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Case Report with a Review of Literature: Pancoast Syndrome—A Rare Presentation of Metastatic Hepatocellular Carcinoma

Lakshmi Sandhya Singuluri[1] Prasanth Ganesan[1] Bheemanathi Hanuman Srinivas[2] Biswajit Dubashi[1] Yadav Nisha[1]

[1] Department of Medical Oncology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India
[2] Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India

Address for correspondence Lakshmi Sandhya Singuluri, MD, DM, Department of Medical Oncology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), JIPMER Campus Rd, Gorimedu, Priyadarshini Nagar, Puducherry, 605006, India (e-mail: drsandhyaprasanth@gmail.com).

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Abstract

Superior sulcus tumors, also known as Pancoast tumors, present in a distinctive way with Horner's syndrome (ptosis, miosis, and anhidrosis), hand weakness brought on by the atrophy of the intrinsic hand muscles, and excruciating pain along the medial aspect of the arm. (1) Primary lung cancers constitute a majority of Pancoast tumors, but Pancoast syndrome can be multifactorial. (2) Here, we present a case of 62-year-old male who presented with right shoulder pain and weakness for 2 months. Clinically, he had a supraclavicular mass with atrophy of the intrinsic muscles of the hand and sensory-motor weakness. Computed tomography showed a mass lesion in the supraclavicular fossa with the erosion of the T1 vertebra and first rib, mimicking carcinoma right upper lobe. However, the biopsy from the mass was suggestive of metastasis from hepatocellular carcinoma (HCC). Our case report identifies HCC as a rare differential for Pancoast syndrome and highlights the unique metastatic presentation.

Keywords

- hepatocellular carcinoma
- Pancoast tumor
- Pancoast syndrome
- metastasis
- hepatoid adenocarcinoma

Introduction

About 5% of nonsmall cell lung cancers present as Pancoast or superior sulcus tumors. They are named after Henry Pancoast, an American radiologist who described them in 1920.[1] These tumors often involve the surrounding anatomical structures of the thoracic inlet and cause a unique constellation of symptoms ("Pancoast syndrome"). Manifestations include shoulder pain, brachial plexus palsy, and Horner's syndrome.[1,2] The American College of Chest Physicians defines Pancoast tumors as primary lung cancer located at the apex of the lung. In contrast, "Pancoast syndrome" may be caused by conditions from primary lung or pleural malignancies, metastasis from other primary sites, and benign diseases caused by infections and inflammation.[3] Here we present a case report of metastatic hepatocellular carcinoma (HCC) mimicking a Pancoast tumor.

Case Report

A 62-year-old male, a chronic smoker (10 pack years) and nonalcoholic, presented with right shoulder pain and right upper limb weakness for 2 months. On examination, his performance status was borderline Eastern cooperative Oncology Group (ECOG 2), and he had a nontender, hard, ill-defined mass in the right supraclavicular region. There was weakness in the right upper limb (power 3/5), sensory loss over the ulnar aspect, and atrophy of the intrinsic muscles of the hand. There were no signs of Horner's syndrome or

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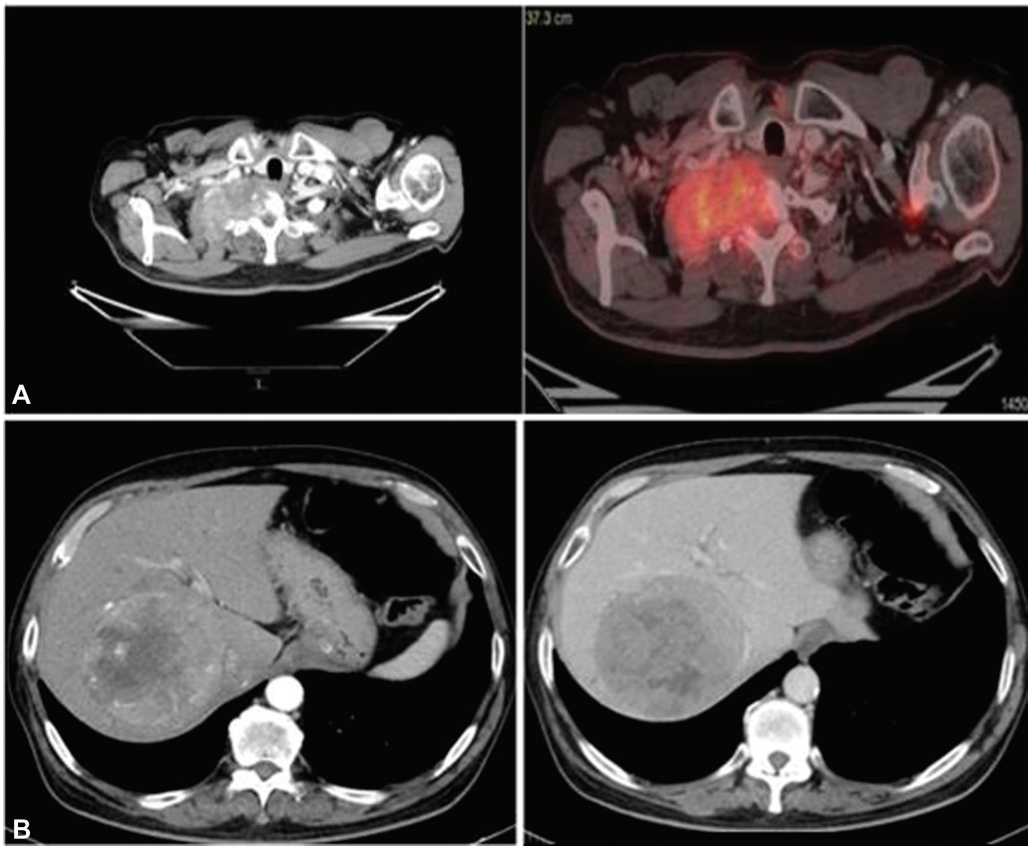

