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Chronicles of Oncology

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A case of isolated metastasis to right level II cervical lymph node from intrahepatic cholangiocarcinoma

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Received: Jan 31, 2017

Accepted: Mar 01, 2018

Published Online: March 10, 2018

Journal: Chronicles of Oncology

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Keywords: Immunohistochemistry; Human papillomavirus; Fluorodeoxyglucose

Abstract

Cervical lymphadenopathy is a common reason for referral to the Otolaryngology – Head & Neck Surgery clinic. The differential diagnosis is broad, and can include infectious, traumatic, anatomical, and neoplastic etiologies. Cervical lymph nodes are the primary site of metastasis for head and neck cancers, but have also been implicated in other forms of cancer, including primary tumors of the lung, gastrointestinal tract, and breast.

The current case report outlines the diagnosis of metastatic intrahepatic cholangiocarcinoma, originally presenting as an isolated level II neck mass in an otherwise asymptomatic patient. Diagnosis was completed using a combination of radiological imaging, biopsy, and tumor biomarkers. This case report is the first with isolated metastasis to the level II nodal group from intrahepatic cholangiocarcinoma in an otherwise asymptomatic patient, and is the first to describe the specific treatment utilized in such a case. Neck mass evaluation is a common consult for all otolaryngologists. This case highlights the importance of both maintaining a broad differential when evaluating neck masses and when searching for a cancer with unknown primary

Introduction

Cervical lymphadenopathy is a common reason for referral to Otolaryngology – Head & Neck Surgery. The differential diagnosis is broad, and can include infectious, traumatic, anatomical, and neoplastic etiologies. In lesions suspected to be malignant in origin, physical examination using flexible nasopharyngoscopy is typically utilized in combination with Fine Needle Aspiration (FNA) in order to confirm both the presence of cancer and the location of the primary tumor. Recently, Human Papillomavirus (HPV) has overtaken smoking as the most common etiology of oropharyngeal cancer [1]. Disease associated with HPV has a higher probability of presenting as a malignant neck mass with unknown primary, particularly in level II [2,3]. Cervical lymph nodes are the primary site of metastasis for many head and neck cancers, but can also be involved by metastases from other primary sites including lung, breast and pancreas [4,5].

Cite this article: Forner D, Bullock M, Rigby M, Wilke D, Lamond N. A case of isolated metastasis to right level II cervical lymph node from intrahepatic cholangiocarcinoma, Chronicles Oncol. 2018; 1: 1003.

Cholangiocarcinoma is a malignant neoplasm arising from the biliary epithelium and has a varying incidence 6. Several risk factors are strongly linked to the development of cholangiocarcinoma, including primary sclerosing cholangitis, choledochal cysts, and liver fluke infection. In most cases, patients with cholangiocarcinoma present with advanced disease at the time of diagnosis [6]. Common presenting symptoms include painless jaundice [7], weight loss, pruritus, and abdominal pain [8]. Cholangiocarcinoma is known to metastasize to the liver, gallbladder, pancreas, branches of the portal system, and regional lymph nodes. Common distant sites of metastasis include the lungs, brain, and bone, with rare sites including skeletal muscle [9], ovaries [10], and spleen [11].

Case Report

A 47-year-old, otherwise healthy male was referred to the Otolaryngology – Head & Neck Surgery clinic after presenting with a two-month history of non-tender right neck mass. The mass initially measured 2 cm in maximal diameter and was contained in level IIa. Aside from a five-pound weightloss in the preceding two months, he was otherwise asymptomatic. He was a non-smoker and only occasionally drank alcohol. Physical exam revealed no further masses of the head and neck and normal flexible nasopharyngoscopy with mucosal surfaces free of lesions or masses. Differential diagnosis for the neck mass at this time remained infectious, anatomical, and neoplastic. Fine needle aspiration was performed to narrow the differential diagnosis, and revealed abundant, nonspecific neoplastic cells with polygonal, elongated shape, supporting the diagnosis of neoplasm.

The patient's neck mass progressed quickly. Subsequent enhanced Computed Tomography (CT) of the neck and chest was performed in order to elucidate a primary source of the neoplastic neck mass. This showed a 3.5 x 2.6 x 5.2 cm conglomerate of centrally necrotic lymph nodesinvolving levels II and III (**Figure 1A**), as well as a 5cm liver lesion. Initially, the differential diagnosis remained broad, with both the neck mass and liver lesion thought to be sites of metastases from a gastrointestinal primary. Given the FNA result, this was believed to be more likely than metastasis of a head and neck primary tumor to the liver.

