Diagnosis of metastatic fibrolamellar hepatocellular carcinoma by endoscopic ultrasound-guided fine needle aspiration

Amanda Crowe, MD, Carrie S. Knight, MD, Darshana Jhala, MD, B. MUS, Steve J. Bynon, MD, Nirag C. Jhala, MD, MIAC*

Address: Department of Pathology, Division of Anatomic Pathology, University of Alabama at Birmingham, Birmingham, AL, USA.

E-mail: Amanda Crowe - aedailey@uab.edu; Carrie S. Knight - carrie.knight@rocketmail.com; Darshana Jhala - djhala@uab.edu; Steve J. Bynon - steve.bynon@ccc.uab.edu; Nirag C. Jhala* - jhalan@uphs.upenn.edu

*Corresponding author

INTRODUCTION

The fibrolamellar variant of hepatocellular carcinoma (FL-HCC) is distinguished from other hepatocellular carcinomas (HCC) by its unique clinical and pathologic features. First described as "eosinophilic hepatocellular carcinoma with lamellar fibrosis" by Edmondson in 1956, FL-HCC is typically diagnosed at a younger age than the age at which conventional HCC is diagnosed. According to Surveillance, Epidemiology, and End Results (SEER) data, FL-HCC accounts for approximately 1% of all primary liver cancer in the United States, with a mean age of 39 years at the time of diagnosis compared with 65 years for conventional HCC. In this age group, other primary mass-forming lesions such as hepatocellular adenoma and focal nodular hyperplasia are more common. Most patients with FL-HCC do not have underlying liver disease, in contrast to the common associations of other...

Abstract

The fibrolamellar variant of hepatocellular carcinoma (FL-HCC) is distinguished from other hepatocellular carcinomas (HCC) by its unique clinical and pathologic features. Cytological features for this tumor on fine needle aspiration (FNA) of primary tumors have been described earlier. We present here a unique case of metastatic FL-HCC diagnosed by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of mediastinal adenopathy. A 32-year-old woman with a history of oral contraceptive use presented with nausea and severe abdominal pain but no ascites or stigmata of cirrhosis. She had a past history of resection of a liver lesion. Serial computed tomography scans revealed mediastinal lymphadenopathy and the patient was referred for endoscopic ultrasound (EUS). A transesophageal EUS-FNA was performed and tissue was collected for cytological evaluation by an on-site pathologist with no knowledge of prior history. Based on morphology correlated with prior history received later, a final diagnosis of metastatic FL-HCC in the retrocardiac lymph node was rendered on the EUS-FNA samples. There are very few reports in the literature where a diagnosis of FL-HCC is rendered at unusual sites. This case highlights that EUS-FNA is a relatively non-invasive, rapid, accurate and effective modality in obtaining tissue from otherwise hard-to-reach areas. It also suggests that metastasis of FL-HCC can be observed in mediastinal nodes and that diagnosis based on cytological features can be rendered even when the tumor is identified at unusual locations.

Key words: Metastatic fibrolamellar variant of hepatocellular carcinoma, endoscopic ultrasound guidance, fine needle aspiration
HCC with cirrhosis and viral hepatitis,\[^{1,3}\]\ and it is quite rare in regions of the world such as China and Japan, which show a high incidence of usual HCC.\[^{3}\]

FL-HCC is detected at a localized stage at diagnosis and receives potentially curative resection or transplantation more commonly than conventional HCC.\[^{2}\]\ FL-HCC patients also have better 1-year (73.3% vs. 26.0%) and 5-year (31.8% vs. 6.8%) survival when compared to all HCC.\[^{2}\]

Cytopathologic features for this tumor on fine needle aspiration (FNA) of the primary tumors have been described earlier.\[^{4-10}\]\ Diagnosis by FNA for this rare tumor, however, poses a unique set of challenges for unsuspecting pathologists, especially when this tumor is aspirated at unusual locations. We report here a unique case in which FL-HCC metastatic to the mediastinum was diagnosed by endoscopic ultrasound-guided FNA (EUS-FNA).