Fig. 1 (A) Positron emission tomography computed tomography (CT) scan shows a right upper lobe mass lesion of size 6.1 4.8 cm with the erosion of C7 and D1 vertebra. (B) Triple phase CT: of the abdomen showing a 9 cm lesion in the segment VI & VII suggestive of HCC (Arterial and portal phase).

superior vena cava obstruction features. There were reduced breath sounds on the right infrascapular region. Abdominal examination was normal. The viral markers (hepatitis B virus surface antigen, hepatitis C virus) were negative, and laboratory tests were unremarkable. A contrast-enhanced computerized tomography of the thorax showed a right upper lobe mass lesion (6.1×4.8 cm) eroding the C7 and D1 vertebra, multiple metastases in the 1st and 6th rib, sternum, and posterior elements of C7, C4 vertebra (►**Fig. 1A**).

Positron emission tomography showed a metabolically active lesion (maximum standardized uptake value: 1.55) in the right supraclavicular region extending from the C7 vertebra to the T1 vertebra and eroding the adjacent right transverse process of C7, T1, and right 1st rib medially. Multiple other sites of metastases were also noted (ribs, clavicle, manubrium, vertebra). It also showed an 18F-fluorodeoxyglucose avid lesion in segments VI and VII of the liver ($8.4 \times 8.9 \times 7.1$cm), suggestive of metastases (►**Fig. 1B**).

With a clinical diagnosis of carcinoma lung with multiple metastases, a core needle biopsy was done from the right upper lobe mass. Histology showed tumor cells arranged in glandular and trabecular patterns, with abundant polygonal eosinophilic cytoplasm and central nuclei with moderate nuclear atypia. On immunohistochemistry (IHC), they showed strong positivity for CK8/18, CD 10 and patchy focal positivity for hepar-1 (►**Fig. 2A**). Tumor cells were negative for napsin A, glypican 3 (GPC3), and arginase is noncontributory. The histomorphology was in favor of HCC (►**Fig. 2**). Serum alpha fetoprotein (AFP) levels were done and were found elevated (2450 ng/mL).

A diagnosis of HCC with Pancoast syndrome and extensive skeletal metastasis was made based on the biopsy report. The patient was started on sorafenib at 200mg twice a day that was increased to 400 mg twice a day from the second month, and palliative radiotherapy of 30 Gy was given to the thoracic inlet. After 3 months of sorafenib, the patient had pain relief, and AFP was reduced to 240 ng/mL. However, imaging was not done. Six months after diagnosis, the patient succumbed to the disease.

Discussion

Henry K. Pancoast first defined Pancoast tumors in 1924 and 1932 among patients presenting with right upper limb pain and radiological characteristics of apical chest tumors.[4] The first to propose a pulmonary origin was Tobías, who defined the clinical presentation of Pancoast tumors in detail. The Pancoast syndrome could be caused by various benign (infections and inflammatory) and malignant conditions, including tumors arising from the lung and metastases from different primary sites.[2] These tumors were considered to have a poor prognosis. However, the outcomes have improved significantly with advances in chemotherapy, radiotherapy, and immunotherapy.

