An Unusual Presentation of A Large Cell Neuroendocrine Carcinoma and Acute Liver Failure

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Introduction

Large cell neuroendocrine carcinomas (LCNECs) are characterized as large cells with areas of necrosis, neuroendocrine traits (palisading, trabeculae, etc.), ample cytoplasm and high mitotic rates. LCNECs are a rare, aggressive form of neuroendocrine tumor known to have high rates of metastasis. Our case highlights acute liver failure with rapid progression to death due to metastatic spread of LCNEC.

Case Presentation

71-year-old male with a history of prostate cancer requiring prostatectomy, hypertension, hyperlipidemia, and tobacco use, presented for shortness of breath and abdominal pain for 3 days. He was a poor historian and was unable to provide much history. Of note, the patient reported that he had imaging performed in Spring 2021 to further evaluate his degenerative disc disease and was told there was concern for a cancerous process. Initial laboratory studies showed an elevated AST and ALT (over 300), and thrombocytopenia, but were otherwise unremarkable. Further imaging was performed, given the patient's history of reported malignancy. Initial chest X-ray was negative for acute findings and an abdominal ultrasound revealed a markedly abnormal appearance of the liver, suggestive of possible hepatic metastatic disease. Computed tomography scan of the chest/abdomen/pelvis showed a left hilar mass measuring 5.5 x 6cm with regional lymphadenopathy. The patient underwent a biopsy of the liver, and was later noted to have worsening liver enzymes, platelets, INR, and renal function, along with a lactic acid. He was transferred to the intensive care unit for further monitoring. Bowel ischemia and portal vein

thrombosis were ruled out, and the patient became continually more acidotic, and had a pulseless electrical activity (PEA) arrest. He was revived and intubated, and placed on pressor support and continuous renal replacement therapy. His family decided to change his code status to “do not resuscitate” and the patient was made comfortable. Final results of the liver biopsy were obtained 2 days later, and showed findings consistent with high grade large cell neuroendocrine carcinoma. Immunohistochemical staining was positive for CD56, synaptophysin, CK7 and CK5/6.

