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Fibrolamellar Hepatocellular Carcinoma. A Case Report

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Abstract: Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare primary liver cancer that affects young adults with no prior liver disease. Multinodular with poor prognosis FLHCC is an uncommon presentation of this tumor. We report in this paper the case of a 20 year old man who presented with abdominal pain of the right hypochondrium associated with hepatomegaly. The imaging studies showed multiple nodular lesions of the liver, the histopathology of which revealed a FLHCC. In this case report, we discuss the characteristics of the FLHCC and we review the literature regarding clinical presentation and treatment.

Keywords: Gastric tumor, alveolar rhabdomyosarcoma, Clinicopathological features.

Case Report

INTRODUCTION

Fibrolamellar hepatocellular carcinoma (FLHCC) is a rare primary liver cancer that has distinctive, clinical, histopathological, and prognostic features. Among these are its frequency among young patients with no history of cirrhosis or chronic liver disease, increased chance of resectability for cure and prolonged survival compared with patients with conventional hepatocellular carcinoma (Ichikawa, T. *et al*., 1999). We report in this paper an unusual observation of a multinodular FLHCC associated with a poor prognosis.

CASE PRESENTATION

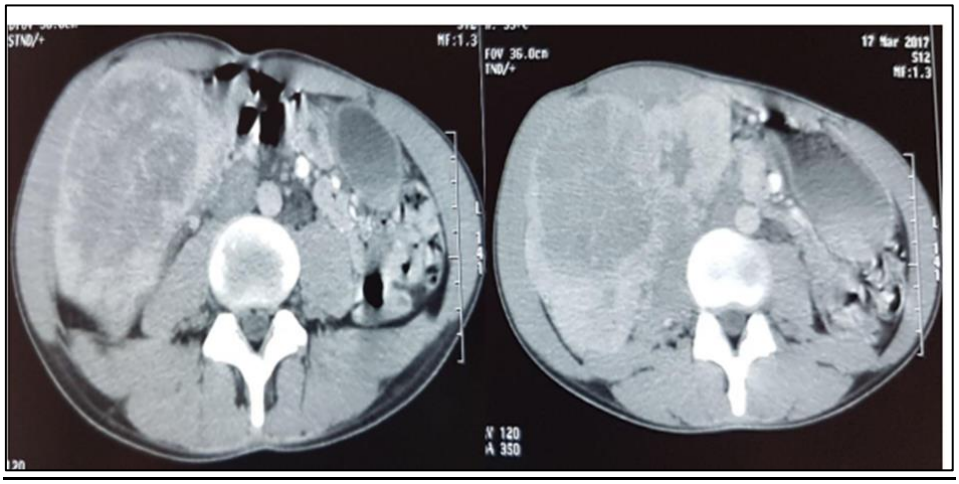
The patient was a 20-year-old man with no remarkable medical history, admitted to our department with progressively worsening chronic abdominal pain of the right upper quadrant without previous trauma evolving for 2 months duration, associated with fatigue, and weight loss estimated at 6 kg within the 2 months period.

Physical examination revealed an important hepatomegaly (Hepatic arrow of 20cm). No other abdominal or extra-abdominal mass was palpated. There was neither jaundice nor lymphadenopathy. The remainder of the physical examination was unremarkable.

His initial laboratory investigation was notable for a slightly elevated aspartate and alanine aminotransferases (AST and ALT) , normal alkaline phosphatase, normal total and direct bilirubin, normal prothrombin time and normal alpha foeto protein.

