Case Report

Metastatic Tumors to Craniofacial Skeleton: Analysis of Two Cases and Review of the Literature

Mohsen Dalband[1], Shoaleh Shahidi[2], Mahdi Gholami[3], Adell khayati[4]

[1]Associate Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Shahid Beheshti University of Medical Science, Tehran, Iran
[2]Professor, Biomaterial Research Center, Department of Oral and Maxillofacial Radiology, School of Dentistry, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Oral & Maxillofacial Diseases Research Center, Mashhad University of Medical Science, Mashhad, Iran
[4]Assistant Professor, Department of Oral and Maxillofacial Surgery, School of Dentistry, Kurdestan University of Medical Science, Sanandaj, Iran

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Abstract

Craniofacial skeletal metastasis is a rare presentation of advanced prostate cancer. This is a report of a 69-year-old man who presented with numbness of the right lower lip and recently ill-fitting lower denture. Based on the medical history of benign prostate hyperplasia (BPH) and suspicion of a metastatic tumor, prostate core needle biopsy was performed. Histology of the prostate biopsy confirmed an adenocarcinoma with Gleason Score of 6/10. The diagnosis of metastatic prostate adenocarcinoma was established by incisional biopsy from the mandibular lesion. Androgen deprivation therapy (ADT) was administered along with bilateral orchidectomy and radiotherapy. He had a significant resolution of trigeminal nerve palsy and the other symptoms at subsequent follow-ups, but after 18 months passed away. The second case was a 65-year-old man with a history of prostate cancer since 5 years ago. He complained of painful swelling in the right side of the face. Radiographic evaluation revealed new bone formation in right mandibular ramus and condylar process as well as the left temporoparietal region. Incisional biopsy from mandibular lesion revealed metastatic prostate adenocarcinoma. Palliative radiotherapy for increasing quality of life started for the patient but he died after 9 months. The related literatures were reviewed.

Keywords: metastatic tumor; prostate cancer; adenocarcinoma; craniofacial skeleton.

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Introduction

Prostate cancer is the second most common malignant tumor in men after lung cancer and the third most common cause of death from cancer after lung and colorectal cancers(1). It is predominantly a tumor of older men and the mean age at diagnosis is 72 years. More than 95% of primary prostate cancers are adenocarcinoma (2). Metastasis to bone is a common and morbid complication of prostate cancer and 85% of men who die of prostate cancer have bone metastasis (3). Although bones of any area can be affected by metastasisspine, proximal long bones, thorax, pelvis and skull are mostly affected. Osteoblastic bone metastasis (bone forming type), which is the predominant type in prostate cancer, results from the disordered proliferation of osteoblasts with incomplete bone calcification (4). Metastatic tumors in oral cavity are rare and only 1-3.2% of all oral cancers are metastasis of primary tumors elsewhere in the body (5, 6). Some tumors more frequently affect the jaw bone as their metastatic target, for example, 11% of jaw bone metastasis in men originate from prostate gland compared with 1.5% observed in soft tissues (7). Mandibular body is the preferred site of these metastases (8).

The purpose of this case report is to emphasize the clinical importance of metastatic tumors to the jaws and cranial bones, especially as an initial manifestation of an underlying malignant disease. We obtained a written consent from the patients and clearance from the Hospital Ethics Committee to report these unusual presentations of an advanced prostate cancer.

Case presentations

Case 1: A 69-year-old white man was referred to our department with the chief complaint of a painful right facial swelling, trismus and numbness of the right side of the lower lip for four months. Also, the patient complained of recently ill-fitting lower denture that seemed to be the result of alveolar bone expansion. His medical history was positive for symptoms of obstructive uropathy including frequency, post voiding dribbling, dysuria and a weakened stream for two months. The diagnosis of benign prostate hyperplasia (BPH) had been made by urologists previously and he had undergone alpha-blocker and 5α- reductase inhibitor therapy. Coincidentally, the patient had generalized musculoskeletal pain and a history of controlled hypertension and chronic smoking but no history of alcohol consumption. Extraoral physical examination revealed a right perimandibular swelling without any cervical lymphadenopathy. Intraoral physical examination revealed complete edentulous arches with a limited range of motion and presence of a mass in the body of mandible with surrounding soft tissues being slightly hyperplastic and fibrotic. Plain panoramic view of the mandible showed an irregular alveolar ridge with sclerotic bone throughout the right mandibular area extending to ascending ramus (Figure 1). According to the history of BPH and generalized musculoskeletal pain, whole body bone scan and prostate-specific antigen (PSA) was requested.

