



Metastatic Cholangiocarcinoma in the Absence of Jaundice Presenting with Neck Swelling in District Hospital

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Cholangiocarcinoma is a malignancy arising from biliary epithelium with incidence rate of less than 2 in 100000. It is the second most common primary liver malignancy. Cholangiocarcinoma usually presents with jaundice with or without abdominal pain. In advanced cholangiocarcinoma, it is extremely rare for cervical swelling to be the initial complaint and presentation.

Case Presentation: A 69-year-old male with underlying diabetes mellitus presented to surgical clinic with painful neck cervical swelling for 1 month with no other associated symptoms. Blood investigations were within normal range. Contrast enhanced computer tomography showed multiple enlarged lymph nodes over the axilla, mediastinal and supraclavicular with small hypodense lesion identified at Segment IV of the liver. Excision biopsy of left supraclavicular was performed which revealed metastatic adenocarcinoma. Immunohistochemistry study with an elevated Ca 19.9 tumour marker confirmed the diagnosis of metastatic cholangiocarcinoma.

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Conclusion: Metastatic cholangiocarcinoma presenting with neck swelling in the absence of jaundice is a rare occurrence and confer diagnostic challenge especially in district hospital. Availability of immunohistochemical study is of paramount important in establishing the diagnosis.

Keywords: Cholangiocarcinoma; neck; cervical; lymph node; lymphadenopathy; jaundice; metastatic.

1. INTRODUCTION

Cholangiocarcinoma is a malignancy arising from the biliary tree [1,2]. It accounts for 3% of all gastrointestinal system malignancies and the second most common primary liver cancer [1,2]. The overall incidence was reported to be less than 2/100 000 [2,3]. However, the incidence of cholangiocarcinoma showed geographical variation with higher incidence reported in Eastern countries compared to Western countries [1,3]. This variation has been attributed to the differences in geographical risk factors and genetic determinants. In Western countries, cholangiocarcinoma has slightly male predominance with the peak age of incidence at seventh decade [1].

Approximately 70% of all cholangiocarcinoma cases occurred without any obvious causes [2]. Among the risk factors that have been identified include parasitic infections, primary sclerosing cholangitis, liver cirrhosis and Hepatitis B and C infection. Cholangiocarcinoma could be classified into three groups based on the anatomical location; intrahepatic, perihilar, and extrahepatic (distal) cholangiocarcinoma. Perihilar cholangiocarcinoma made up about 50% to 60% of all cholangiocarcinoma [1].

Cholangiocarcinoma is usually diagnosed at advanced stage. In advanced stage, cholangiocarcinoma may metastasize to liver, pancreas, lung, lymph nodes and bones. Despite that, it is extremely rare for cervical swelling to be

the initial presentation of an advanced cholangiocarcinoma in the absence of jaundice. To the best of our knowledge, only 2 such cases have been reported.

2. CASE PRESENTATION

A 69-year-old Malay man with underlying diabetes mellitus presented to a private hospital with painful left cervical swelling for 1 month. The swelling gradually increasing in size but no obstructive symptoms were reported. He denied dysphagia, odynophagia or any shortness of breath. He reported significant weight loss but was unable to quantify. Physical examination revealed left supraclavicular neck swelling measuring 3cm x 3cm [Fig. 1].



Fig. 1. Left supraclavicular neck swelling

Blood investigations were unremarkable as shown in Table 1.

Table 1. Blood result during first presentation

	Result	Normal range
Hemoglobin (Hb)	13.0 g/dL	13.0 – 17.0 g/dL
Total white cell count (WCC)	6.3 x 10 ⁹ /L	4.0 – 10.0 x 10 ⁹ /L
Platelet Count	280 x 10 ⁹ /L	150 – 410 x 10 ⁹ /L
Urea	4.3 mmol/L	1.7 – 8.5 mmol/L
Creatinine	83 umol/L	71 – 115 umol/L
ALT (SGPT)	13 IU/L	10 – 41 IU/L
ALP	78 IU/L	0 – 119 IU/L
AST (SGOT)	14 IU/L	16 – 40 IU/L
Total Bilirubin	4 umol/L	3 – 20 umol/L

Contrast enhanced computer tomography (CECT) of thorax, abdomen and pelvis revealed multiple supraclavicular, axillary and mediastinal lymph nodes with the largest nodes measuring about 4cm x 3cm in the left supraclavicular region. There was hypodense liver nodule in segment IV about 1.5cm x 1cm and right upper lobe lung nodule measuring 1.3 x 1.6 cm.

