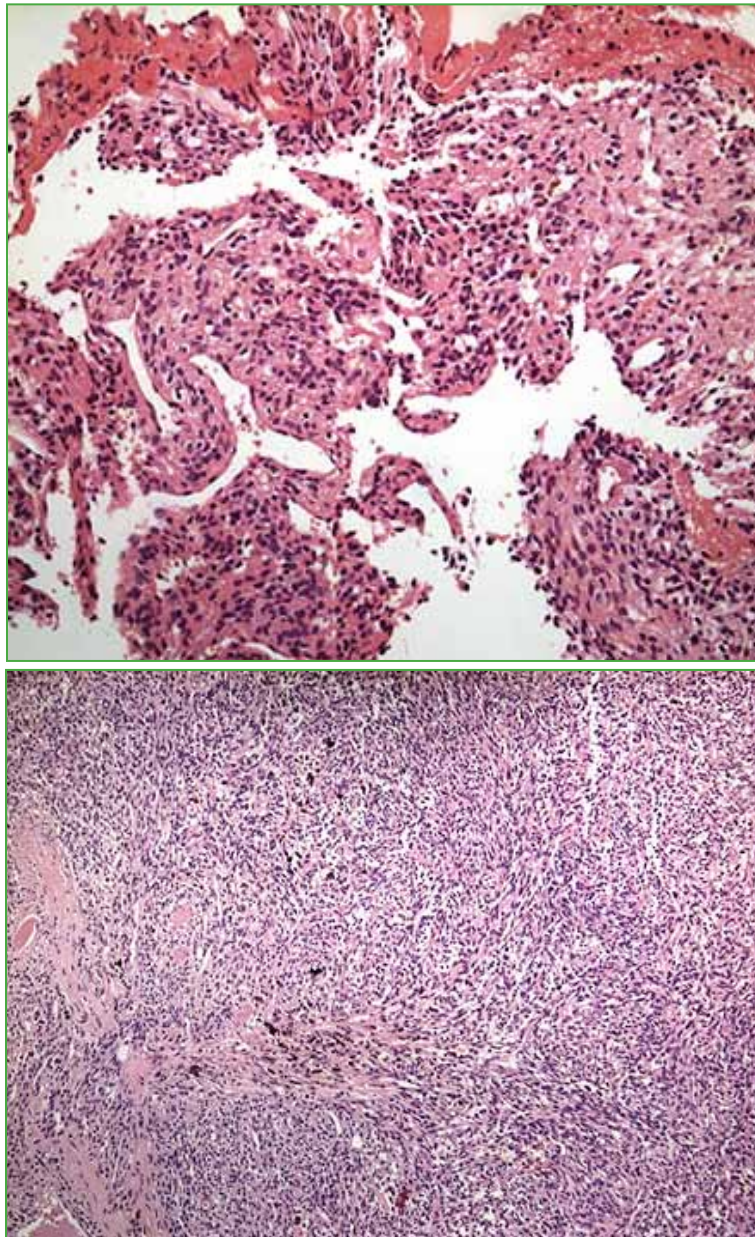


Figure 3. Low-grade spindle cell proliferation with branching vessels exhibiting a hemangiopericytoma-like (“staghorn”) pattern.

Initially, surgical treatment with oncological margins was considered, which was flatly rejected by the patient; consequently, she was prescribed analgesia and told not to bear weight on that limb, monthly control visits were scheduled, and an interconsultation with endocrinology was requested. A significant increase in the size of the mass was observed six months after the first consultation.

As the patient refused surgery, in a multidisciplinary meeting, it was decided to start using burosumab, a monoclonal antibody that binds to fibroblast growth factor 23. It is a protein responsible for phosphate-calcium metabolism. This antibody binds in the kidney and inhibits it, thus correcting the hypophosphatemia, since it increases the reabsorption of this nutrient. After three months of application, it was not possible to reverse the phosphorus values in the blood and the symptoms described continued to worsen. Having exhausted all medical treatment options, the benefits and comorbidities of surgery were discussed with the patient; thus, a surgical resolution was chosen by the patient together with her family and the Oncology and Endocrinology Services as a curative treatment.

A two-stage surgery was planned. The original idea was to remove the tumor and place a preformed spacer to limit the local infectious process, and then, in a second stage, to perform definitive surgery with an unconventional implant.

We planned the approach and reconstruction with a spacer with antibiotics designed with 3D printing (Figure 4).