**CASE REPORT**

A 32-year-old woman with a history of oral contraceptive use presented with nausea and severe abdominal pain. She had no fever, weight loss or history of viral hepatitis. On examination, her spleen was not enlarged and there was no ascites or stigmata of cirrhosis. Her blood counts, including platelet count, were within reference ranges. She had a past history of resection of a liver lesion.

Serial computed tomography (CT) scans revealed small lesions at the base of the lungs that slowly increased in size. Mediastinal lymphadenopathy was also present and the patient was referred for EUS. EUS revealed a 41 mm x 31 mm lymph node in the lower paraesophageal/retrocardiac area. A transesophageal EUS-FNA was performed.

Air-dried, Diff Quik-stained slides and alcohol-fixed smears were prepared and the Diff Quik-stained slides [Figure 1] were examined on-site. The moderately cellular smears showed many individual cells and occasional aggregates of fibrous tissue. Individual cells were enlarged and had low nuclear to cytoplasmic ratios, with abundant granular and eosinophilic cytoplasm. Frequently, the cells demonstrated sharply outlined cytoplasmic vacuoles as well as bile pigment in the cytoplasm. The nuclei were enlarged and had prominent nucleoli. Naked nuclei with prominent nucleoli were also noted. The possibility of a metastatic hepatic lesion was considered. The smears did not reveal some of the features associated with usual HCC, such as vessels traversing groups of hepatocytes, nor was the “basketing” pattern of endothelial cells surrounding groups of hepatocytes observed in these smears. FNA smears also revealed large polygonal cells with sharply outlined cytoplasmic borders with centrally placed nuclei. Unlike the neoplastic cells, these cells demonstrated small, pyknotic nuclei with regular nuclear membranes without prominent nucleoli or intranuclear cytoplasmic inclusions. These cells represented contamination by surface esophageal mucosal cells. Other possibilities were also considered. Considering the unusual location for hepatocytes, further history was requested in the EUS suite from the referring clinician.

Additional, history suggested that 2 years ago a CT scan of the abdomen revealed a mass in the right lobe of the liver. Imaging study at the time did not reveal features of cirrhosis. Serum alpha-fetoprotein AFP levels were also within the reference range. A clinical diagnosis of hepatic adenoma was considered and the lesion was resected. Later, cells from the FNA sample were compared with the previously resected liver tumor that had revealed FL-HCC [Figure 2].
A final diagnosis of metastatic FL-HCC in the retrocardiac node was rendered on the EUS-FNA samples.

DISCUSSION

This case highlights several challenges in the diagnosis of FL-HCC for which cytopathologic features have been previously described. FNA specimens from these tumors generally show variably cellular smears with large, discohesive tumor cells with abundant granular and eosinophilic cytoplasm, centrally placed vesicular nuclei, prominent nucleoli and low nuclear to cytoplasmic ratios. The so-called “pale plasm,” centrally placed vesicular nuclei, prominent nucleoli and binucleation is not uncommon. Bland, spindled cells arranged in parallel bands may also be seen, representing the bundles of collagen fibers and fibroblasts seen in the histologic sections. The trabecular arrangement of conventional HCC is not seen. Intranuclear pseudo-inclusions may be present and binucleation is not uncommon. Bland, spindled cells arranged in parallel bands may also be seen, representing the bundles of collagen fibers and fibroblasts seen in the histologic sections.

In addition to the cytologic diagnosis of this uncommon tumor at a metastatic site, another unique aspect of our case is that the FNA was performed under EUS guidance. It is difficult to aspirate retrocardiac/lower paraesophageal lymph nodes with other imaging modalities. Prior to the advent of EUS, it would have required more invasive techniques to obtain tissue samples to document metastatic FL-HCC in these nodes. Thus, EUS provides better access to these hard-to-reach lymph nodes. Furthermore, our setting allows for immediate assessment of not only sample adequacy but also on-site diagnosis. EUS-FNA for the detection of metastatic malignancy is a very sensitive and specific modality. Our results have also demonstrated an excellent concordance rate between on-site and final diagnosis. This case also underscores the value of effective communication between the endoscopist and the on-site pathologist to ensure specimen adequacy as well as availability of relevant clinical information and also to provide rapid and accurate diagnosis for informed patient management.