Ultrasound (US) of the patient's abdomen revealed 4 nodular lesions of the liver, 3 of which were hyperechogenic located at the segments I, IV and VIII measuring respectively 55, 130 and 18mm of diameter, and one hypoechogenic lesion of 13mm of diameter located at the segment VII. The abdominal computerized tomography (CT) (Figure 1) showed a large hypodense heterogenous tumor of the segment VIII measuring 71 x 93mm associated with multiple other hypodense nodular lesions of variable size, the largest ones were involving the segments III and V measuring respectively 44mm and 33mm. The other nodular lesions were supra-centimetric with different sizes involving the right and the left liver. Enlarged metastatic lymph nodes were also detected including the hepatic hilum, the celiac, and the periaortic lymph nodes. There was no signs of cirrhosis or portal hypertension which was suggestive of a FLHCC. An ultrasound guided liver biopsy was then performed, the histopathology of which reported a fibrolamellar-type HCC. The CT

findings were suggestive for a FLHCC stage IVB with staging T3N1M1 (8th TNM Classification of Malignant Tumors edition 2017). The fibrolamellar hepatocellular carcinoma invaded more than 80% of the hepatic parenchyma without surgical possibility of resection or liver transplantation because of the extensive liver involvement and the presence of extrahepatic disease (periaortic lymph nodes) . The patient was then transferred to the oncology department to start palliative chemotherapy but died 6 months later from tumor progression leading to a chronic liver failure.



DISCUSSION

The FLHCC was first described in 1956 by Edmondson as a distinctive form of primary hepatocellular carcinoma (HCC) (EDMONDSON, H. A. 1956). Although HCC is one of the most common malignancies worldwide, the fibrolamellar variant is rare and occurs in a distinctly different group of patients (Stipa, F. *et al*., 2006]. Unlike conventional nonfibrolamellar hepatocellular carcinoma (NFL-HCC), the etiology of FLC is still unknown. It typically affects younger patients without underlying liver disease such as viral hepatitis or cirrhosis (Mavros, M. N. *et al*., 2012).

The reported incidence for FLHCC seems to vary by geographical region (Liu, S. *et al*., 2009). It represents less than 1% of all primary liver tumors diagnosed in the United States (Chakrabarti, S. *et al*., 2019). In Africa, where the HCC incidence is particularly high, FLHCC represents 3.3 % of all liver cancers in children < 14 years of age (Liu, S. *et al*., 2009). Overall, FLHCC represents a small proportion of liver cancers as compared with typical HCC, which accounts for 60 – 80 % of all primary hepatic tumors (Liu, S. *et al*., 2009). FLHCC typically affects younger individuals, 5 to 35 years of age, although there appears to be two peak incidences: one at age 10 to 30 years and another at age 70 to 79 years 3. FLHCC seems to occur with equal frequency in males and females in general (Liu, S. *et al*., 2009) .

Macroscopically FL-HCC usually presents as a single, scirrhous, white-brownish, slow-growing and well-circumscribed mass (Depauw, L. *et al*., 2019). Histologically it is characterized by eosinophilic neoplastic hepatocytes separated into cords by lamellar fibrous strands (Maniaci, V. *et al*., 2009). The neoplastic cells in the fibrolamellar variant do not produce a-fetoprotein (AFP). They do commonly express biliary markers, including cytokeratin CK7 and CK19, and molecular markers such as epithelial membrane antigen (EMA), monoclonal carcinoembryonic antigen (mCEA), cancer antigen 19 (CA19) and epithelial cell adhesion molecule (EpCAM) (Depauw, L. *et al*., 2019). Overall, the pathological diagnosis of FLHCC is based on the following triad: 1) large tumor cells with a deeply eosinophilic cytoplasm, 2) the presence of macronucleoli, and 3) abundant fibrous stroma arranged in thin parallel lamellae around tumor cells (Liu, S. *et al*., 2009).

The clinical presentation ranges from asymptomatic and indolent to clinically significant with aggressive features when locally invasive or metastatic (Depauw, L. *et al*., 2019). The clinical symptoms are usually non-specific and often comprise abdominal pain, weight loss, nausea and malaise. The most common physical finding is an abdominal mass or hepatomegaly (Maniaci, V. *et al*., 2009). Jaundice may be present in up to 40 % of cases (Liu, S. *et al*., 2009).

