IMAGES

Pleomorphic giant cell-rich hepatocellular carcinoma presented as a right atrial mass

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A 50-year-old nonalcoholic male presented with swelling of lower limbs, abdominal distension, and conjunctival discolourization of 1-month duration as well as altered sensorium and oliguria of 1 day duration. Ultrasonogram (USG) of the abdomen performed 1 month previous to hospitalization showed ascites with no other abnormalities. On examination, the patient had jaundice, pedal edema, ascites, and altered sensorium (E2 M5 V1). Patient's pulse was feeble and blood pressure was not recordable. Bilateral crepitations were present in the lower chest.

Laboratory investigations revealed normal hemoglobin and total leukocyte counts, along with thrombocytopenia (20,000/mm^3) and elevated bilirubin (direct-15.4 mg%, indirect-12 mg%), prothrombin time (1 min), serum glutamic pyruvic transaminase (SGPT, 292 IU), alkaline phosphatase (4560 IU), as well as elevated blood urea (161 mg%). The present USG of the abdomen showed a mass in segment VII of the liver with continuation in the inferior vena cava (IVC). Echocardiography also showed a right atrial (RA) mass with extension into the IVC. A provisional clinical diagnosis of HCC with extension into the IVC and RA, with subsequent cardiogenic shock and hepatic encephalopathy, was made. However, the possibility of an aggressive RA tumor (sarcoma) extending into the IVC and liver infiltration could not be ruled out.

During his short hospital stay, the patient received only supportive treatment for shock in the form of inotropes, oxygen inhalation, intravenous antibiotics and was ventilated. In spite of these measures, the patient deteriorated and died on the same day of admission.

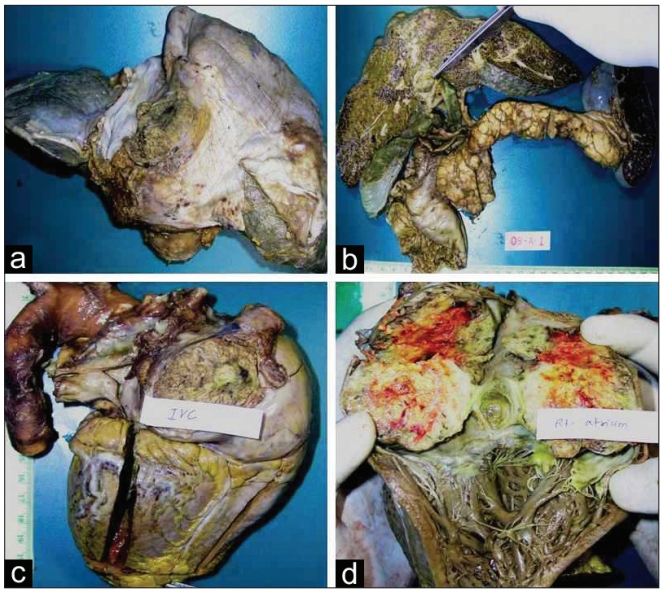

Figure 1: Grossly enlarged liver shows multifocal gray tumor nodules in a background of markedly bile stained cirrhotic liver. IVC shows tumor invasion (a and b). Gross specimen of heart shoes enlarged atrial cavities with IVC embolization. The right atrium is clogged with a tumor mass with a heterogeneous cut surface (c and d)

Hepatomegaly with diffuse micronodularity of the capsular surface was seen [Figure 1a]. On cutting, an irregularly infiltrative, multifocal, grayish white tumor in the liver was seen with areas of necrosis and hemorrhage [Figure1b]. Rest of the liver showed a nutmeg appearance, varying size nodules, cholestasis, and congestion. The tumor was seen to extend through the IVC caudally up to the level of renal veins and cranially reaching up to and filling the whole right atrium with a bulge into the right ventricle, without any infiltration into the atrial wall or tricuspid valves [Figure 1c and d]. The infiltration of the branches of intrahepatic portal vein with luminal thrombi formation was seen. Lymph nodes were enlarged at the porta hepatis and mesentery.