In summary, we showed that EUS-FNA is a relatively non-invasive, rapid, accurate and effective modality to obtain tissue from otherwise hard-to-reach areas. This case also shows that diagnosis of FL-HCC can be made based on cytologic features even when the tumor is identified at unusual locations.

COMPETING INTEREST STATEMENT BY ALL AUTHORS

No competing interest to declare by any of the authors.

AUTHORSHIP STATEMENT BY ALL AUTHORS

Each author acknowledges that this final version was read and approved. All authors qualify for authorship as defined by ICMJE http://www.icmje.org/#author. Each author participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article.

ETHICS STATEMENT BY ALL AUTHORS

Our institution does not require approval from the Institutional Review Board (IRB) for a case report without identifiers.
REFERENCES

1. Craig JR, Peters RL, Edmondson HA, Omata M. Fibrolamellar carcinoma of the liver: A tumor of adolescents and young adults with distinctive clinico-pathologic features. Cancer 1980;46:372-9.

2. El-Serag HB, Davila JA. Is fibrolamellar carcinoma different from hepatocellular carcinoma? A US population-based study. Hepatology 2004;39:798-803.

3. McLarney JG, Rucker PT, Bender GN, Goodman ZD, Kashtani N, Ros PR. Fibrolamellar carcinoma of the liver: Radiologic-pathologic correlation. Radiographics 1999;19:453-71.

4. Perez-Guillermo M, Masgrau NA, Garcia-Solano J, Sola-Perez J, de Agustin P. Cytologic aspect of fibrolamellar hepatocellular carcinoma in fine-needle aspirates. Diagn Cytopathol 1999;21:180-7.

5. Mansouri D, van Nhieu JT, Couanet D, Terrier-Lacombe MJ, Brugieres L, Cherqui D, et al. Fibrolamellar hepatocellular carcinoma: A case report with cytological features in a sixteen-year-old girl. Diagn Cytopathol 1999;21:180-7.

6. Kunz G Jr, Chung J, Ali SZ. Hepatocellular carcinoma - fibrolamellar variant: Cytopathology of an unusual case. Diagn Cytopathol 2002;26:257-61.

7. Montero A, Allende H, Tallada N, Ramon y Cajal S, Margarit C, Viladomiu L. Fine needle aspiration cytology of massive bilateral ovarian metastasis of fibrolamellar hepatocellular carcinoma. Acta Cytol 2007;51:682-3.

8. Sarode VR, Castellani R, Post A. Fine-needle aspiration cytology and differential diagnoses of fibrolamellar hepatocellular carcinoma metastatic to the mediastinum: Case report. Diagn Cytopathol 2002;26:95-8.

9. Jain M, Niveditha SR, Bharadwaj M, Pathania OP. Cytological features of fibrolamellar variant of hepatocellular carcinoma with review of literature. Cytopathology 2002;13:79-82.

10. Suen KC, Magee JF, Halparin LS, Chan NH, Greene CA. Fine needle aspiration cytology of fibrolamellar hepatocellular carcinoma. Acta Cytol 1985;29:867-72.

11. Bakdounes K, Jhala N, Jhala D. Diagnostic usefulness and challenges in the diagnosis of mesothelioma by endoscopic ultrasound guided fine needle aspiration. Diagn Cytopathol 2008;36:503-7.

12. Pugh JL, Jhala NC, Eloubeidi MA, Chhieng DC, Eltoum IA, Crowe DR, et al. Diagnosis of deep-seated lymphoma and leukemia by endoscopic ultrasound-guided fine-needle aspiration biopsy. Am J Clin Pathol 2006;125:703-9.

13. Jhala NC, Eltoum IA, Eloubeidi MA, Meara R, Chhieng DC, Crowe DR, et al. Providing on-site diagnosis of malignancy on endoscopic-ultrasound-guided fine-needle aspirates: Should it be done? Ann Diagn Pathol 2007;11:176-81.

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