Current Problems in Cancer 45 (2021) 100704

Contents lists available at ScienceDirect

Current Problems in Cancer

journal homepage: www.elsevier.com/locate/cpcancer

Nasal hemangiopericytoma presenting with oncogenic osteomalasia: A case report and literature review

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ABSTRACT

Sinonasal type hemangiopericytoma is a rare soft tissue tumor. Oncogenic osteomalacia (tumor-induced osteomalacia) is a rare syndrome that develops especially due to benign mesenchymal tumors. Nonspecific general bone pain and weakness delay the diagnosis and treatment of oncogenic osteomalacia, and it is difficult to determine the localization of the primary tumor causing oncogenic osteomalacia.

A 43-year-old male patient with nasal hemangiopericytoma with symptoms of oncogenic osteomalacia is presented. The patient had musculoskeletal complaints at first and was diagnosed with lumbar disc herniation and surgery was performed. When his complaints recurred 1 year later, he was re-evaluated and diagnosed with hypophosphatemic osteomalacia. Despite the various treatments he received, his complaints did not decrease but increased, so a detailed examination was decided. When the positive PHEX mutation and very high fibroblast growth factor 23 level were detected, PET-CT imaging was performed with a prediagnosis of possible oncogenic osteomalacia, but no finding was found. Then he was evaluated with Ga-68 DOTATATE, and the soft tissue mass filling the right ethmoidal sinus was detected. Due to the relation of the mass with surrounding structures, it was considered unsuitable for total excision and incomplete surgical excision was performed. Pathologic evaluation revealed sinonasal type hemangiopericytoma (glomangiopericytoma). A significant remission in the patient's complaints was observed after the operation.

☆ Conflict of Interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

☆☆ Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

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https://doi.org/10.1016/j.currproblcancer.2020.100704

Young patients with osteomalacia with unknown causes should be evaluated for malignancy, and screening and further examinations should be performed.

ARTICLE INFO

Keywords: Nasal hemangiopericytoma; Oncogenic osteomalacia; Fibroblast growth factor 23

Introduction

Hemangiopericytomas (HPC) take their names from their origin cells, pericytes, which are myofibroblast-like cells surrounding capillaries and venules.[1] HPC is most common in the extremities.[2] Head and neck HPCs are more rarely seen and constitute 15% of all HPCs.[3] Besides, 2.5% of all vascular sinonasal tumors are HPC.[4]

Sinonasal type hemangiopericytoma has the characteristics of both myoid cell-originated glomus tumor and pericytic cell-originated hemangiopericytoma.[5] It can be seen in all age groups.[6] It is most common in the ethmoid sinus (44.8%) and generally causes unilateral polypoid tissue formation in the nasal cavity.[6,7] The mean tumor size was found to be 3.9 cm, but it can reach up to 14 cm.[6] Epistaxis and nasal obstruction are the most common signs and symptoms.[6] Sinonasal HPC with aggressive behavior (malignant SHP) is an extremely rare form. The factors such as tumor size larger than 5 cm, bone invasion, prominent nuclear pleomorphism, increased mitotic activity (>4/10 high power fields), necrosis, and proliferation index greater than 10% are the determinants of aggressive behavior.[8] Histologically, sinonasal HPCs have a diffuse growth pattern and "staghorn" branching vasculature, and rarely show necrosis.[9,10] In addition, they have a diagnostic, distinctive perivascular hyalinization.[10] While CD34 is negative or focal positive in the sinonasal type of HPC, it is more common and strongly positive in soft tissue type.[11,12]

Open surgery or endoscopic resection is preferred primarily in the treatment.[6] Due to the no difference in recurrence rates and endoscopic resection is being a less invasive surgical option with reduced morbidity than open surgery, endoscopic resection has been applied more frequently.[13] Resection may be complete or incomplete depending on the case. Local recurrence usually develops due to incomplete surgical excision and has been reported in 7%-40% of the cases.[14] Overall, the prognosis for this type of tumor is very good and survival rates for 5 years as 88.1% and 10 years as 65.3% have been reported.[10] The recurrence rate is about 20% and occurs generally 3 years after initial treatment.[10]