Tc-99m methylene diphosphonate (MDP) bone scintigraphy revealed multiple zones of increased radiotracer activity in the right mandible, sternum, spine, ribs, pelvis and left femur. The scan findings were suggestive of skeletal metastases involving the above-mentioned areas. His serum prostate-specific antigen level (12.5ng/ml) and bone-specific alkaline phosphatase level (3025 IU/L) were found to be elevated. With the suspension of prostate cancer, the patient was referred to the urology department. Prostatic adenocarcinoma, histological grade 6 on Gleason score, was confirmed by performing Trans Rectal Ultrasonography (TRUS) guided biopsy of the prostate. Histopathologic study of the specimen revealed fragments of fibrous stroma infiltrated by tubules and columns of atypical cells with clear cytoplasm and hyperchromatic nuclei (Fig.2). Biopsy of the mandibular lesion revealed a neoplastic gland tissue infiltrated within bony trabeculae and compatible with prostatic origin adenocarcinoma (Fig. 3).

According to the patient's age, symptoms and presence of distant metastases, the following treatment options were selected. The most common symptoms were originated from the lower urinary tract and bone metastasis. Palliation of symptoms of the lower urinary tract was done with transurethral resection of prostate (TURP) and palliation of symptoms of bone metastasis was performed with hormonal therapy (luteinizing hormone-releasing hormone agonist and anti-androgens), bilateral orchiectomy and radiation therapy. The therapy was primarily effective in improvement of signs and symptoms of the primary and metastatic lesions which resulted in decreased serum level of PSA to 3.5ng/ml. Nevertheless, the risk of prostate cancer progression and death persisted throughout the follow-up period and the patient died after 18 months**.**

Case 2: A 65-year-old male patient was referred to our department with the chief complaint of a painful swelling in the right side of the face. There was a history of prostate cancer since 5 years ago. Radical prostatectomy, bilateral orchiectomy and radiation therapy were done for the patient at that time. Then he was under close follow up with serial serum PSA assay and annual whole body bone scanning. Panoramic view showed evidence of speculated new bone formation in the right side of mandibular ramus extending to the coronoid and condylar process. Loss of continuity of cortex in the sigmoid notch region was found. Right

maxillary tuberosity also had evidence of new bone formation (Fig. 4). Spiral CT scan of the head and face confirmed the panoramic findings and revealed skull metastasis in the left temporoparietal region as well (Fig. 5). Incisional biopsy from anterior border of ramus was performed. Histopathologic examination revealed osteoblastic metastatic adenocarcinoma of prostatic origin to the jaw. Because of involvement of different parts of body, palliative radiotherapy for increasing quality of life was started for the patient; however he died after 9 months.

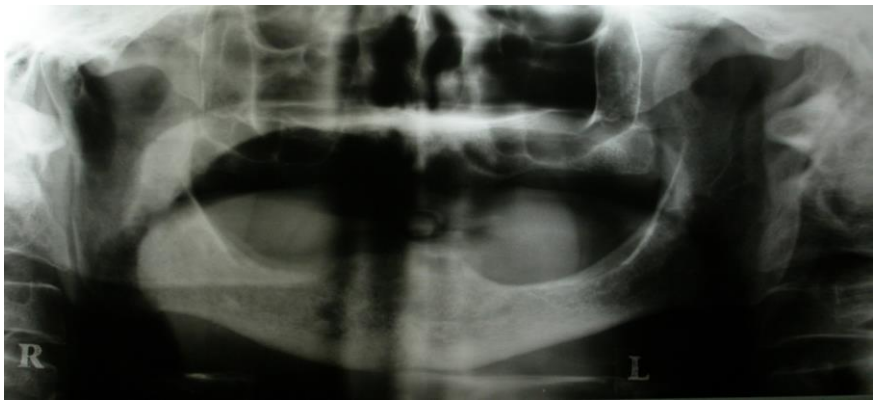

Figure1. Plain panoramic view of the mandible showing an irregular alveolar ridge with sclerotic bone throughout the right mandibular body and ramus

