

CASE REPORT

Unusual mandibular metastasis of bladder cancer in a patient and two synchronous malignancies, bladder cancer and chronic lymphocytic leukemia, in an inguinal lymph node: A case report

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Abstract

Metastatic lesions to the mandible are rare, comprising less than 1% of all malignancies. Breast, lung and colon cancer are the most common primary tumors with a mandibular mass as the initial presentation of metastatic disease. The following report describes an unusual case of a mandibular mass in a patient with recurrent bladder transitional cell carcinoma (TCC) with a past medical history of chronic lymphocytic leukemia (CLL), as well as the synchronous presence of both cancers during the evaluation of an inguinal enlarged lymph node. The sudden appearance of an isolated lesion in the head and neck region should always raise suspicion in a patient with a history of cancer that rarely metastasizes to this site. The co-existence of two malignancies in the same lymph node is extremely rare, and, to our knowledge, this is the first case of metastatic bladder cancer and CLL in the same lymph node.

Key words

Bladder cancer, Mandible, Metastasis

1 Introduction

Metastatic tumors to the jawbones are uncommon. The clinical presentation of the metastases varies between different locations in the oral region. In the jawbones most patients complain of edema, pain and paresthesia which developed in a short period. Because of its rarity and the lack of extensive literature, mandibular metastatic disease usually presents as case reports and case series; the diagnosis of a metastatic lesion in the oral region is challenging, both to the clinician and to the pathologist, in recognizing the type of the lesion and in determining the site of origin^[1-3].

Bladder cancer is a very common urologic malignancy. In 2012, approximately 430,000 new cases were diagnosed worldwide. In the Western population, the majority of cases are transitional cell carcinoma. The most common site of metastatic disease outside the pelvis is bone (35%); among these lesions, 40% involve the vertebrae, and the rest of them

frequently appear in the iliac bones and the ribs. A mandibular mass accompanied by underlying osteolysis is a peculiar first presentation of bone metastases [4, 5].

Lymph nodes are the most common metastatic site inside the pelvic cavity and can be detected radiographically or clinically. However a definitive diagnosis can only be made with histology examination especially if there is a history of hematologic malignancy that mainly affects the lymph nodes, as in this case report. Synchronous occurrence of multiple neoplasms is rare. In such a case though, it can be difficult to assess the staging of each neoplasm and to determine optimal treatment according to the stage of each disease [6].

2 Case presentation

We report here in the case of a seventy-three year old male who presented with a chief complaint of gross hematuria in our oncology clinic in 2009. His past medical history comprised of chronic lymphocytic leukemia (CLL) diagnosed in 2004 and transitional cell carcinoma (TCC) of the bladder diagnosed in 2007. At the time of diagnosis (2007) the patient's bladder cancer stage was 0 (pTaN0M0, low grade by the WHO classification), and he remained asymptomatic until the time he visited our department.

In 2009, after the presentation of recurrent symptoms, he underwent cystoscopy with biopsies taken from suspicious areas in the bladder. The pathology report confirmed Grade III TCC with infiltration of muscular layer (pT2). Subsequently, the patient had computed tomography (CT) scan of the chest, abdomen and pelvis in order to exclude metastatic disease. Neither pelvic lymphadenopathy nor distant lesions were detected. The patient underwent radical cystoprostatectomy, and pathology revealed locally advanced disease with involvement of the prostate, spermatic cords, perivesical adipose tissue and three iliac lymph nodes (stage IV, pT4N2Mx). He received six cycles of adjuvant chemotherapy with Gemcitabine - Cisplatin.

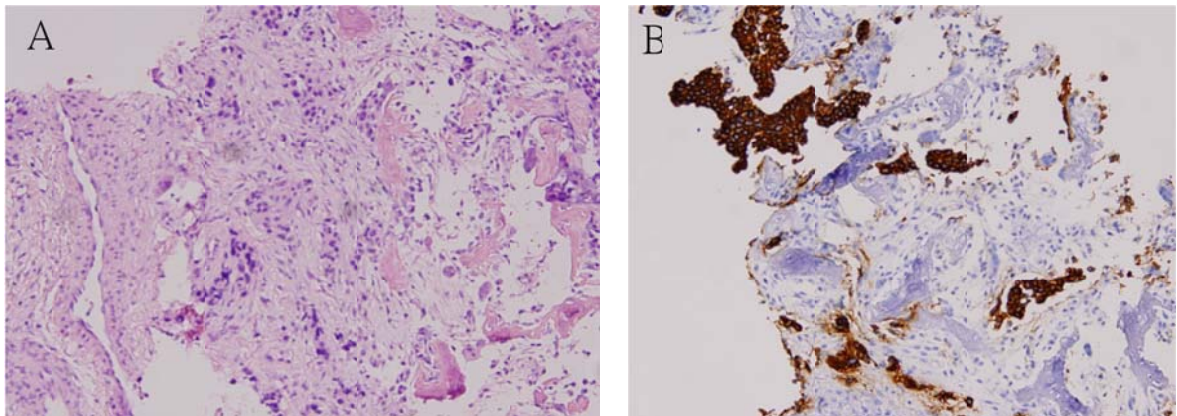


Figure 1. A: Hematoxylin eosin staining of mandibular biopsy. B: Cytokeratin 7 positive transitional cell cancer cells of the bladder in a mandibular biopsy. Expression of CK7 is seen in the majority of primary urinary bladder carcinomas [3, 13].

