Malignant phosphaturic mesenchymal tumor, mixed connective tissue variant of the tongue

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Oncogenic osteomalacia has recently been recognized to be a phosphate wasting state caused by the secretion from a tumor of fibroblast growth factor-23 (FGF-23), which inhibits the renal tubular epithelial phosphate transport [1]. The majority of the oncogenic osteomalacia-associated mesenchymal tumors are considered to belong to the category of phosphaturic mesenchymal tumors, mixed connective tissue (PMTMCT) variant [2].

PMTMCT typically follows a benign clinical course [2], and malignant cases are very rare [3].

We herein report a case of a recurrent malignant PMTMCT variant which arose in the tongue. This report was approved by The University Committee for Medical Research.

Case report

In 2002, a 48-year-old male consulted our clinic due to symptoms of oral bleeding. The physical examination revealed gibbosity and a 3×5 cm hard tumor in the middle of the tongue (Fig. 1). He had been receiving vitamin D, calcium, and phosphate for 2 years from a local community

hospital. The serum calcium and parathyroid hormone level showed a normal concentration when he visited our clinic. However, the serum phosphate level was markedly decreased (1.0 mg/dl, normal; 2.2-4.4 mg/dl). Radiographs revealed deformity of the thoracic and lumbar vertebrae, and thinning of the cortical bone.

The tumor was marginally resected, having been diagnosed to be a benign giant cell tumor by the biopsy prior to the operation. However, based on an examination of the surgical specimen, the tumor was diagnosed to be a malignant PMTMCT variant as focal areas of high nuclear grade, high cellularity, and elevated mitotic activity (Fig. 2). After the operation, the hypophosphatemia improved. The expression of the FGF-23 gene product was detected by a reverse transcriptase polymerase chain reaction (RT-PCR) analysis from the tumor (Fig. 3).

In 2003, the tumor recurred in the oral floor. An additional resection was thus performed with reconstruction using a scapular-latissimus dorsi osteocutaneous flap. In 2004, the tumor recurred at the oral cavity and the cervical lymph nodes. As surgery with sufficient margins was expected to result in severe morbidity, the patient was treated with radiotherapy (66 Gy).

The oral tumor and the lymph nodes thereafter markedly decreased. The tumors did not completely disappear; however, hypophosphatemia has not progressed for 2 years while the tumor slowly growing (Fig. 4).

~~Discussion~~

Since oncogenic osteomalacia was first described in 1959, it has been recognized that mesenchymal tumor-associated osteomalacia is resistant to high-dose vitamin D therapy and that a complete tumor resection results in a dramatic reversal of both hypophosphatemia and hyperphosphaturia [4]. In accordance with the tumor recurrence and resection, the hypophosphatemia in our case progressed and improved. These findings seen in our patient are therefore consistent with the typical course of oncogenic osteomalacia.

The production of FGF-23 was considered to be a main pathophysiology of oncogenic osteomalacia [1, 5]. Interestingly, the serum phosphate level did not decrease after radiotherapy while the tumor has been very slowly regrowing after it initially decreased in size during radiotherapy. So far, we could find no report that regarded such a unique

phenomenon.

Most cases of PMTMCT variant behave in a benign fashion [2]. Even in histologically malignant tumors, either local recurrence or distant metastasis is extremely rare [3]. In general, definitive radiotherapy is not considered as an effective treatment. However, this case tells us that PMTMCT is capable of acting in a rather malignant manner, and the FGF-23 producing property of the tumor might be changed by the radiotherapy. Radiotherapy may therefore be considered as an alternative treatment for a malignant PMTMCT if a meaningful resection is not possible.