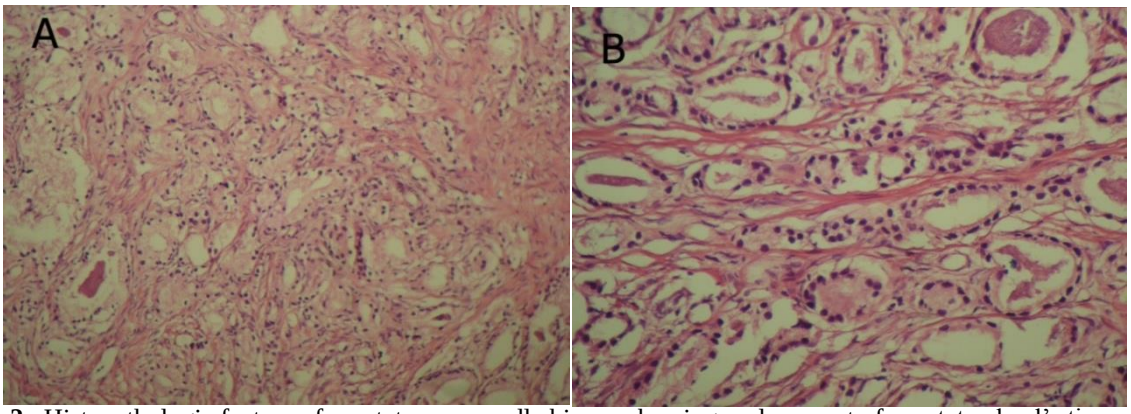

Figure 2. Histopathologic feature of prostate core needle biopsy showing replacement of prostate gland's tissue by neoplastic adenocarcinoma cells. Hematoxylin and eosin; original magnification ×100 (A) and ×200(B)

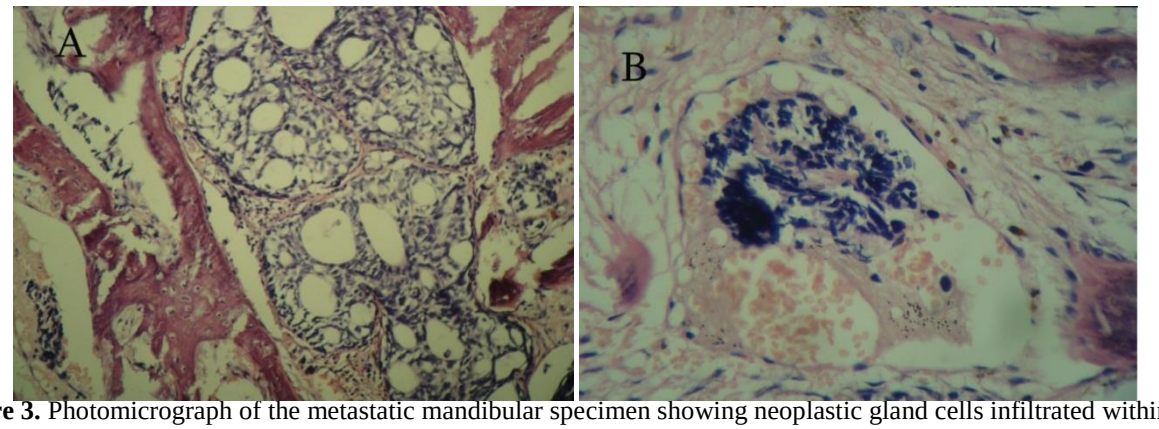

Figure 3. Photomicrograph of the metastatic mandibular specimen showing neoplastic gland cells infiltrated within bony trabecular (A). Vascular invasion by neoplastic cells is also seen (B)