The patient remained stable and disease free with frequent follow up evaluation for two years. In 2011, he returned to our clinic with a solid mass in the posterior region of the right mandible. On physical examination, a hard, non-tender, localized, well-defined round swelling was palpated. There were no palpable regional lymph nodes. Oral cavity examination did not reveal the existence of any ulcer, fistula or wound. The involved mandibular area was edentulous, and the mucosa over the mass was intact. The skin over the mass was normal in color and texture.

A CT-guided biopsy of the mandibular mass (see Figure 1) was performed, and the histology report confirmed that it was infiltrated by malignant transitional cells with similar morphology and immunohistochemical characteristics as those detected in the patient's bladder cancerous lesion. Chemotherapy with Methotrexate-Vinblastine-Doxorubicin-Cisplatin

was initiated, and the patient completed six cycles. In the radiological findings, such as the bone metastatic disease and abdominal lymph nodes were improved.

A year later, the patient's physical exam revealed enlarged inguinal lymph nodes in the right groin. Inguinal lymph node biopsy showed not only infiltration with transitional carcinoma cells but also by CLL cells (see Figure 2). The CT of abdomen/pelvis showed progression of the disease in the para-aortic lymph nodes as well as a metastatic lesion in the left iliac bone. Treatment resumed with Vinflunine and radiation treatment but the patient did not respond completely to it and after several relapses passed with metastatic disease three years later.