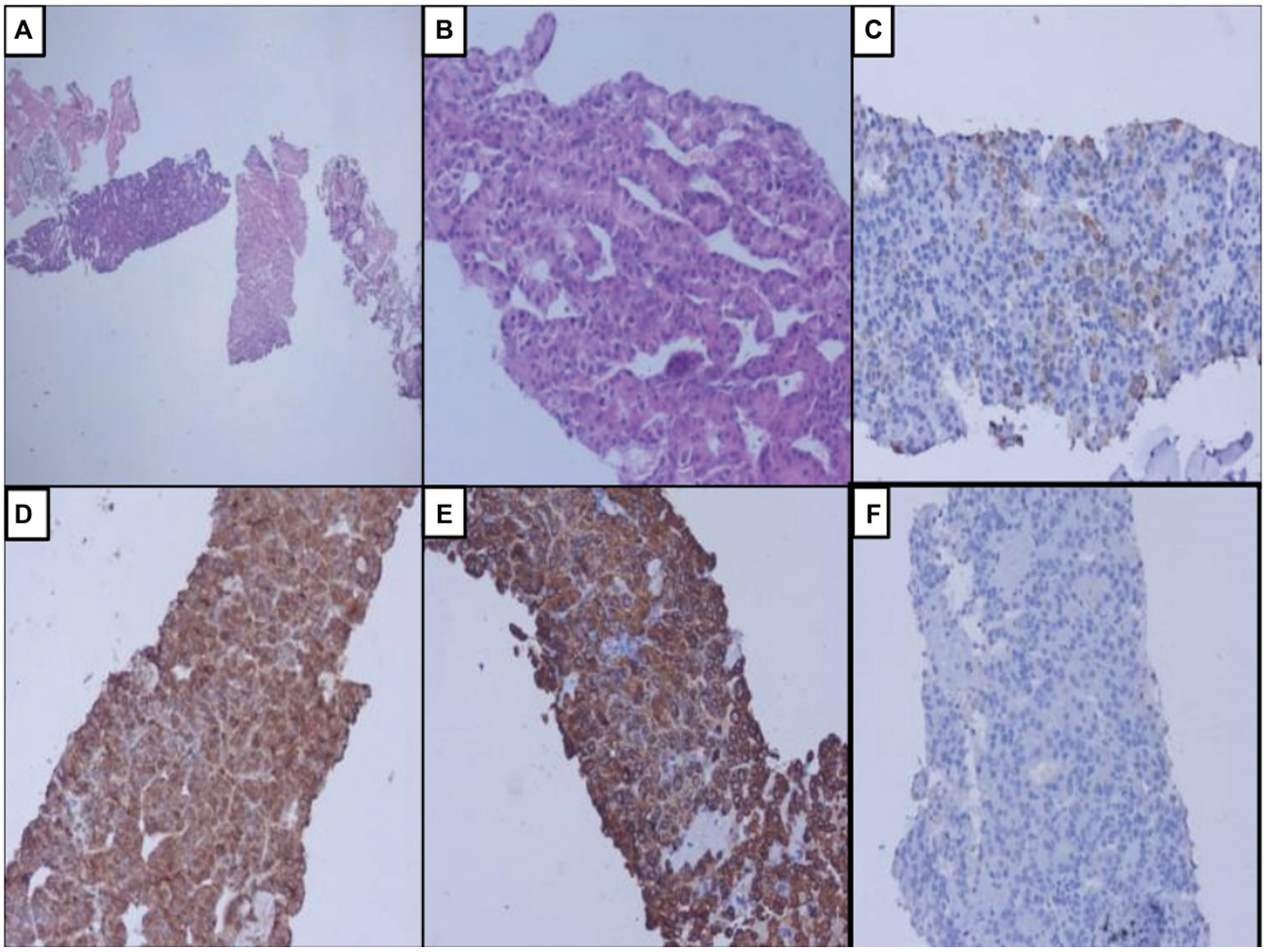

Fig. 2 Photomicrographs of (**A**) biopsy from the right lung shows fragmented cores of tissue comprising off skeletal muscle fragments, coagulative tumor necrosis, and viable tumor (hematoxylin and eosin [H&E] x40). (**B**) Tumor composed of cells arranged predominantly in trabecular pattern (H&E X200). Immunohistochemistry (**C**) tumor cells show focal positivity for hepar-1 (DABXl00). (**D** and **E**) Diffuse strong positive for CD 10 as well as CK 8/18 (DABX100). (**F**) Negative for napsin A, thyroid transcription factor1 and CK7, CK20, and chromogranin (DABX100).