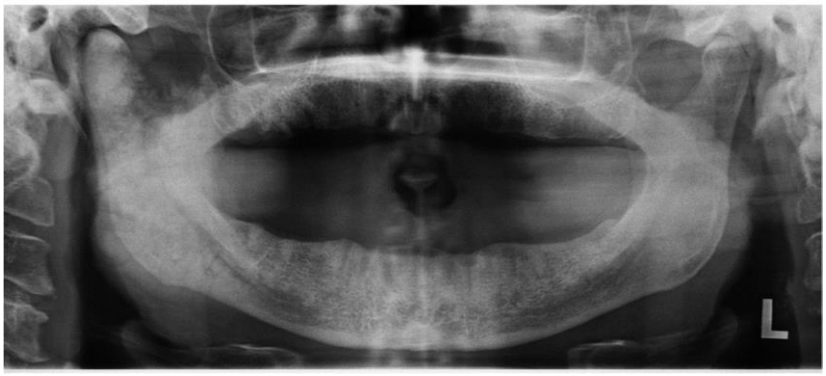

Figure 4. Plain panoramic view of the mandible showing evidence of speculated new bone formation in the right ramus extending to the coronoid and condylar process

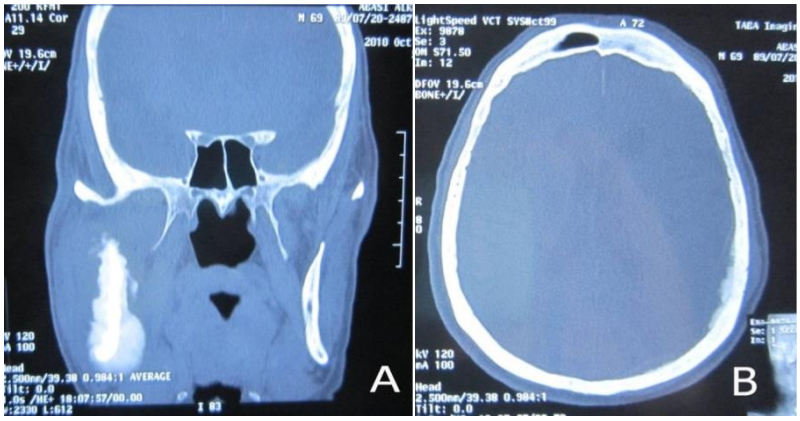

Figure 5. Helical CT scan of the head confirming the panoramic findings (A) and revealing skull metastasis in the Left temporoparietal region (B)

Discussion

Prostate cancer is the second most common cancer in men, accounting for 1 in 9 of all new cancers, and with more than 670,000 new diagnoses worldwide annually (9). The metastatic spread is primarily in the axial skeleton in which lesions are often located in vertebra and ribs via dissemination through Batson's venous plexus. The spread in bone also follows the distribution of adult red bone marrow, that is skull, thorax, pelvis, spine, proximal long bones (10,11), subsequently progressing to involve adjacent cortical bone.

Although metastatic prostate carcinoma is predominantly osteoblastic (bone forming type), osteoclast activation also has an important role in the growth of sclerotic metastasis in bones. In a study of 68 patients with prostatic bone metastasis who underwent surgery for stabilization of pathological fracture or impending fracture, most lesions were osteoblastic and only 29.1% were osteolytic or mixed (12).

Histopathologic analysis of metastatic prostate tumors typically shows substantial numbers of osteoblasts adjacent to prostate cancer cells, whereas few or no osteoblasts can be seen in normal bone or in metastatic bone lesions from other types of cancers (kidney, lung, and most cases of breast cancer) in which most often exist plenty of osteoclasts in cancer-affected areas. Increased osteoblast activity in metastatic prostate cancer lesions of bones is accompanied by elevated serum level of osteoblast proliferation markers such as bone-specific alkaline phosphatase in the affected patients similar to the reported cases here (13).

Skeletal metastases occur in approximately 90% of patients presenting with advanced prostate cancer and the extent of bone disease directly correlates with survival (14, 15); however, Metastasis to jaw bones is uncommon. The identification of these lesions can become a real diagnostic challenge because they present non-specific symptoms. Nevertheless, they have a diagnostic (a quarter of them reveal unknown cancer) and prognostic significance (their presence is correlated with limited survival of the patient) (7, 16).