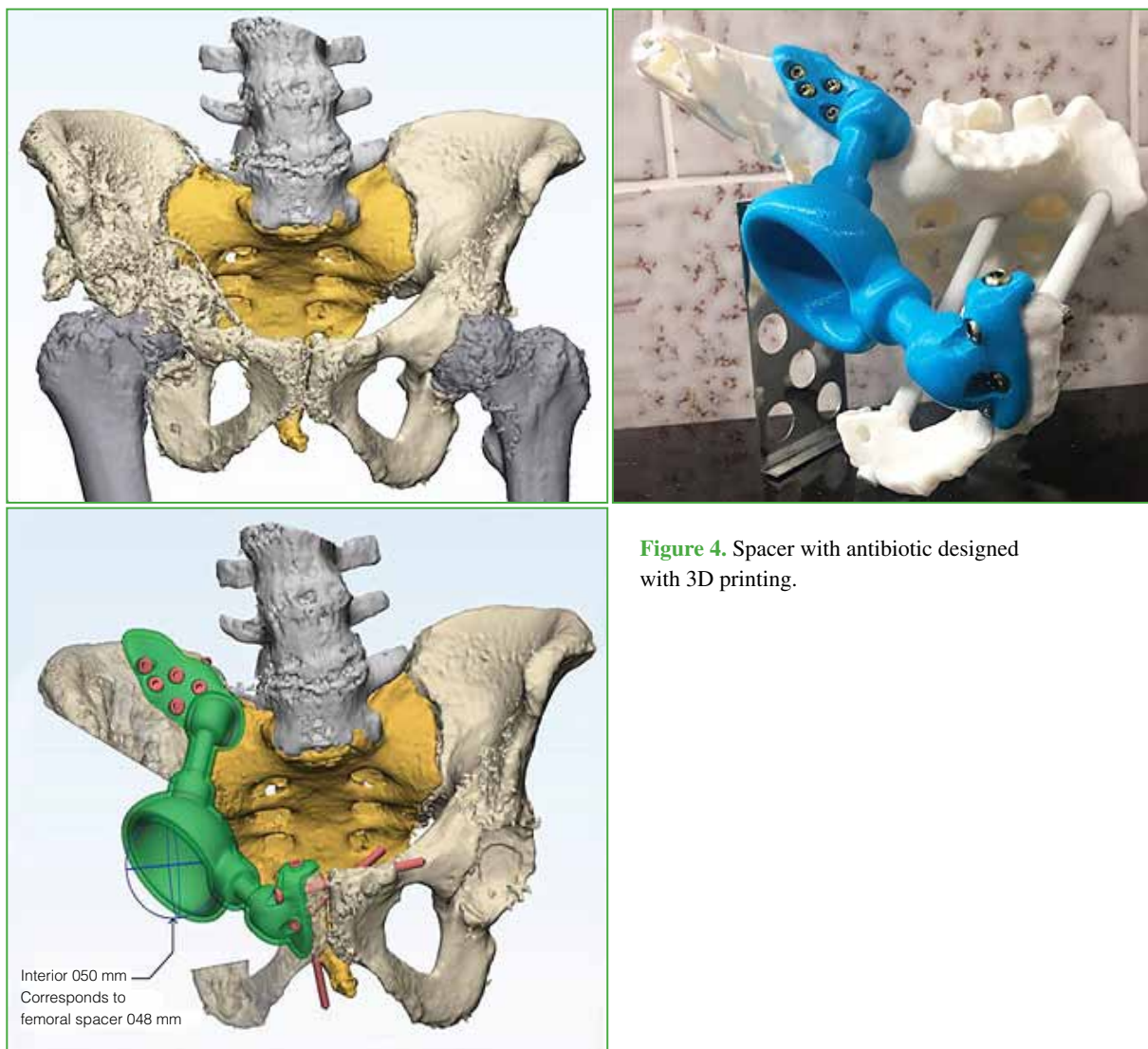


Figure 4. Spacer with antibiotic designed with 3D printing.

The retroperitoneum was accessed by mobilizing the peritoneum. The inguinal ligament was divided and the anterior superior iliac spine was disinserted, freeing the femoral and iliac vessels with the vascular surgery team. After mobilizing the iliofemoral bundle, the superior pubic ramus was accessed and dissected in its entirety until reaching the pubic symphysis. Next, a pubic osteotomy was performed, the superior and inferior pubic rami were dissected, and, subsequently, an osteotomy of the femoral neck was performed. Soft-tissue dissection of the external face of the pelvis was performed, preserving the gluteal muscles and the gluteal pedicle, as well as the pelvic tilt muscles. The right sacroiliac joint was identified and, by means of a proximal osteotomy, the release of the retroperitoneal soft tissues (psoas and iliacus muscles) was completed, preserving the femoral and greater sciatic nerves.

Oncological resection of the iliac and periacetabular region was performed, and the piece was sent for anatomopathological study (Figure 5); then, the pelvic ring was reconstructed with an implant and a preformed spacer was placed (Figure 6). The subsequent histopathological study indicated clear margins.



Figure 5. Resection of the surgical piece.



Figure 6. Oncological resection of the iliac and periacetabular region plus reconstruction of the pelvic ring with an implant and placement of a preformed spacer.

On the third day, the patient suffered cardiogenic shock and required high-dose norepinephrine plus vasopressin, orotracheal intubation, and mechanical ventilation. On the seventh day, sedation was discontinued and she was extubated. One week later, she was diagnosed with dyspnea, desaturation, and tachycardia and was transferred to the Coronary Care Unit, with a diagnosis of pulmonary thromboembolism. She was given low-molecular-weight heparin for two weeks and then switched to acenocoumarol for four months.