Multiple FNA and core biopsies of the neck were performed for further immunohistochemistry staining and showed nests of poorly differentiated carcinoma (**Figure 2A**). Cells were positive for CK7, GATA3 and AE1/3 and negative for CK20, vimentin, CD45, S100, TTF1, napsin, synaptophysin, OCT4, SALL4 and p63 (**Figure 2B,2C**). Positron emission tomography (PET)/CT scan demonstrated intense Fluorodeoxyglucose (FDG) avidity of the known right neck mass and liver lesion (Figures 1B and 3B, respectively). Further investigation revealed a markedly elevated carbohydrate antigen 19-9 (CA19-9) to 90,000 U/mL. Triphasic liver CT showed a dominant hepatic mass within segments 7 and 8, demonstrating arterial rim enhancement, microlobulated border, and heterogeneous central cystic necrosis and enhancement (**Figure 3A**).

Given his biomarker, immunohistochemistry, and radiological imaging results, he was diagnosed with metastatic intrahepatic cholangiocarcinoma to the right neck.

During the period of diagnostic work up, the patient's neck mass had rapidly expanded to include levels II to IV, causing displacement of the larynx. He became symptomatic with severe neck pain, poorly responsive to analgesia, and decreased cervical range of motion. On follow up physical examination he was noted to have a new ipsilateral Horner's syndrome. Based on the diagnosis of metastatic cholangiocarcinomahe was started on 1st line palliative chemotherapy using gemcitabine and cisplatin.

He tolerated chemotherapy welland pain control did improve while tumor biomarkers decreased (CA19-9 to 20,000 U/mL). Despite achieving symptomatic control, the neck mass remained unchanged in size and follow-up CT imaging revealed slight interval increase of the intrahepatic disease. Following four cycles of chemotherapy, palliative radiotherapy was to be undertaken, originally intended as 60Gy in 20 fractions. Ultimately only 15 Gy in 5 fractions was delivered as the patient had a rapid decline in performance status and was admitted to hospital for end of life care.

Discussion and Literature Review

The current case is the first report of metastastic intrahepatic cholangiocarcinoma presenting as a solitary high neck mass in an otherwise asymptomatic patient, without known hepatobiliary disease or symptomatology. While cholangiocarcinoma has been described to metastasize to cervical lymph nodes in some instances, these cases are reported in endemic areas with high rates of liver fluke infection [12]. Outside of endemic areas, the occurrence of cervical lymph node metastases from cholangiocarcinoma has been described twice. The first case report of cholangiocarcinoma presenting with neck mass was from the United States in 2002. This described a 50-year-old man who presented with cholangitis and was found to have a low neck mass in left level IV, which appears, on the provided imaging, to represent a supraclavicular node, a well-described presentation of intra-abdominal malignancy known as Virchow's node [13]. This presentation strongly suggests biliary tract malignancy and is in sharp contrast to the currently presented case, in which an otherwise asymptomatic patient without known hepatobiliary disease presented with a high, right-sided neck mass.

The only other case report in the literature was from 2004 in Japan, and described a 56-year-old woman presenting with a right neck mass [14]. Specific nodal group involvement is not clear from this report. However, initial evaluation identified evidence of significant liver dysfunction and subsequent investigation identified the presence of metastases in cervical, paraaortic, and peripancreatic lymph nodes, as well as both lungs and other organs. The development of cervical lymphadenopathy in the setting of widespread metastases is in contrast to the currently presented case, in which cervical lymph node involvement was the sole site of metastasis.

The differential diagnosis of neck mass is broad, and includes infectious, congenital, inflammatory, and neoplastic etiologies. Infectious etiologies are numerous and include bacterial, viral, and fungal agents but were less likely in our case given the clinical time course and lack of other supporting signs and symptoms. Neoplastic etiologies of neck mass are also diverse, and include head and neck primary cancers, for example oropharyngeal and nasopharyngeal cancer (NPC). In our case, level II was the primary nodal group involved, making oropharyngeal cancer the most likely neoplastic etiology. Shah and colleagues demonstrated that over 80% of regionally metastatic oropharyngeal cancers display level II involvement [15]. Similarly, NPC has a propensity for level II nodal group metastasis, with 70% of NPC presenting with lymphadenopathy showing level II involve-

ment [16].