In an extensive review of metastatic tumors to jaw bones, Hirshberg et al. observed that the most common primary cancer site was breast, followed by lung, adrenal, kidney, bone, colorectal and prostate (17). In accordance with results from other studies, they also showed that the most common site of metastatic tumors

was the mandible (85%) and only 13.6% of the metastatic tumors happened in maxilla (5, 17, 18, 19).

In most patients who present with a metastatic tumor, as in our second case, the distant primary tumor has already been diagnosed, and in most cases treated. However, as in our first case, the discovery of a metastatic tumor leads to detection of an occult primary malignancy elsewhere in the body (17, 19, 20). In such cases, the histopathologic features of the metastatic tumor may provide an evidence for detection of primary tumors.

Compatible with other authors' descriptions, our first patient's chief complaints were swelling, ill-fitting denture, pain, trismus and paresthesia (5, 17, 21, 22). Metastatic Prostate cancer tends to be osteoblastic and leads to make the surrounding bone thicker and denser, whereas many other metastatic cancers to the bones tend to be osteolytic. The metastatic deposits of prostate cancer cells in the mandible around the inferior alveolar nerve can cause pain and paresthesia characterized as numb chin syndrome (NCS) (23, 24).

Although most cases of NCS are of benign origin (e.g., dental disease, dental anesthesia or trauma, diabetes mellitus, sarcoidosis, multiple sclerosis, amyloidosis or osteomyelitis), in the absence of trauma or dental history, especially in elderly people, malignancies must be included in the differential diagnoses of NCS (24,25).

Systemic diseases such as diabetes mellitus, lupus erythematosus or sarcoidosis usually present as mononeuropathy multiplex, not as numbness restricted to the distribution of the mental nerve. Giant cell arteritis is another unusual cause of NCS (26).

On the other hand, metastasis to temporal bone typically presents with the classical triad of otalgia, periauricular swelling and facial nerve palsy (27). Also, increased bone volume due to metastatic lesion, in some cases, can lead to trismus (5, 17, 22).

Detection of an asymptomatic metastatic disease in prostate cancer is greatly affected by the staging tests performed. Radionuclide bone scans are currently the most widely used tests for metastases to bone, which is the most common site of distant tumor spread. Magnetic resonance imaging (MRI) is more sensitive than radionuclide bone scans but is impractical for evaluating the entire skeletal system.

Some evidence suggests that serum PSA levels can predict the results of radionuclide bone scan in newly diagnosed patients. In one series, only 2 of 852 patients (0.23%) with a PSA of less than 20 µg/l, had a positive bone scan in the absence of bone pain (28). In another series of 265 prostate cancer patients, 0 of 23 patients with a PSA of less than 4µg/l, had a positive bone scan, and 2 of 114 patients with a PSA of less than 10 µg/L had a positive bone scan (29).

Detection of bone metastases indicates progression to lethal prostate carcinoma (30). At this stage, complete remissions are rare and onset of complications of bone metastases is likely. Survival of the patient with prostatic carcinoma is related to the extent of tumor. When cancer is confined to the prostate gland, median survival in excess of 5 years can be anticipated. Patients with locally advanced cancer are not usually curable and a substantial fraction will eventually die of the tumor, though median survival may be as long as 5 years. If prostate cancer has spread to distant organs, current therapy will not cure it. Median survival is usually 1 to 3 years and most such patients will die of prostate cancer (31).

In the two reported cases, in addition to hormonal therapy, local treatment of mandibular metastasis was performed by radiotherapy, which usually subsides pain and functional loss. Even in this group of patients, however, indolent clinical courses lasting for many years may be observed, but finally, death from cancer is inevitable.

Conclusion:

Although rare and with atypical symptoms, metastatic urogenital malignancies have been shown in jaws and cranium. A hamatogenous mechanism for spread from the primary site has been postulated and widely accepted. So, unusual symptoms such as a recently ill-fitting denture, chin numbness or generalized musculoskeletal pain should be considered the result of metastasis of cancer until proven otherwise. Consequently, physicians should be aware of the disorder and seek the cause when it is detected.

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Corresponding Author:
Mahdi Gholami
Assistant Professor, Oral & Maxillofacial Diseases Research Center,
Mashhad University of Medical Science, Mashhad, Iran
Tell: 05138829511
E-mail: gholamimh@mums.ac.ir