The patient was discharged 25 days after the operation. Fifteen days later, she was admitted to the Emergency Department with purulent discharge due to wound dehiscence and soft tissue exposure (Figure 7).



Figure 7. Wound dehiscence with soft tissue exposure (40 days after surgery).

Biochemical analyses were requested, which yielded the following values: white blood cells 9000/mm³, erythrocyte sedimentation rate 62 mm/h, and C-reactive protein 5.2 mg/dl. In computed tomography, findings compatible with a fluid collection were observed in the right inguinal region (Figure 8).



Figure 8. Computed tomography of the pelvis. A fluid collection is observed in the right hemipelvis.

The following day, a debridement was performed with sample collection plus placement of a negative suction system, and antibiotic treatment with intravenous vancomycin and imipenem was indicated. Methicillin-sensitive *Staphylococcus aureus* was identified from the sample and the antibiotic was switched to cefazolin for one week. The patient was discharged and prescribed cephalexin until completing 21 days of treatment.

After 18 months, laboratory parameters were normal, both inflammatory values (C-reactive protein 0.3mg/dl, erythrocyte sedimentation rate 15mm/h, white blood cell count 5600/mm³) and phosphocalcic metabolism values (calcium 9.3mg/dl, phosphorus 3 mg/dl); there were no clinical signs of active infection. After discussion in a multidisciplinary conference, definitive reconstruction surgery of the right hemipelvis was proposed to the patient, which she flatly refused, because she had no pain and walked without difficulty with a walker. According to the Endocrinology Service, the plan will be to continue treatment with burosumab for an indefinite period of time and carry out bimonthly calcium and phosphorus controls. Currently, the radiograph shows the correct position of the spacer, with no signs of loosening or active disease (Figure 9).



Figure 9. Panoramic radiograph of the current pelvis (18 months post-surgery).

DISCUSSION

Osteomalacia-inducing tumors are an extremely rare paraneoplastic entity, and finding their anatomical location is one of the greatest challenges. The average time from the onset of symptoms to the diagnosis of PMT often exceeds 2.5 years.¹ In our case, this characteristic did not cause major inconvenience due to the large size of the neoplasm in the pelvis. Oncogenic osteomalacia is characterized by hypophosphatemia with increased urinary phosphate excretion and a deficient or normal value of 1.25(OH)-D, in the presence of normal calcemia. The reason for consultation is usually insidious bone pain, polymyalgia, difficulty walking, and incomplete pathological fractures. Our patient presented right coxarthralgia of several years of evolution, which had not been cured despite previous intervention and treatment with state-of-the-art drugs.

Some alternative treatments to surgery are radiofrequency ablation,⁴ subcutaneous octreotide,⁵ and monoclonal antibodies against fibroblast growth factor 23 (KRN23), a substance produced by osteocytes whose physiological function is to regulate plasma phosphorus levels in the kidney, producing phosphaturia. Of these antibodies, burosumab is the most widely used today, it binds to fibroblast growth factor 23 and inhibits it, thus correcting hypophosphatemia. This monoclonal antibody has been shown to reduce fatigue, improve quality of life, normalize serum phosphorus, and improve histomorphometric parameters after 48 weeks of administration. Although it has emerged as a promising therapy, information on its long-term efficacy and safety is still lacking. Furthermore, since burosumab does not stop the progression or growth of the causative tumor, its use should be limited to patients with unresectable or unidentified tumors.⁶

In the 1970s, Enneking and Dunham were the first to publish a series of resections of pelvic bone tumors trying to avoid amputation, surgeries with a high rate of morbidity and mortality, but which provided the patient with a greater chance of survival and better quality of life.⁷ In recent years, a wide range of surgical techniques has emerged intending to shorten intraoperative time and provide a better mechanical solution to the bone defect after resection, such as three-dimensional designed reconstruction.^{8,9} Detailed and accurate preoperative planning is essential to achieve the expected outcomes.

Due to their locally aggressive nature, PMTs are prone to local recurrence and may even generate distant metastases.¹⁰ Resection of PMT with oncological margins is the only curative option; medical treatment is reserved for patients with inoperable tumors or who opt out of surgery. It is a technically demanding procedure with a high rate of surgical complications, the most common being infection associated with necrosis and dehiscence of the surgical wound. Its treatment is based on aggressive surgical debridement associated with intravenous antibiotic treatment.

As a single case report, one limitation of this study is that it lacks value as evidence. However, it records a rare event, contains useful details on the diagnosis of the disease and its differential diagnoses, and describes an unusual, interesting, and highly complex method of treatment.

CONCLUSION

PMT is an extremely rare condition, clinically characterized by the production of a paraneoplastic syndrome called oncogenic osteomalacia. The multidisciplinary approach is essential to treat the patient. As a curative criterion, the treatment of choice is surgery.

Conflict of interest: The authors declare no conflicts of interest.

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