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Sarcomatoid hepatocellular carcinoma in a young African female

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Abstract

Sarcomatoid hepatocellular carcinoma is a rare primary malignant liver cancer. The pathogenesis is unclear; however, the risk factors may be similar to that of conventional hepatocellular carcinoma. We present an 18-year-old female who was admitted due to generalized tonic–clonic convulsions. On examination, we palpated a large non-tender mass in the right upper quadrant. An abdominal computed tomography identified it as hepatocellular carcinoma, and spindle-shaped cells were seen on histopathology. She was counseled on her prognosis but opted for local herbal medications rather than chemotherapy, but unfortunately passed away. We present a rare subtype of hepatocellular carcinoma in a young female which is commonly seen in males above the age of 50 years, and despite its grade and stage, overall survival is poor.

Keywords

Sarcomatoid, hepatocellular carcinoma, non-cirrhotic liver, young adult, Tanzania

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Introduction

Hepatocellular carcinoma (HCC) is the main type of liver cancer, accounting for up to 75%–85% of cases.[1] Males are mainly affected with a male-to-female ratio exceeding 2.5 for both incidence and mortality.[2] More than 80% of HCC cases occur in low-income and lower-middle-income countries, particularly in Eastern Asia and sub-Saharan Africa.[3]

Sarcomatoid hepatocellular carcinoma (SHC) is a rare type accounting for less than 5% of HCC, which consists of epithelial and mesenchymal spindle cells.[4,5] SHC is a distinct subtype of HCC identified histologically by spindle-shaped cells with increased mitotic activity.[6] We present an 18-year-old female with a large liver mass in the absence of cirrhosis and major risk factors, with spindle-shaped cells on histopathology.

Case report

An 18-year-old female was admitted with a complaint of generalized tonic–clonic convulsions 24 h before admission. She reported three episodes of convulsions each lasting within 2 min and preceded by a frontal headache. She was healthy-looking, and not pale with a hemoglobin of 13.9 g/dL. She was not jaundiced, and there were no palpable lymph nodes. Her abdomen was asymmetrically distended with an irregular hard liver 7 cm below the right costal margin, and there was no palpable spleen. She did not present with any bone or joint pain and swelling. She was initially loaded with diazepam and later switched to phenytoin due to poor control of her convulsions. No further convulsions were observed during the rest of her stay at the hospital.

Her blood workup showed normal serum total protein and albumin of 71.3 and 48.4 g/L, respectively. The total bilirubin was 14.6 mmol/L with a direct bilirubin of 5.6 mmol/L, an international normalized ratio of 1.25, and aspartate aminotransferase of 35 U/L. She scored 5 points on the Child–Pugh score[7] labeling her as Class A. Her alpha-fetoprotein level was 5.6 IU/mL (normal = 0–6 IU/mL). She tested negative for human immunodeficiency virus, hepatitis B, and hepatitis C. Her urine for a pregnancy test was negative.

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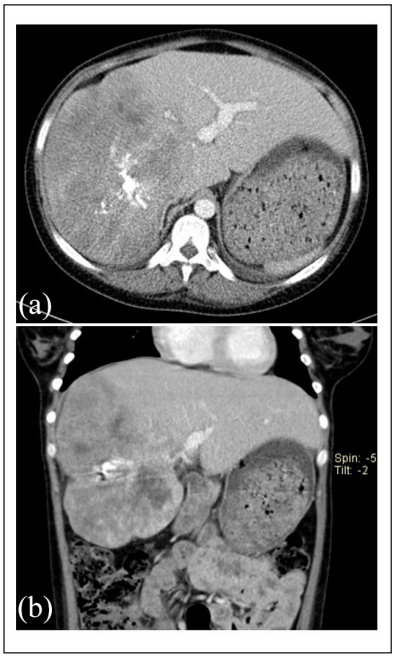

Figure 1. CT axial (a) and coronal (b) views show a poorly marginated mass occupying segments V, VI, VII, and VIII of the liver, which appears heterogeneous with central calcification.

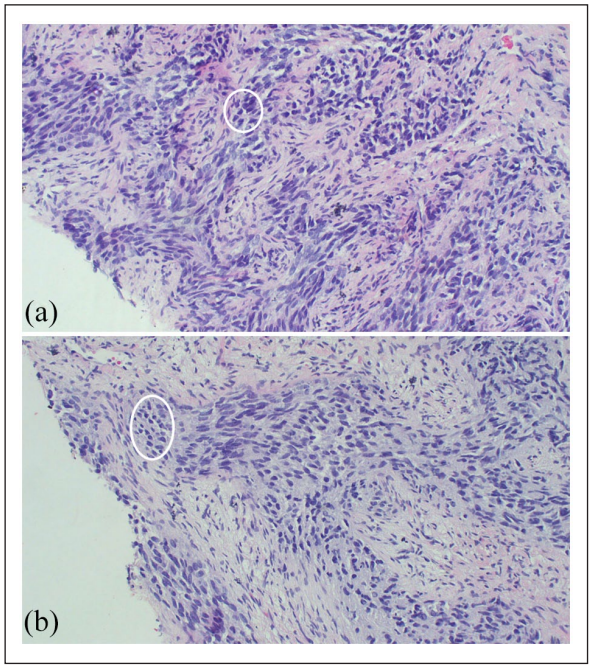

Figure 2. (a) and (b) Different liver core biopsies with mainly spindle cell lesions invading the fibrous stroma in clusters and strands with foci of epithelioid cells (white circle).