References

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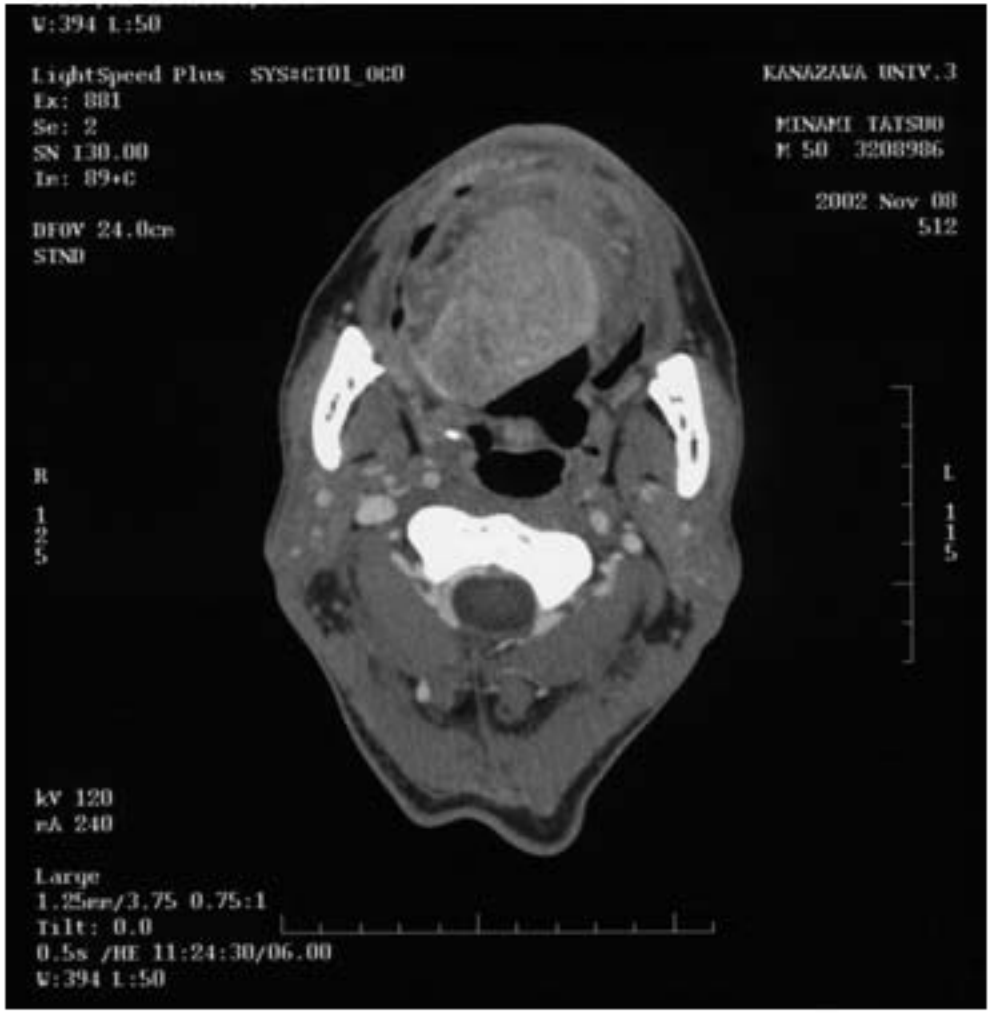
Figure legends

Fig. 1: The tumor located at the center of the tongue.

Fig.2: A histological analysis of the tumor (a; x100, b; x400). The tumor was diagnosed to be a malignant PMTMCT, based on the focal areas of a high nuclear grade, high cellularity, and elevated mitotic activity.

Fig.3: A RT-PCR analysis for the FGF-23 transcript expression. A 303-bp band presenting FGF-23 was present in this tumor lane.