Oncogenic osteomalacia (tumor-induced osteomalacia) is a rare syndrome that develops especially due to benign mesenchymal tumors and is characterized by the secretion of fibroblast growth factor 23 (FGF23).[15] FGF23 decreases phosphate reabsorption in the renal tubule, urinary phosphate excretion increases, and hypophosphatemia develops.[16] It also inhibits the 1a-hydroxylation of vitamin D, causing a decrease in calcitriol (the active form of vitamin D made in the kidney) levels.[17] Low levels of calcitriol lead to a decrease in calcium absorption, secondary hyperparathyroidism, and phosphate loss in the urine.[18] Ultimately, all these affect bone mineralization and cause osteomalacia. Progressive bone pain, muscle weakness, and walking disability are observed in patients with osteomalacia.[19] Nonspecific general bone pain and weakness delay the diagnosis and treatment of oncogenic osteomalacia, and it is difficult to determine the localization of the primary tumor causing oncogenic osteomalacia.[19]

Case

A 43-year-old male patient presented with low back and hip pain, weakness in extremities, difficulty walking, and joint stiffness. His complaints started about 3 years ago, and he was diagnosed with lumbar disc hernia in the first evaluation at this time, subsequently, a surgical operation was performed on L4-5. One year after the operation, the patient was diagnosed with hypophosphatemic osteomalacia with recurrent low back and hip pain, difficulty walking and sitting. Although the patient was under treatment, his complaints continued, and also the joint stiffness, which was lasted 30-60 minutes in the morning and reduced with movement during the day, appeared. Therefore, a year later, treatment was started with the diagnosis of ankylosing spondylitis. Six months later, closed reduction procedure and internal fixation operation were performed due to non-traumatic femoral head fracture.

In the physical examination, he needed support while sitting and walking. He could walk only short distances with crutches. There was localized pain in the forearm and tibia upon palpation. The range of motion of the hip joint was limited and painful. Loss of muscle strength was 4 of 5 in the upper extremities, 3 of 5 in the lower extremities, and deep tendon reflexes were normal, there was no sensory defect.

Laboratory examination results were as follows: BUN: 28 mg/dL (7,9-21), creatinine: 0.9 mg/dL (0,84-1,25), Na: 140 mmol/L (136 -146), K: 4.4 mmol/L (3,5-5,1), ALT: 50 U/L (0-45), AST: 38 U/L (0-35), ALP: 288 U/L (30 -120), GGT: 88 U/L (0-55), albumin: 4.4 g/dL (3,5-5,2), Ca: 9.7 mg/dL (8,8-10,6), P: 0.9 mg/dL (2.5-4.5), Mg: 2.3 mg/dL (1,8-2,6), PTH: 68 pg/mL (12-65 ng/L), and viral his serology was negative. Repeated radiographic examination showed diffuse osteopenia, and the DEXA scan revealed T and Z scores of L1-5 interval were -3.8 SD, -3.6, respectively; T and Z scores of the femoral neck were -3.7 SD, -3.1 SD, respectively. The patient did not respond to previous treatments such as vitamin D, calcitriol, zoledronic acid, sülfasalazin, and anti-TNF drugs. Due to these results, it was decided to conduct a detailed examination. Other biochemical tests including CRP, ESR, autoimmune markers, vitamin B12, 25-OH vitamin D level, thyroid function tests, muscle enzymes, hormone levels, and tumor marker levels, glucose and amino acid excretion in urine, protein electrophoresis in urine and blood, immunoelectrophoresis tests were performed and resulted within normal limits.

The PHEX gene mutation and FGF23 level tests were done with a prediagnosis of possible oncogenic osteomalacia. The PHEX mutation was positive and the FGF23 level was 442 RU/mL (5-195 RU/mL). Thereupon, PET-CT scan was performed with a pre-diagnosis of malignancy of unknown origin, but no finding was found. The patient was then evaluated with Ga-68 DOTATATE, and a soft tissue mass of 46×22mm, filling the right maxillary sinus and destructing the bone, was detected (Fig. 1). A paranasal sinus CT scan was obtained for detailed evaluation, and a massive soft tissue was detected filling the right ethmoid sinus, destructing the nasal concha in the midline, causing thinning of the bony structure in the orbital medial wall, nasal septum, and ethmoid cell walls, and displacing the nasal septum to the left with axial dimensions of 48×24 mm and craniocaudal dimensions of approximately 36 mm. Due to the relation of the mass with surrounding structures, it was considered unsuitable for total excision and incomplete surgical excision was performed. Pathology results from the material, which stained positively for NSE and CD56, and negative for CD34, were consistent with glomangiopericytoma; sinonasal type hemangiopericytoma.