Brain computed tomography (CT) showed no pathology. An abdominal CT (Figure 1) showed a heterogeneous mass in segments V, VI, VII, and VIII of the liver with chunky central calcifications, infiltration into the gallbladder, and no portal vein thrombosis were seen. A biopsy of the lesion (Figure 2) showed spindle cells, and the diagnosis was SHC. Immunohistochemistry of the biopsy showed cytokeratin negative and vimentin negative stains; however, there was background uptake of myoblast determination protein 1 though no nuclear expression (Figure 3).

In the discussion with the oncology team, due to the unresectable nature of the tumor, she was advised on palliative chemotherapy. The patient and family were counseled on her prognosis but opted for alternative therapy instead, and she was discharged home with phenytoin. Regular telephone follow-up and a physical follow-up visit 3 months later reported no complications. However, she reported using local herbal medicine as means of alternative therapy. Unfortunately, 2 months after the follow-up visit, the relatives reported that she had passed away at home.

Discussion

This study describes a young female with an incidental finding of a large distinct subtype of HCC. Similar to the conventional HCCs, the sarcomatoid subtype is predominantly seen in males and older ages between 58 and 62 years.[5,8] In addition, the liver enzymes, serum bilirubin, and alpha-fetoprotein tend to be within the normal range,[8] similar to this study.

The risk factors for the development of SHC are similar to that of conventional HCCs, being hepatitis B, hepatitis C, and liver cirrhosis.[8] The pathogenesis is not well-understood but is possibly caused by anti-cancer therapy accelerating the proliferation of the sarcomatous cells being a secondary transformation of the conventional HCC.[9] Although, in this study, no risk factor was identified similar to other studies demonstrating the incidence without any prior exposure to anti-cancer therapy,[10] as SHC can occur in up to 22.5% without an underlying etiology.[8]

Compared with conventional HCC, patients with SHC tend to have poorly differentiated large tumor size, frequent tumor necrosis, advanced stage, higher grade at presentation, and higher rates of lymph node metastases.[5,11] The CT imaging typically shows peripheral ring enhancement and no enhancement in the center. The delayed and prolonged peripheral enhancement correlates with extensive interstitial space, allowing slow diffusion of contrast between interstitial and vascular spaces.[12]

SHC must be distinguished from hepatic sarcoma, as the diagnosis is based on a combination of immunohistochemistry, morphology, and no epithelial differentiation. Despite the close morphological similarity between SHC and carcinosarcoma, the spindle cells are positive for keratin while the converse holds in carcinosarcoma.[13] Spindle cell rhabdomyosarcoma has been reported in the liver with the cells being positive for myoblast determination protein 1.[14] SHC must be differentiated from combined tumors with separate primary foci of HCC and sarcoma, as the absence of mixing of different tumors on

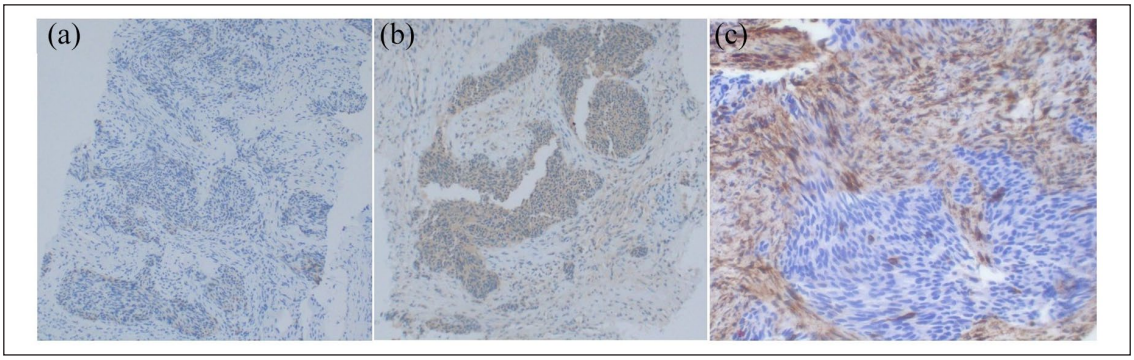

Figure 3. Immunohistochemistry shows cytokeratin negative (a), background uptake of myoblast determination protein 1 without nuclear expression (b) and vimentin negative (c).

histopathology and immunohistochemistry in the different tumors is diagnostic.[11] This study was unable to demonstrate the positivity of either cytokeratin or vimentin in epithelial or mesenchymal marker of the sarcomatoid lesions. However, there have been cases whereby only a third of the cases demonstrate both cytokeratin and vimentin positivity.[15]

To date, there are no specific treatment options for patients diagnosed with SHC. Surgical resection remains the primary treatment option; however, the long-term overall survival of patients with stage II SHC and above was similar to that of patients with advanced stage.[5] However, chemotherapy[16] and an immune checkpoint inhibitor[17] have been observed to improve overall survival.

In Tanzania, the estimated incidence of HCC is 6.8% for males, with a mortality rate of 5.3%.[18] A retrospective study reported that HCC death occurred twice in males than females at 11.3% and 5.1%, respectively.[19] Children and young adults undergoing cancer treatment have expressed physical and financial concerns regarding care and treatment in Tanzanian hospitals.[20] In this study, the patient and family did not want to be financially burdened hence opted for an alternative treatment method; however, the outcome was fatal.

Conclusion

We present a sarcomatoid subtype of HCC based on spindle-shaped cells on histopathology. It is an aggressive tumor associated with a rapid clinical course, large tumor size, and advanced stage at the time of presentation. An early diagnosis, using CT and histological analysis, and treatment through appropriate examination, surgical resection, and chemotherapy may improve patient prognosis.

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Ethical approval

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Informed consent

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