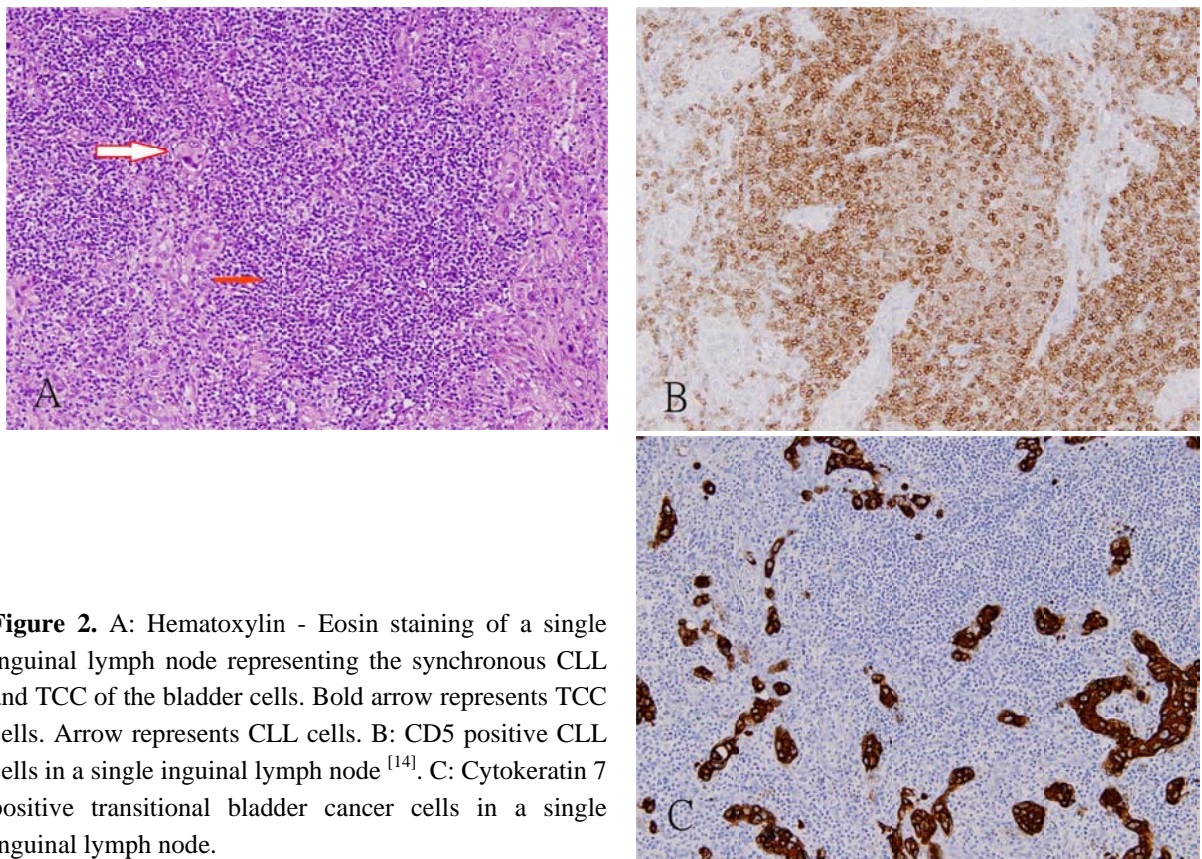


Figure 2. A: Hematoxylin - Eosin staining of a single inguinal lymph node representing the synchronous CLL and TCC of the bladder cells. Bold arrow represents TCC cells. Arrow represents CLL cells. B: CD5 positive CLL cells in a single inguinal lymph node^[14]. C: Cytokeratin 7 positive transitional bladder cancer cells in a single inguinal lymph node.

3 Discussion

Bladder cancer represents a neoplasia that is frequently attributed to environmental factors, mostly to smoking. Incidence is three times higher in men compared to women, and the incidence and mortality exponentially increase after 60 years of age^[7].

TCC, the most common type of bladder cancer, is often multifocal with 30%-40% of patients having more than one tumor sites at diagnosis. Painless gross hematuria and irritable bladder symptoms such as dysuria, increased frequency and urgency are the most common clinical manifestations^[8].

The treatment of non-muscle-invasive bladder cancer (Ta, T1, carcinoma in situ) begins with transurethral resection of the tumor and subsequent intravesical chemotherapy or immunotherapy with BCG. Radiation therapy is often combined with chemotherapy to make the radiation more effective. The combination of radiation therapy and chemotherapy after transurethral bladder surgery can eliminate cancers that would otherwise need to be treated with cystectomy. This approach can be used to treat smaller tumors as long as there are no signs of kidney blockage. High rate of recurrence and

progression in muscle-invasive cancer though underscores the importance of careful follow-up studies. NCCN 2012 guidelines specify that cystoscopy and urinary cytology should be performed every three to six months for the first two years followed by every six months for the subsequent two to three years, and then annually thereafter ^[9, 10].

Metastatic tumors to the oral region are infrequent and account for approximately 1% of all malignant oral tumors. However, metastatic tumors to the mandibular bone are not a rare phenomenon. Many cases with metastatic breast carcinoma to the mandible have been reported. Metastases in the oral region can occur in oral soft tissues or the mandibular bone. Metastatic tumors to the mandibular bone are more frequently reported than those in the oral mucosa. To our knowledge this is the first report of a mandibular metastasis from bladder cancer ^[10, 11].

A comprehensive study in 2001 indicated that patients with CLL have increased risk of subsequent neoplasms. The study measured the risk of second cancers among 16,367 patients with CLL under the population-based surveillance, epidemiology and end results (SEER) program. The possibility of a second primary cancer in patients, who were exposed to chemotherapy as first course of treatment, was reciprocal to the risk of those who did not receive treatment. Significant surplus was found for Kaposi sarcoma, malignant melanoma, and cancers of the larynx and the lung. Gastric cancer, tumors of the central nervous system among men and bladder cancer among women also had significant higher numbers after exposure to chemotherapy for CLL. Additional research is needed to explore the role of immunologic deterioration and other etiologic influences after the CLL treatment. Overall risk of developing a second cancer is elevated, independent of initial treatment, in people with CLL compared with those in the general population. Although the importance of shared factors responsible for that remains unclear, the pattern of increased cancer prevalence in CLL survivors implies an influence of immunodeficiency associated with CLL along with the long survival after the CLL diagnosis. Given the increased survival of CLL patients, it is important for physicians to be aware of the potential of second primary malignancies, particularly when new symptoms or physical findings arise. It is also prudent to discourage patients with CLL from carcinogens such as tobacco use and excessive sunlight. Further studies of second cancers in CLL are needed to clarify the role of immunologic impairment and other determinants. When feasible, molecular probes could clarify the underlying mechanisms of tumors associated with CLL ^[10, 12]. In our case the patient did not receive treatment for the CLL.

As a conclusion, despite their rarity, metastatic tumors should be considered in the differential diagnosis of new lesions of the jaws. Also, a patient with a history of CLL carries an elevated risk to develop a second malignancy, such as in this case, which to our knowledge, is the first case reporting bladder cancer and CLL simultaneously in a single (inguinal) lymph node. It is also rare to have metastatic disease in an already infiltrated lymph node. We emphasize the significance of a complete and careful work-up with particular attention to detailed medical history as well as careful clinical, radiographic and histopathologic examinations. Because these lesions are associated with a poor prognosis, early detection is extremely critical.

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