Fig. 4: Treatment course and serum phosphate level.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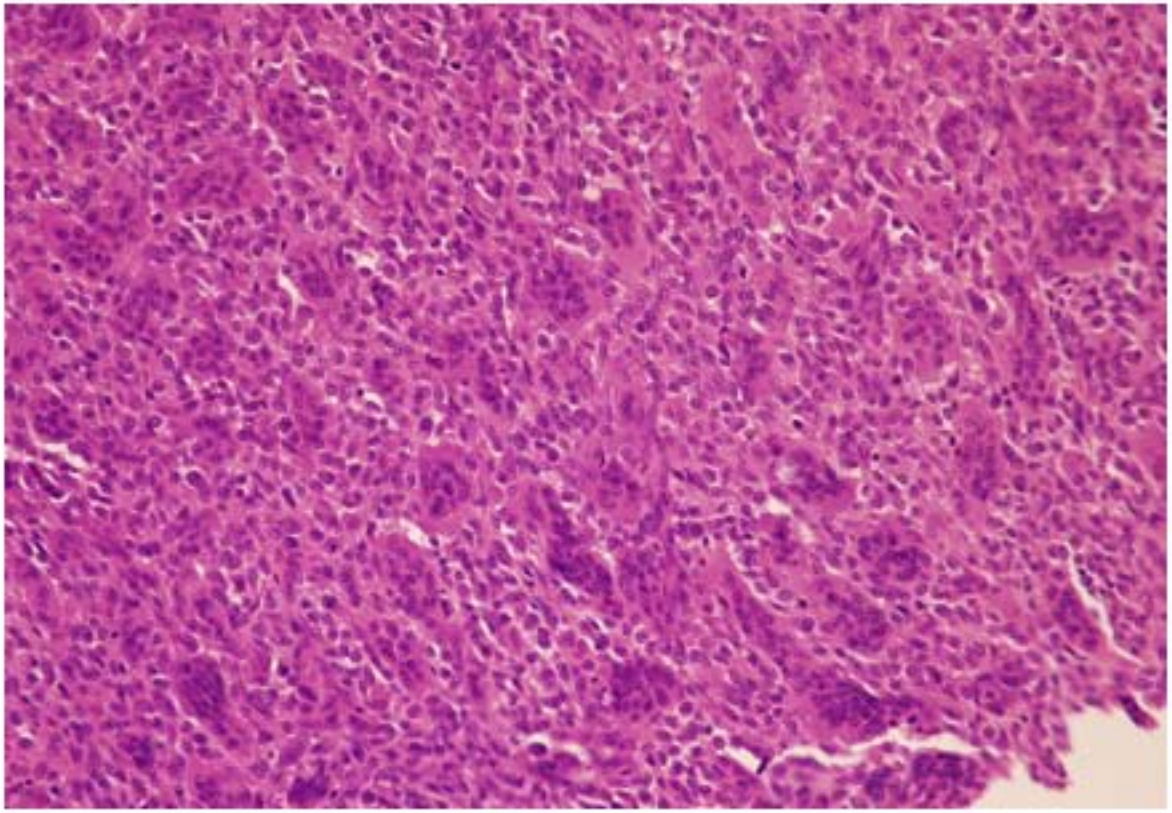
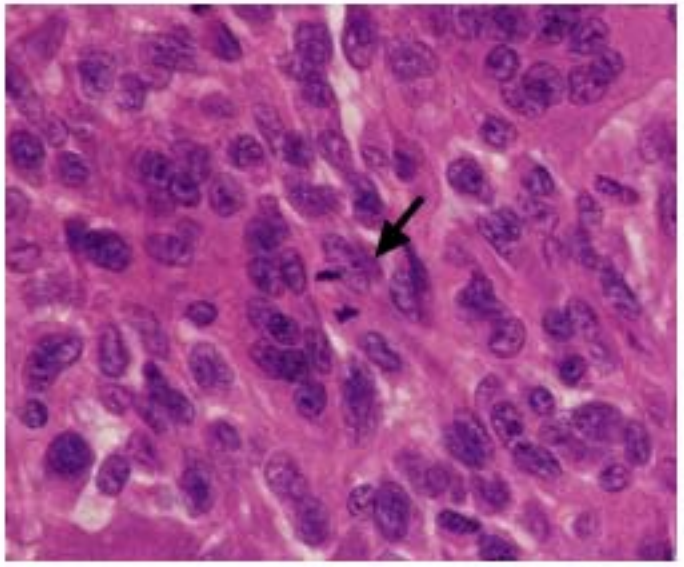
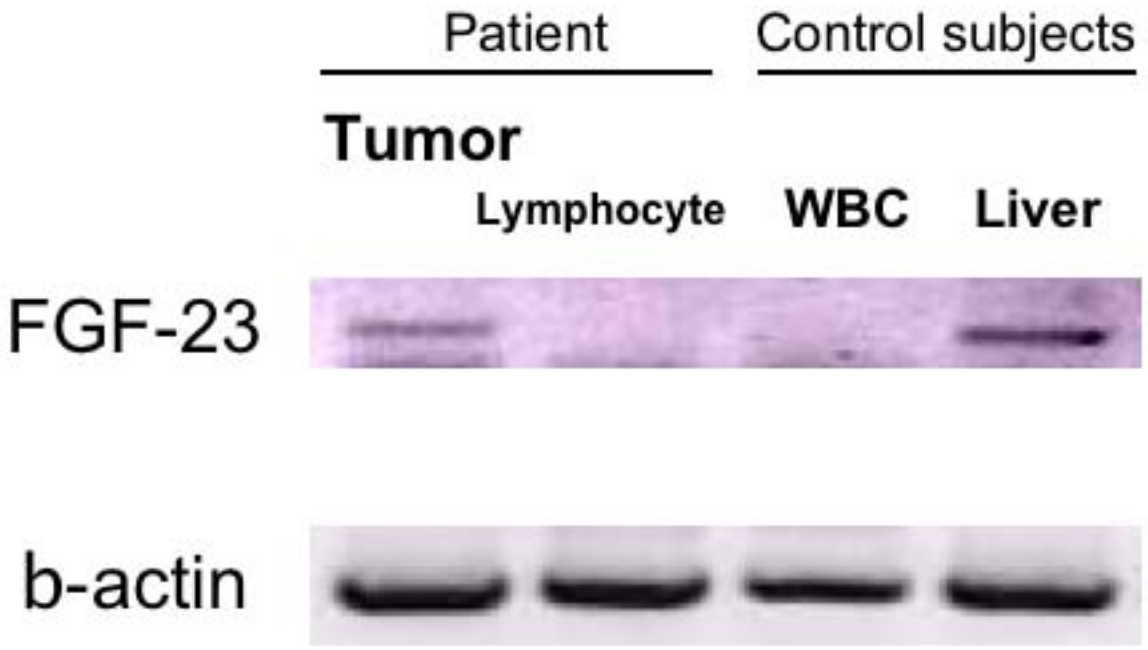