Excision of left supraclavicular lymph node was subsequently performed. Histopathological examination (HPE) reported as metastatic

deposits of moderate to poorly differentiated adenocarcinoma [Figs. 2 and 3]. Immunohistochemistry (IHC) panel comprising TTF-1, CK7, AMACR, CD45 were performed. However, due to financial constraint, he was subsequently referred to the public district hospital for further workout.

Flexible laryngoscope, esophagogastroduodenoscopy (OGDS) and colonoscopy were performed to identify the primary malignancy. However, no suspicious

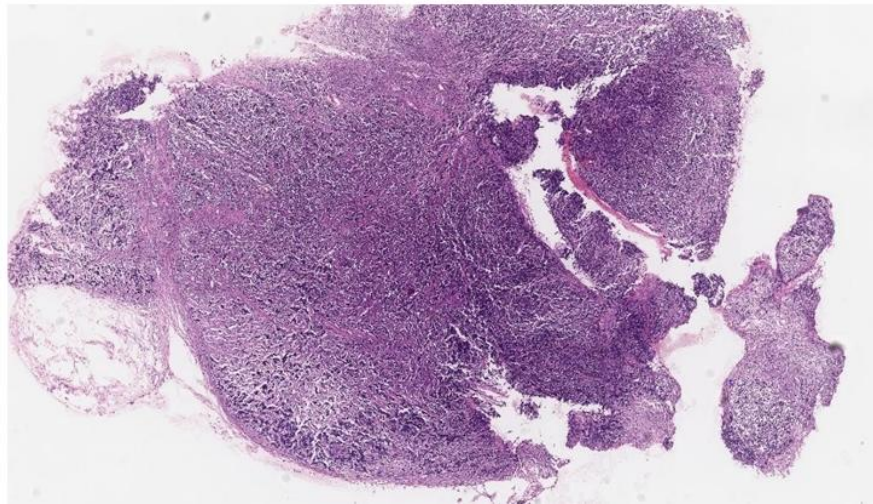


Fig. 2. Sections of the fragmented left supraclavicular lymph node exhibit effacement of lymph node architecture by diffuse infiltration of malignant cells. (hematoxylin & eosin, magnification x10)

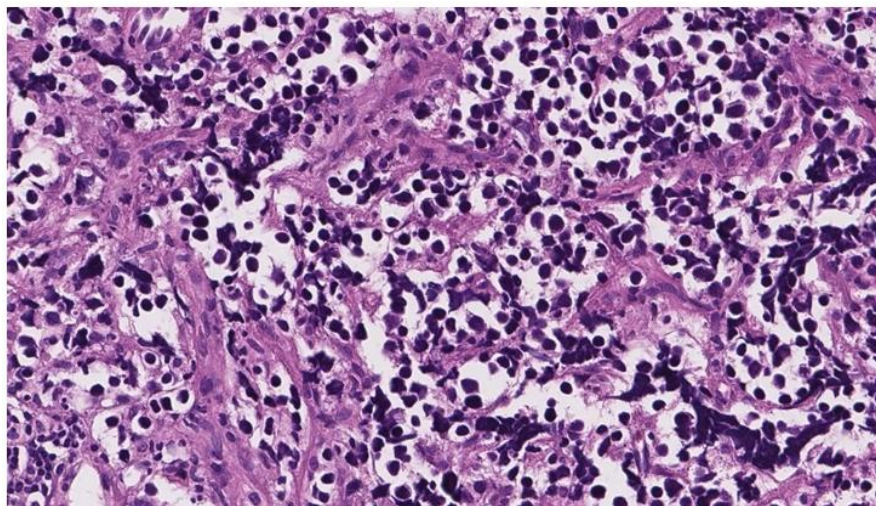


Fig. 3. Microscopic image showed individual cells are relatively large in configuration, displaying vesicular nuclei with prominent nucleoli (hematoxylin & eosin, magnification x40)