Liver function enzymes, ALT (alanine transaminase) and AST (aspartate transaminase), are typically normal or are only mildly elevated (Liu, S. *et al*., 2009). Only small proportions of patients show minor elevation in Alpha-fetoprotein (Liu, S. *et al*., 2009). Other authors have suggested neurotensin as a biomarker, though it has not been

proven sensitive or specific enough to be a diagnostic marker (Depauw, L. *et al*., 2019).

Diagnosis of FL-HCC merely depends on imaging studies, including US, CT and MRI (Depauw, L. *et al*., 2019). Fibrolamellar HCCs have non specific sonographic features and are seen as well-defined masses of variable echogenicity on ultrasound. Multiphasic CT using a liver protocol or dynamic contrast-enhanced MRI is usually required for further characterization (Ganeshan, D. *et al*., 2014). On CT scan, tumors are typically sharply demarcated or lobulated heterogeneous hepatic masses with a central scar, sometimes with calcification, usually occurring in noncirrhotic or otherwise normal livers. The lesion seen on the CT scan is usually hypodense, which may show a marked enhancement after contrast injection (Liu, S. *et al*., 2009). Tumor necrosis may be seen, but intratumoral hemorrhage is uncommon (Ganeshan, D. *et al*., 2014). Many investigators have stated that FLHCC may closely resemble the benign masses of FNH or hepatic adenoma. However, unlike the heterogenous hypervascular enhancement seen in 90% of cases of FLHCC, FNH and adenomas tend to show homgenous hypervascular enhancement on hepatic arterial CT or MR images (Ichikawa, T. *et al*., 1999). On MRI, fibrolamellar HCC is usually hypointense on T1-weighted images and hyperintense on T2-weighted images. The fibrous central scar is typically hypointense on both T1- and T2-weighted images. Calcification may be difficult to identify on MRI. Gadolinium contrast enhancement characteristics of fibrolamellar HCC mimic the patterns seen on CT, showing marked heterogeneous contrast enhancement on the arterial phase and becoming isointense or hypointense on the portal venous and delayed phase (Ganeshan, D. *et al*., 2014). FDG-PET might be useful to reveal lymph node metastasis and extrahepatic manifestations (Depauw, L. *et al*., 2019). When imaging studies do not provide clarity about the diagnosis, a biopsy can be considered to differentiate between FL-HCC, HCC and FNH (Depauw, L. *et al*., 2019).

At presentation, 70 % of FLHCC patients has metastatic lymphadenopathy. 5 Lymph node metastasis has been shown to be associated with worse outcomes (Chakrabarti, S. *et al*., 2019). Lymph node and peritoneal metastases are believed to be more common in FLHCC than in conventional HCC . Nearly half of the patients develop distant metastasis. The reported common sites for FLHCC metastasis include the mediastinum, ovary, pericardium, os ilium, and skeletal muscle (Liu, S. *et al*., 2009).

Given the rarity of the disease, minimal progress has been made in identifying effective therapeutic regimens for the management of FLHCC (Chakrabarti, S. *et al*., 2019). Overall, the key to successful management of FLHCC is early diagnosis and the cornerstone for treatment is surgical resection with adequate lymph node dissection (Liu, S. *et al*., 2009). Surgical resectability is associated with prolonged survival but a high relapse rate ranging from 36 to 100% and there is currently no proven effective adjuvant systemic therapy (Depauw, L. *et al*., 2019; Maniaci, V. *et al*., 2009). For recurrence, repeated resections or an orthotopic liver transplantation are advised given the low sensitivity of the tumor to alternative treatment (Depauw, L. *et al*., 2019). Systemic chemotherapy has been proposed as a potential beneficial option for inoperable tumors . Unfortunately, the response rates on chemotherapy in FL-HCC patients are low (Liu, S. *et al*., 2009). Commonly used chemotherapeutic agents are cisplatinum, epirubicin, 5-fluorouracil, or their combination (Liu, S. *et al*., 2009). For FLHCC patients who do not respond to chemotherapy and who are not candidates for liver transplantation, hepatic artery chemoembolization can be used as an alternative treatment approach (Liu, S. *et al*., 2009).