Malignant cervical adenopathy in the absence of a known primary is becoming more common due to the increased incidence of HPV-associated oropharyngeal cancer [17]. HPV-associated oropharyngeal cancer frequently presents with unilateral level II neck mass and has a higher likelihood to present in the absence of an identifiable primary tumor within the oropharynx compared to non-HPV associated disease [17]. Despite up to 90% of cancers of unknown primary involving the cervical lymph nodes ultimately being diagnosedas HPV-associated head and neck cancer [17], the reported case highlights the possibility of rare presentations from other malignancies, including intrahepatic cholangiocarcinoma. We outline the preferred diagnostic approach, beginning with pathological tissue acquisition in the form of FNA. Failure of FNA to provide adequate tissue may be reconciled with the use of core needle biopsy. Radiological imaging in neck mass investigation is key for identification of both the possible neoplastic process, as well as assessing possible upper aerodigestive tract crisis. Finally, failure to identify a head and neck primary for the undifferentiated neck mass should prompt further investigation, such as chest and abdominal imaging.

In summary, cervical lymph node metastasis from cholangiocarcinoma is rare and has only been reported twice in North America. This case report is the first with isolated metastasis to the level II nodal group in an otherwise asymptomatic patient, and is the first to describe the specific treatment utilized in such a case. Neck mass evaluation is a common consult for all otolaryngologists. This case highlights the importance of both maintaining a broad differential when evaluating neck masses and when searching for a cancer with unknown primary.

Figures

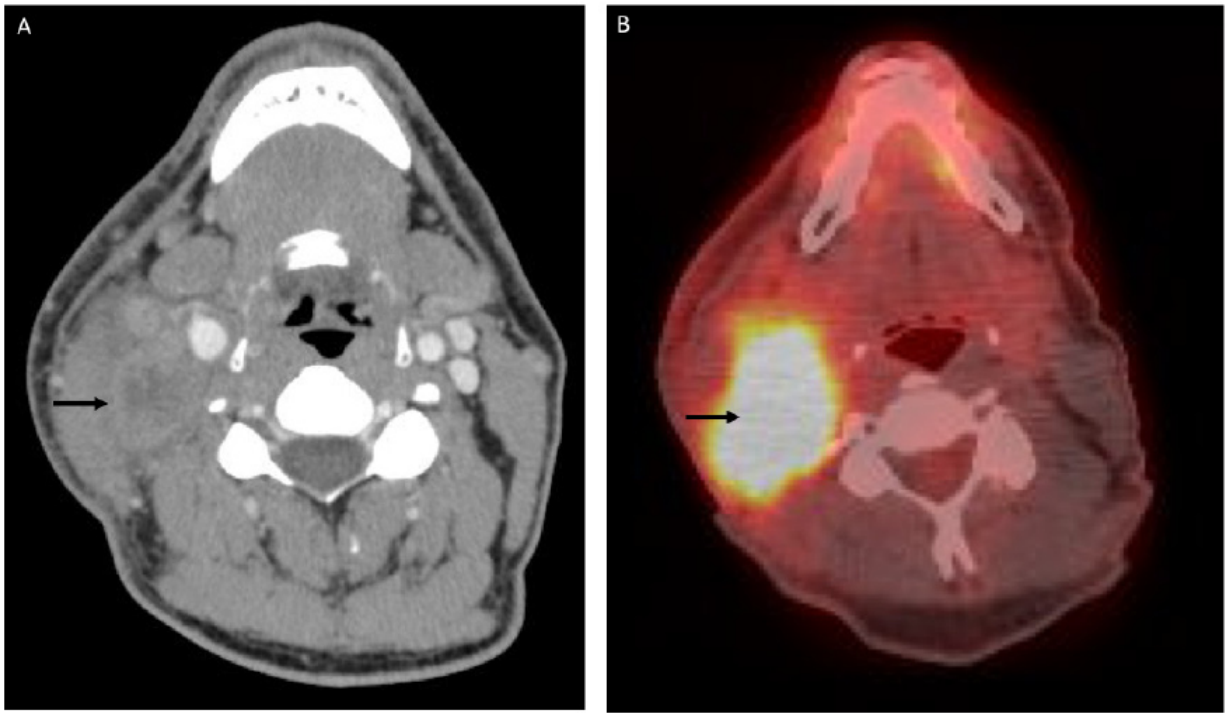

Figure 1: Imaging findings of right level II neck mass. A) Axial orientation of enhanced CT scan demonstrating conglomerate of centrally necrotic lymph nodes (black arrow) and B) Axial orientation of PET scan demonstrating intense FDG avidity in the right neck (black arrow).