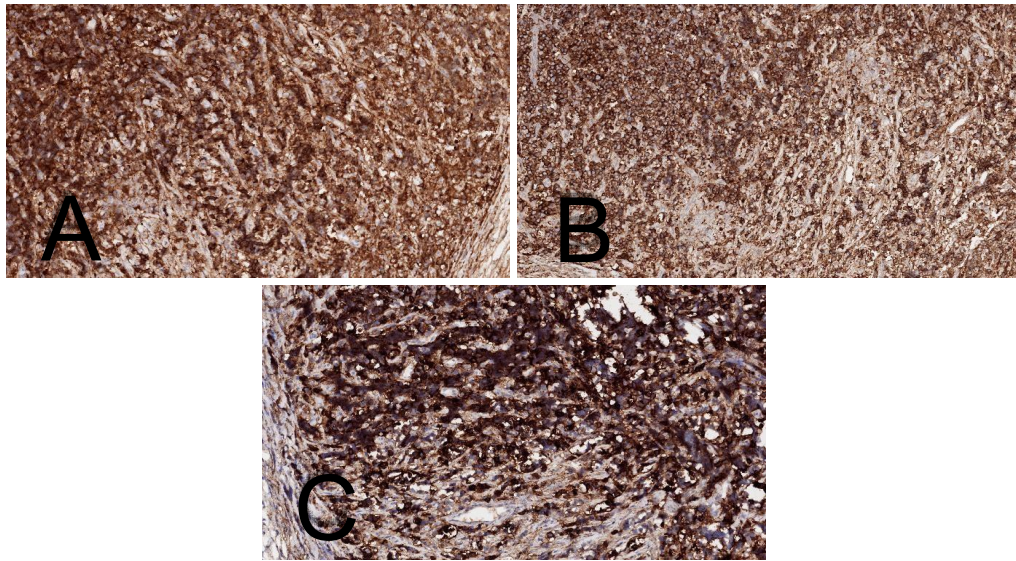


Fig. 4. Immunohistochemistry study of the excised cervical lymph node
A) Stained positive for CK7 B) Stained positive for AE1/AE3 C) Stained positive for CA 19.9

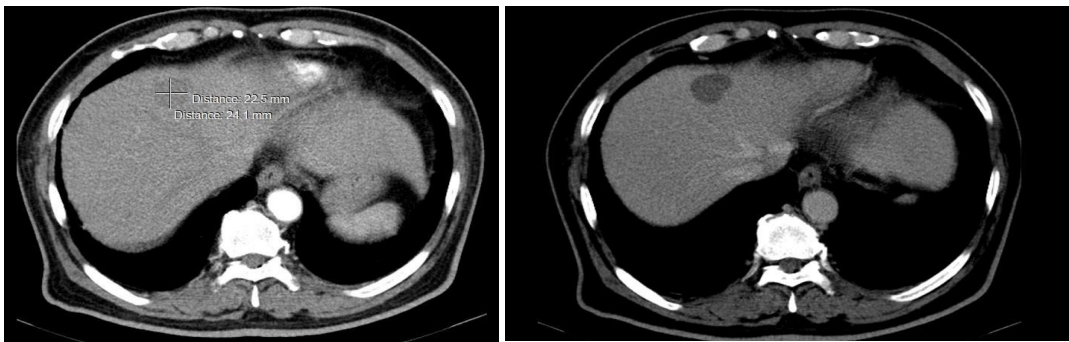


Fig. 5. Well defined hypodense lesion during arterial phase (left) and venous phase (right) at Segment IV of the liver

tumor was identified. The IHC study from the excised lymph node was then traced from the private hospital and it turns out to be poorly differentiated malignant epithelial cells, strongly positive for CK7, pankeratin AE1/AE3 and CA 19.9 (Fig. 4). The tumor element was negative for TTF-1 and Synaptophysin. IHC study concluded as metastatic deposit of cholangiocarcinoma. Serum CA 19.9 was 435.3 U/ml (normal range < 37 U/ml).

CECT Pancreatic Protocol was performed for further evaluation. A well-defined nonenhancing hypodense lesion noted at the periphery of segment VII of the liver measuring 2.1 cm x 2.6 cm x 1.9 cm which showed isodense to hypodense on plain and arterial scan, with no enhancement on portovenous and delayed scan

[Fig. 5]. Complimentary ultrasound showed a well-defined hypoechoic lesion with peripheral tubular anechoic structure, which may represent focal ductal dilatation.

