A case of tumor-induced osteomalacia in which recurrence and bilateral lung metastases occurred following tumor resection

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**CASE: 32-years-old female Japanese**

**Chief Complaint:** General fatigue and walking difficulty

**Past medical problems:** No significant

**Family History:** No osteomalacia

**History of Present Illness 1:** up to first surgery

The patient began experiencing right hip pain around 2007 and became unable to walk. In 2008, osteomalacia and hypophosphatemia were identified at a local orthopedic surgery department, and the patient was referred and admitted to our hospital.

Marked hypophosphatemia was observed (serum Ca, 5.5 mg/dl; P1, 1.6 mg/dl; and total serum osteocalcin (700) was diagnosed due to high levels of intact PTH (25 ng/ml), TRF (1.14 mg/ml), and FGF23 (225F1/205F1730 pg/ml), normal, 10-50 pg/ml).

A high level of FGF23 (1000 pg/ml) was detected from the right femur vein with venous saphenous sampling (Fig. 1), and a 26-mm mass was evident at the posterior right hip bone on right leg X-ray (Fig. 2).

Resection of the right bone tumor was performed in June 2011.

Hypophosphatemia promptly recovered postoperatively and FGF23 also normalized to 23 pg/ml (Fig. 2). The patient regained the ability to walk independently and returned to work and activity.

The pathological diagnosis was phosphatofructokinase-tumor (Fig. 4).

**History of Present Illness 2:** process from post-1st surgery to 2nd surgery

However, serum P1 (1.8 mg/dl) began to decrease and FGF23 again increased since October 2011 reaching 223 pg/ml. Oral renatal phosphorus formulation and active vitamin D formulation were restarted, as a result, malaise was improved (Fig. 3).

In May 2014, right knee MRI was performed with consideration of recurrent TIO, but no significant findings were found. June 2014, multiple nodules were detected by the left upper leg in sinus CT (Fig. 4). In July 2014, right knee MRI was performed again, showing that a 25 mm mass was detected in the posterior region of the right knee (Fig. 5). The patient complained of pain in the posterior right knee and chest CT showed uptake into both lung fields corresponding to multiple nodules. (Fig. 6) Nodules of 10 mm were then diagnosed.

On September 30, 2011, we performed right knee tumor resection. The pathological diagnosis was metastatic phosphatofructokinase tumor. However, high levels of FGF23 continued postoperatively at 85 pg/ml as compared to 150 pg/ml preoperatively. Hypophosphatemia did not improve, suggesting that it was due to residual tumor and lung metastasis. Immunohistochemical resection (SSTR2 expression) was expressed in the resected specimen on IHC (Fig. 7). The patient was admitted in the hospital for the treatment of somatostatin analog (Fig. 8-12).

**Treatment for Tumor-Induced Osteomalacia**

- **Surgical treatment**
- **Medical treatment**
  - Neutral phosphorus formulation and active vitamin D formulation
  - **Treatment with octreotide**
  - Treatment with anti-FGF23 antibody (currently undergoing trial)
  - Anti-cancer drug therapy using molecularly targeted drugs

**Fig. 9 RT-PCR shows expression of SSTR2 mRNA**

**Fig. 10 Laboratory finding on admission**

<table>
<thead>
<tr>
<th>Hematologic</th>
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<tbody>
<tr>
<td>WBC 4500/μ</td>
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<tr>
<td>Hb 11.7 g/dl</td>
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<tr>
<td>Ht 35 %</td>
</tr>
<tr>
<td>RBC 4.05 × 1012</td>
</tr>
<tr>
<td>PLT 203 × 104</td>
</tr>
<tr>
<td>Na 130 mEq/l</td>
</tr>
<tr>
<td>K 3.9 mEq/l</td>
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<tr>
<td>Cl 100 mEq/l</td>
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<td>Ca 9.9 mg/dl</td>
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**Fig. 11 Endocrinological examination**

- **[Pituitary](#)**
  - ACTH 13.8 μg/ml
  - GH 1.49 μg/ml
  - TSH 1.16 μg/ml
  - LH 4.6 IU/ml
  - FSH 5.3 IU/ml
  - PRL 10.3 μg/ml

- **[Adrenal](#)**
  - Cortisol 11.4 μg/ml
  - PRA 0.3 μg/ml
  - PRC 30 μg/ml

- **[Thyroid](#)**
  - T4 2.33 μg/ml
  - TSH 2.86 μg/ml

**[Somatostatin analog](#)**

**Glucagon-like peptide 1 (GLP-1)**

**Cell-cycle arrest**

**Apoptosis**

**Conclusions**

1. We encountered a case of malignant tumor-induced osteomalacia that recurred and metastasized to both lungs.
2. Although SSTR2 was detected in the tumor, FGF23 could not be suppressed with octreotide treatment.
3. Only symptomatic therapy is available in cases of metastasis, and no definitive method of treatment has yet been established.