In contrast, the prognosis of metastatic HCC is poor, with a median survival of 3.5 to 6 months.[5,6] Survival depends on the stage of the disease and the residual liver function. Driven by the Child-Pugh class, the prognosis of class A metastatic HCC, when treated with sorafenib, is 10.7 months.[7] In the era of immunotherapy, bevacizumab with atezolizumab has improved overall survival compared to sorafenib alone at 12 months (67.2 vs. 54.6%),[8] but its use is limited by cost.

HCC most commonly occurs in viral cirrhotic liver disease, followed by alcoholic and nonalcoholic liver disease.[9] It also occurs in a small proportion of noncirrhotic liver diseases. Though the etiology of HCC differs, the pattern of metastasis is similar, with the lung being the most common site (65%).[10] Other metastases sites are abdominal lymph nodes, bones, adrenal gland, peritoneum, omentum, and brain.[11]

Advanced HCC with a higher T stage is more likely to have metastasis at multiple sites, predominantly lung.[4] Brain metastases are associated with poor survival (1-year overall survival of 5.9%).[12] Skeletal involvement from HCC is less common (25% of all extrahepatic metastases).[13] Most HCC-associated bone metastases are in the thoracic (70%) and lumbar spine (20%), which are expansile and osteolytic and often associated with extensive soft tissue masses.[14] Various case reports of HCC presenting with neurological symptoms have been described, which are secondary to compressive symptoms caused by the soft tissue component of the osteolytic bony metastasis.[15,16]

In this patient, the Pancoast-like presentation was due to soft tissue extension from the vertebral metastasis involving C7 to T1 vertebral level, an unusual clinical presentation prompting a detailed pathological evaluation for diagnosis.

Imaging is the primary modality of diagnosis in a suspected case of HCC. The American Association for the Study of Liver Disease, the European Association for the Study of Liver, and National Comprehensive Cancer Network have guidelines to utilize imaging criteria for noninvasive diagnosis in patients at risk of HCC.[17] Pathological diagnosis is warranted when a patient presents with a diagnostic dilemma. HCC cells can be well-differentiated to poorly differentiated.[18] Based on the 2019 World Health Organization classification, multiple subtypes of HCC, include clear cell, fibrolamellar, macrotrabecular, neutrophil rich, lymphocyte rich, and steatohepatitis, are described.[19] IHC aids in the differential diagnosis of a patient with rare metastasis sites (hepatocyte paraffin 1 [HepPar1],

arginase1, cytoplasmic thyroid transcription factor1 [TTF1], CK8, CK18, [GPC3]).[19] Arginase 1 is the most sensitive marker for all levels of differentiation, and GPC3 is highly sensitive for poorly differentiated tumors originating from hepatocytes.[20] Well-differentiated HCC is also positive for HepPar1, TTF1, and CK8/18.

The diagnosis of HCC must be differentiated from hepatoid adenocarcinoma (HAC), a rare variant of extrahepatic adenocarcinoma with similar clinical and pathological presentations. The clinical features of HAC depend on the location of the primary tumor.[21] The lung, followed by the stomach, is the most common primary site of HAC and occurs in older people with frequent metastasis to the liver and lymph nodes.[22] HAC may be misdiagnosed as HCC and should be considered a differential diagnosis among patients with a rare presentation of HCC in the absence of hepatitis, fibrosis, or cirrhosis.[23] HAC is highly aggressive and less responsive to conventional therapy. It is challenging to differentiate these tumors pathologically based on morphology alone. HAC shows positive staining for AE1/AE3, CK18 and CK 19 and GPC-3 (100%) on IHC. AFP can be positive in both HCC and HAC; neither IHC staining nor serum levels help differentiate between them. HepPar 1 shows a higher positivity in HCC (73–93%) than in HAC (38.1%), which can help in differentiating the two.[24]

Given the presenting signs and symptoms and similar morphological features on hematoxylin and eosin of all adenocarcinomas, this patient had a clinical and pathological diagnostic dilemma, but IHC helped diagnose HCC. The choice of therapy would depend on the primary diagnosis; hence, it is crucial to differentiate the pathology for treating appropriately.

Conclusion

HCC presenting with Pancoast syndrome as the initial presentation is uncommon, and differentiating HCC from primary metastatic lung cancer and hepatoid adenocarcinoma of the lung is vital for further management.

Patient Consent

The authors certify that written informed consent was obtained in an appropriate format informing the patient that clinical information and images will be reported in the journal. The patient understands that his name and initials will not be published, and efforts will be made to deidentify any personal identity or information. However, anonymity cannot be guaranteed.

Conflict of Interest

None declared.

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