Case was referred to Hepatobiliary Team at a tertiary hospital. Patient was subsequently referred to the oncologist for further management in view of the advanced stage of the disease.

3. DISCUSSION

Most cancers with cervical lymphadenopathy usually arise from the head and neck. Nonhead and neck malignancies that may metastasis to cervical lymph nodes include from lung, breast and liver [4].

A study conducted by Taweevisit et al from Thailand reported that, of the 72 patients with metastatic adenocarcinoma to the cervical lymph node, the most common primary source is thyroid gland which accounts for 41% [5]. Lung malignancy accounts for 25% followed by bile duct malignancy at 17% [5]. However, the percentage is lower in the western countries if we compared to the Asian counterpart. This has been attributed to higher liver fluke infection in Asia.

The first ever reported case of cholangiocarcinoma metastasized to cervical lymph node was by Hardeman et al in 2002 [6]. A 50-year-old man with biliary tract mass, presented to otolaryngology clinic to evaluate left neck mass identified on follow-up positron-emission tomography (PET) scan. Flexible fiberoptic nasopharyngoscopy revealed 1cm x2cm lymph node in left neck. Subsequent excision biopsy confirmed the diagnostic of metastatic cholangiocarcinoma.

From our literature review, only 2 cases were reported of metastatic cholangiocarcinoma with cervical swelling as initial presentation or chief complaint. The first case was reported by Imamura et al in 2004. A 56-year-old woman with right neck mass was noted to have deranged liver function test. Imaging showed multiple lymph nodes metastasis over cervical, paraaortic and peripancreatic. Subsequent investigations confirmed the diagnosis of cholangiocarcinoma [7,8]. Forner et al meanwhile reported the second case in a 47-year-old male with non-tender right neck mass with no other symptom. Fine needle aspirate cytology with core biopsy were performed. Immunohistochemical study with radiological imaging confirmed the diagnosis of cholangiocarcinoma [8].

Our case was the only third case ever reported. Our case was almost identical to the second case as liver function tests were normal. Diagnosis was significantly helped by the availability of immunohistochemical (ihc) study and tumor marker (ca 19.9). In the absence of these modalities, the tumor will likely be classified as cervical adenocarcinoma of unknown primary site.

Extrahepatic and intrahepatic cholangiocarcinoma may present differently. Extrahepatic cholangiocarcinoma typically presents with biliary obstruction symptom, most commonly painless jaundice. Meanwhile, intrahepatic cholangiocarcinoma usually

presented with similar fashion as hepatic mass, such as abdominal pain, night sweat and cachexia. Serum bilirubin level would be lower at the time of presentation in intrahepatic cholangiocarcinoma, compared to perihilar or extrahepatic cholangiocarcinoma [9]. Our case is a typical example of intrahepatic cholangiocarcinoma in which no biliary obstruction demonstrated as evidence by normal serum bilirubin level. The size of the tumour is too small (2.1cm x 2.6cm x 1.9cm) to exert any compressive symptoms.

Early diagnosis of cholangiocarcinoma patients is of paramount importance as 5-year survival is 80% if submitted to early radical surgery [9,10]. Unfortunately, most are diagnosed at advanced stage as cholangiocarcinoma is clinically silent and only exhibit symptoms in advanced stage [9]. Hyperbilirubinemia, raised CA 19.9, extrahepatic metastases, and lymph node involvement were recognized as poor prognostic factors [11].

Singal et al in their study reported that 1-year and 3-year survival was 71% and 42% with surgical resection offered better 5-year survival compared to non-surgical therapy [11]. Benefit of chemotherapy and radiotherapy in cholangiocarcinoma showed conflicting results owing to limited randomized controlled trial available. Adjuvant chemoradiotherapy therapy should be considered based on individual basis.

4. CONCLUSION

Cholangiocarcinoma in advance stage may present atypically and confer diagnostic challenge especially in a district hospital as we lack full histochemical staining. The availability of IHC study is of paramount important in determining the primary site of metastatic adenocarcinoma.

CONSENT

All authors declare that 'written informed consent' was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

Ethical approval is not required at our institution to publish an anonymous case report.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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