The evaluation after the operation revealed that muscle strength was 5 of 5 in the upper extremities, 4 of 5 in the lower extremities, deep tendon reflexes (DTR) were normal, no loss of sensation, and there was a significant increase in the distance in which he could walk with or without support.

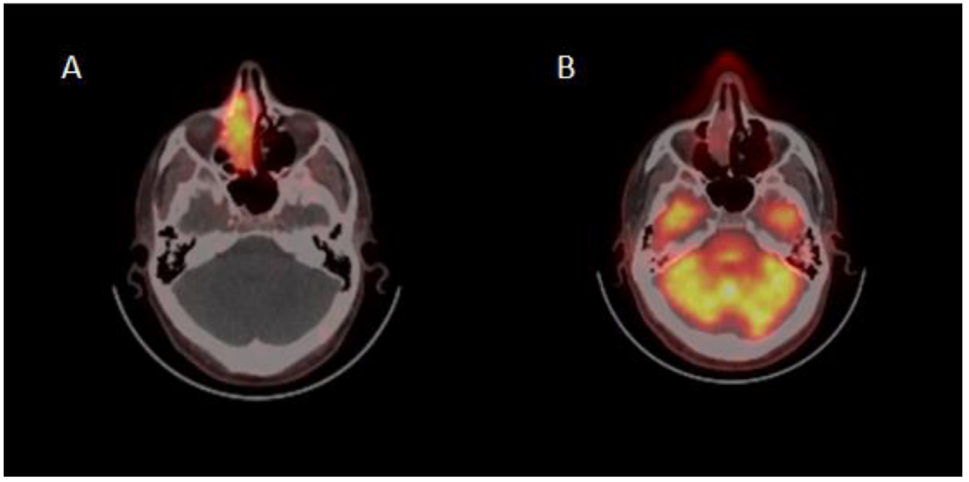

Fig. 1. (A) Ga-68 DOTATATE image of nasal soft tissue mass (B) PET-CT scan of nasal soft tissue mass. (Color version of figure is available online.)

Discussion

Sinonasal type hemangiopericytoma is a soft tissue tumor that is most commonly seen in the ethmoid sinus (44.8%)[6] and generally forms unilateral polypoid tissue in the nasal cavity.[7] In our case, there was a 5 cm soft tissue mass filling the right ethmoid cell and destructs the nasal concha in the midline. According to the immunohistochemical examination of the mass, it was stained positively for CD56 and negative for CD34, which was compatible with sinonasal type hemangiopericytoma.

Patients with osteomalacia have complaints of progressive bone pain, muscle weakness, and gait difficulty,[19] and our patient also had these complaints. Besides, hypophosphatemia and slightly elevated PTH values were compatible with hypophosphatemic osteomalacia. T- and Z-scores revealed by the DEXA scan were less than -2.5, were consistent with osteoporosis. Furthermore, the positive PHEX mutation and very high FGF23 values were found in the patient's condition in favor of oncogenic osteomalacia. In addition, it is difficult to determine the localization of the primary tumor causing oncogenic osteomalacia,[19] and further investigation was required in our patient to determine the primary tumor location, as well.

Oncogenic osteomalacia due to sinonasal HPC is extremely rare. According to Li et al, 12 cases of oncogenic osteomalacia due to sinonasal type HPC have been reported since 1995.[19] Patients with oncogenic osteomalacia caused by HPC generally do not show sinonasal symptoms, and our patient was the same. Although he had musculoskeletal symptoms related to oncogenic osteomalacia, there were no significant symptoms for sinonasal type HPC such as epistaxis and nasal obstruction,[6] he just had a headache. Although there was a clinical finding in our case, the primary tumor could not be detected by other imaging methods. Ga-68 DOTA-TATE PET was performed to determine the primary functional tumor tissue and a polypoid mass in the right ethmoid sinus was detected. The tumor size being approximately 5 cm and the presence of bone metastasis are in favor of malignancy of sinonasal HPC. Complete surgical resection usually leads to the recovery of oncogenic osteomalacia. The patient's persistent osteomalacia complaints, which did not be treated despite various previous treatments, improved with surgical resection of primary sinonasal HPC. No recurrence or metastasis was detected in the 3-month follow-up of the patient after treatment.

Conclusion

In conclusion, screening for malignancy and further examinations should be performed in osteomalacia of unknown causes at an early age. Our case presents the importance of tumor screening in cases of persistent osteomalacia that do not improve with various treatments.

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