Figures

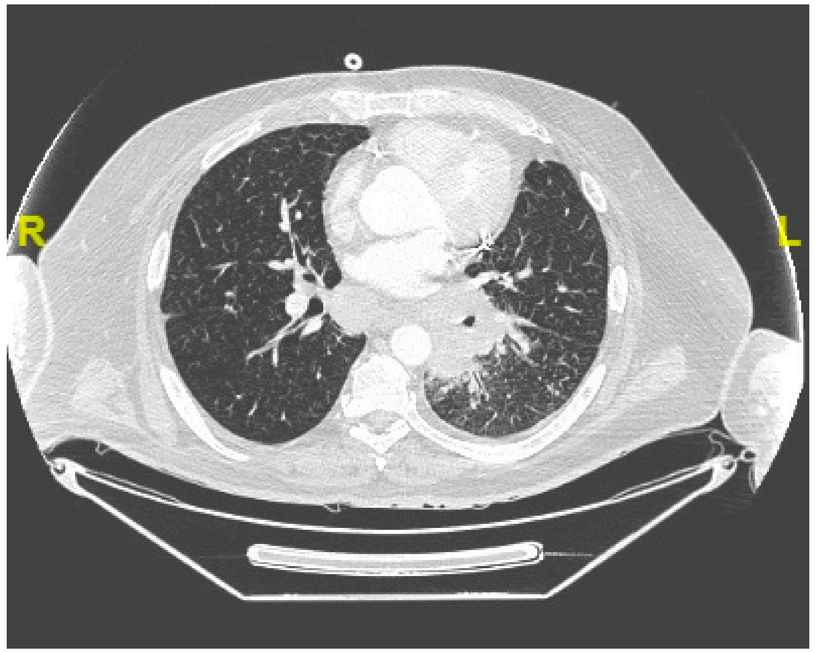

Figure 1: axial view showing left-sided hilar mass

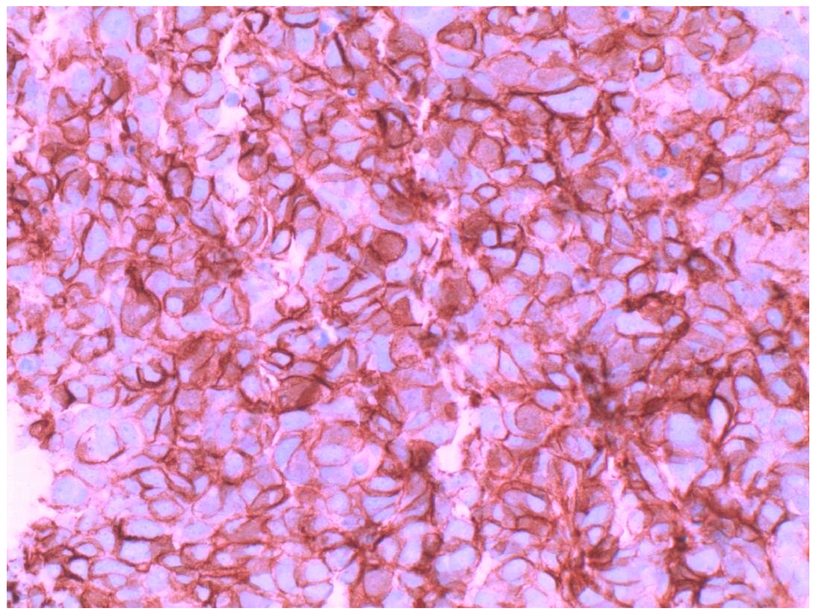

Figure 2: CD56 positive stain for our patient’s liver biopsy sample, indicating a pulmonary tumor with neuroendocrine differentiation

Discussion

The World Health Organization guidelines released in 2015 categorize lung neuroendocrine tumors into 4 distinct subtypes: LCNEC, SCLC, carcinoid tumor and diffuse idiopathic pulmonary neuroendocrine cell hyperplasia [5]. Neuroendocrine features and positive immunohistochemical markers (synaptophysin, chromogranin, or CD56) must be present for the diagnosis to be confirmed [5]. Various other markers can be tested to determine the etiology of the primary tumor as well, including CK7, CK20, CK5/6, and thyroid transcription factor-1 (TTF-1) [6].

Primary LCNECs are peripherally located, whereas our case had a centrally located tumor encasing the left lower lobe bronchus. The location of the lesion likely could have contributed to the likely rapid spread of disease due to the relative adjacency of the nearby pulmonary vessels, similar in nature to the patient presented by Bhamidipati et. al [6]. Our patient demonstrated dyspnea upon presentation, however denied a prolonged history of his prior to the hospitalization. Zacharias et. al [7] noted that only 4 of 21 patients with LCNEC presented with hemoptysis or cough, whereas the others were found to have nonspecific symptoms such as chest pain, dyspnea or asymptomatic lung nodules.

There is limited information available for the treatment of LCNECs given the low survival rates of the disease. No single treatment regimen has been shown to be superior, and patients often times are treated with the same chemotherapy used for SCLC [8]. Per Swarts et. al [4] platinum-etoposide based chemotherapy regimens are preferred in patients with later stage disease, while surgery is generally preferred in the early stages. Even in patients with complete surgical resection of the primary tumor, there is a high rate of recurrence. Sarkaria et. al [9] postulated that neoadjuvant chemotherapy in patients with advanced disease may allow for a “survival advantage.” There are newer therapies that are being developed based upon certain immunohistochemical markers, including VEGF, c-KIT and HER-2, but have been unproven as of yet [10]. There have been instances in the literature of hepatectomy for liver metastases for solitary lesions which showed a decreased rate of recurrence 6 months post-operatively [3].

LCNEC is an uncommon and aggressive disease that can spread rapidly and cause substantial damage throughout the body. Distant metastasis is usually found by the time a confirmed diagnosis is made. In a population based study by Derks et. al, 180 out of 383 patients with Stage IV LCNEC were found to have metastases to the liver [11]. Yang et. al stated that the most common site of metastasis for pulmonary LCNEC was to the brain, although also noted that there were higher rates of metastasis to the liver than with other non-small cell lung cancers [12]. Yamane et. al also demonstrated a case of pulmonary LCNEC with liver involvement, where the patient ultimately underwent a laparoscopic hepatectomy [3]. If diagnosed early, it is possible to intervene, although no definitive treatment modality has yet been established.

Conclusion

Liver metastasis has been documented throughout the literature for other carcinomas, however very few in regards to LCNEC. Acute liver failure in such a short span of time, as in our case, highlights the mortality associated with LCNECs, and the difficulty in diagnosing the condition early in the disease course.

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