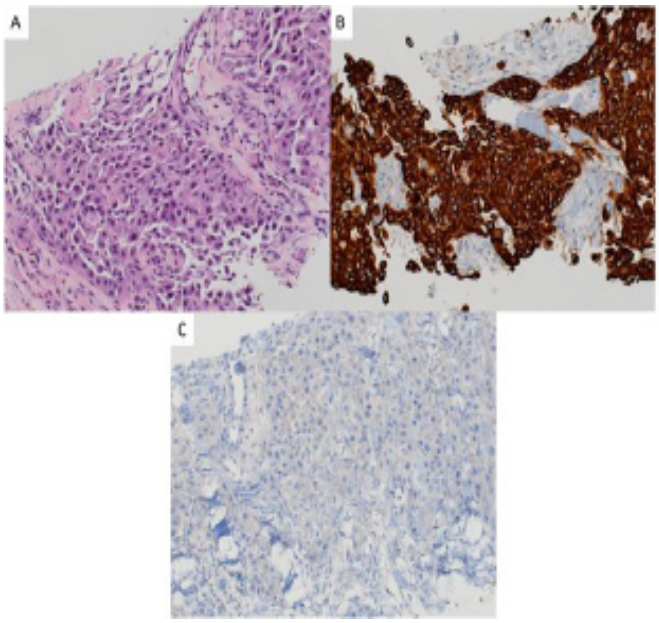

Figure 2: Photomicrographs of the neck core biopsy showing poorly differentiated carcinoma. A) The tumor showed no glandular or squamous differentiation (H&E, 200x), B) The tumor displayed CK7 positivity (brown) and C) The tumor was negative for p63 (blue). Immunohistochemistry was therefore compatible with a pancreatico-biliary primary tumor.

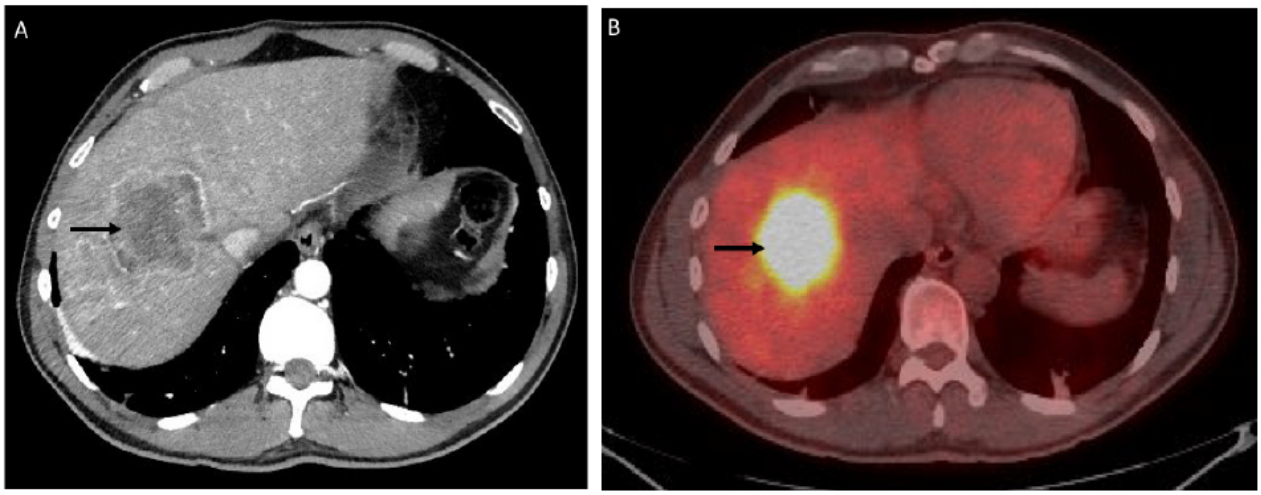

Figure 3: Imaging findings of intrahepatic cholangiocarcinoma primary tumor. A) Axial orientation of triphasic CT scan demonstrating arterial rim enhancement and microlobulated border (black arrow) and B) Axial orientation of PET scan demonstrating intense FDG avidity in the liver (black arrow).

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