The prognosis of fibrolamellar HCC has been a topic of debate in the recent years. Although many authors have reported that fibrolamellar HCC has a better prognosis than conventional HCC, others have reported that the prognosis of fibrolamellar HCC is similar to conventional HCC without cirrhosis (Ganeshan, D. *et al*., 2014). The reported 5-year natural survival rate for FLHCC is 34 %, and the rate increases to 63 % if the tumor has been completely resected (Liu, S. *et al*., 2009). However, For unresectable patients, median survival is estimated at 12 months (Stipa, F. *et al*., 2006). Factors that are of favorable prognostic value in patients with FLHCC include younger age, absence of thrombosis or invasion to hepatic vessels, absence of lymph node metastasis, free surgical borders, and normal liver function Liu, S. *et al*., 2009).

CONCLUSION

In conclusion, FL-HCC is a rare histologic variant of common HCC which occur in younger patients who do not have underlying liver disease. Cross-sectional imaging plays an important role in diagnosis differentiating the tumor from other liver lesions. The cornerstone for cure in FLHCC is complete agressive resection of the tumor along with regional lymphadenectomy given the low sensitivity of the tumor to alternative treatment.

REFERENCES

1. Ichikawa, T., Federle, M. P., Grazioli, L., Madariaga, J., Nalesnik, M., & Marsh, W. (1999). Fibrolamellar hepatocellular carcinoma:

imaging and pathologic findings in 31 recent cases. *Radiology*, *213*(2), 352-361.

2. EDMONDSON, H. A. (1956). Differential diagnosis of tumors and tumor-like lesions of liver in infancy and childhood. *AMA journal of diseases of children*, *91*(2), 168-186.
3. Stipa, F., Yoon, S. S., Liau, K. H., Fong, Y., Jarnagin, W. R., D'Angelica, M., ... & DeMatteo, R. P. (2006). Outcome of patients with fibrolamellar hepatocellular carcinoma. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *106*(6), 1331-1338.
4. Mavros, M. N., Mayo, S. C., Hyder, O., & Pawlik, T. M. (2012). A systematic review: treatment and prognosis of patients with fibrolamellar hepatocellular carcinoma. *Journal of the American College of Surgeons*, *215*(6), 820-830.
5. Liu, S., Chan, K.W., Wang, B., & Qiao, L. (2009). Fibrolamellar hepatocellular carcinoma. *American Journal of Gastroenterology, 104(10), pp.2617-2624.*
6. Chakrabarti, S., Tella, S. H., Kommalapati, A., Huffman, B. M., Yadav, S., Riaz, I. B., ... & Smoot, R. L. (2019). Clinicopathological features and outcomes of fibrolamellar hepatocellular carcinoma. *Journal of Gastrointestinal Oncology*, *10*(3), 554.
7. Depauw, L., De Weerdt, G., Gys, B., Demeulenaere, S., Mebis, W., & Ysebaert, D. (2019). Pediatric fibrolamellar hepatocellular carcinoma: case report and review of the literature. *Acta Chirurgica Belgica*, 1-7.
8. Maniaci, V., Davidson, B. R., Rolles, K., Dhillon, A. P., Hackshaw, A., Begent, R. H., & Meyer, T. (2009). Fibrolamellar hepatocellular carcinoma–Prolonged survival with multimodality therapy. *European Journal of Surgical Oncology (EJSO)*, *35*(6), 617-621.
9. Ganeshan, D., Szklaruk, J., Kundra, V., Kaseb, A., Rashid, A., & Elsayes, K. M. (2014). Imaging features of fibrolamellar hepatocellular carcinoma. *American Journal of Roentgenology*, *202*(3), 544-552.