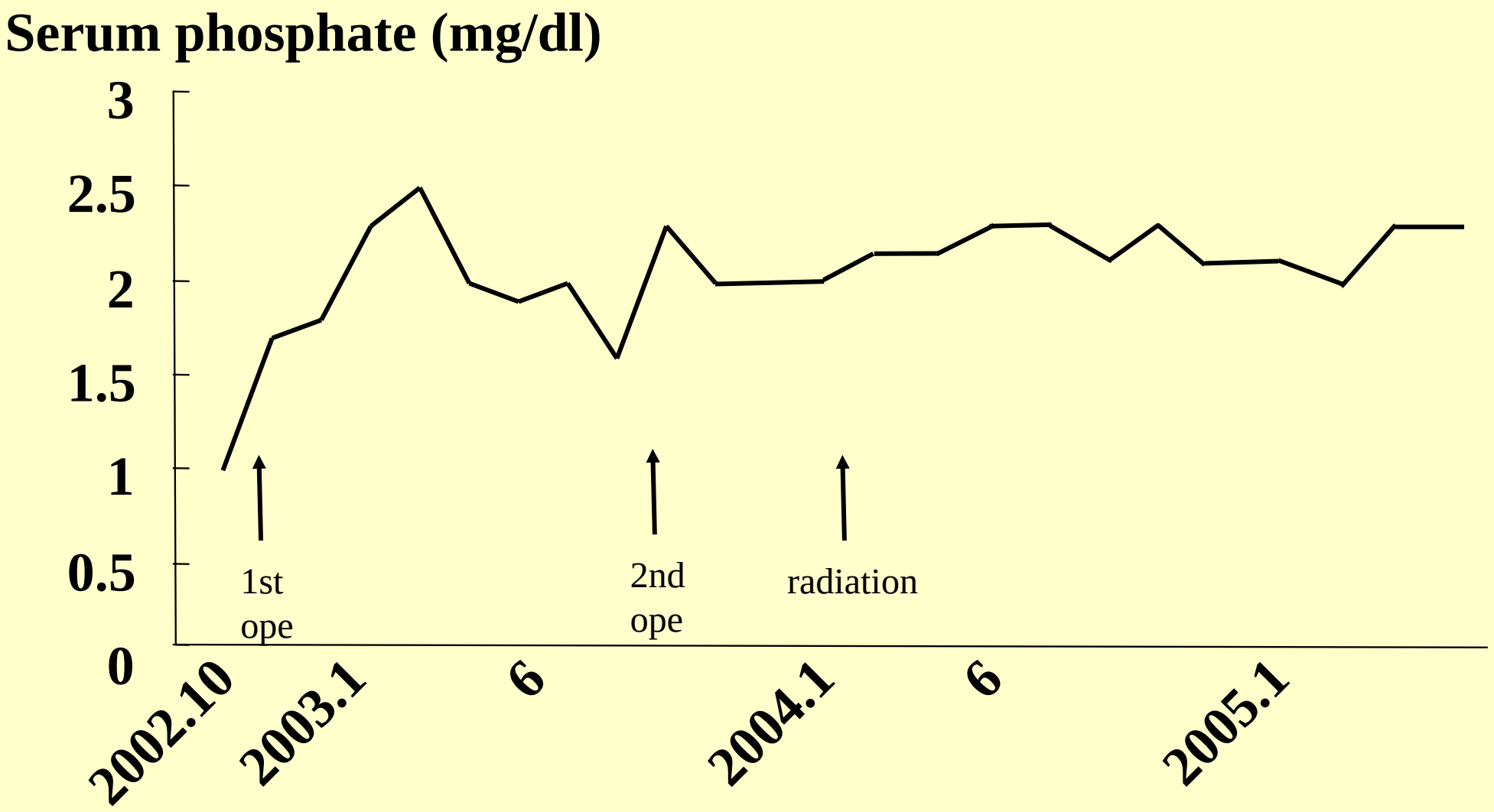


Expression of mRNA for FGF-23 in the Tumor



sense primer: 5'GGCGCACCCCATCAGACCATC3'

antisense primer: 5'GCCCGTTCCCCCAGCGTGCGTGTT3'


Serum phosphate (mg/dl)
3
2.5
2
1.5
1
0.5
0
1st ope
2nd ope
radiation
2002.10
2003.1
6
2004.1
6
2005.1