A tumor embolus was identified grossly in the right bronchial artery. Aspirated hemorrhagic contents were seen in tracheobronchial tree. Bilateral pleural

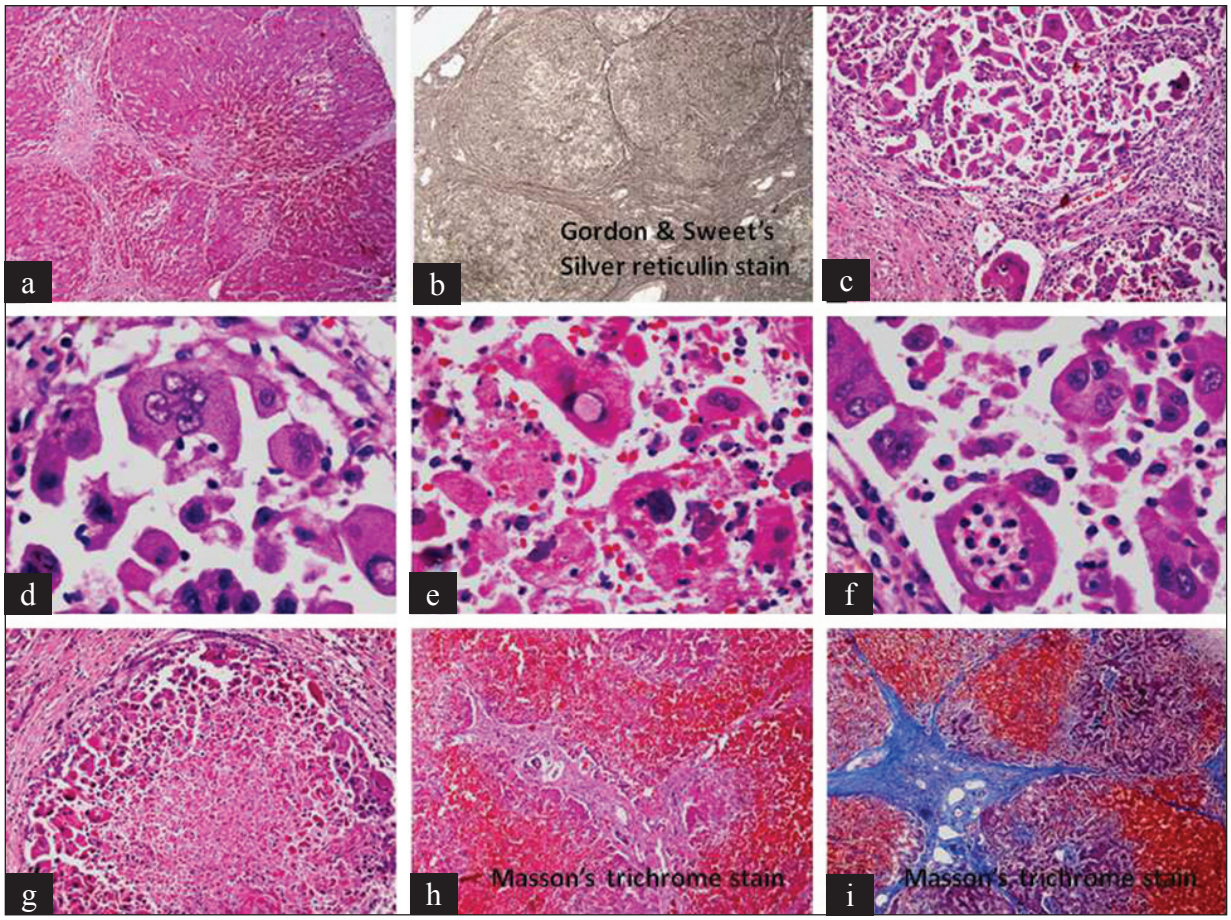

Figure 2: Photomicrograph shows mixed nodular cirrhosis (a and b; a, H and E, ×40; reticulin stain, ×40). The tumor mass shows multiple pleomorphic tumor giant cells (c-e; c, H and E, ×100; d and e, H and E, ×400). The giant cells show cell cannibalism along with central necrosis (f and g; f, H and E, ×400; g, H and E, ×40]. Rest of the liver shows Budd-Chari syndrome-like changes [h and i; h, H and E, ×40; i, Masson's trichrome, ×40)

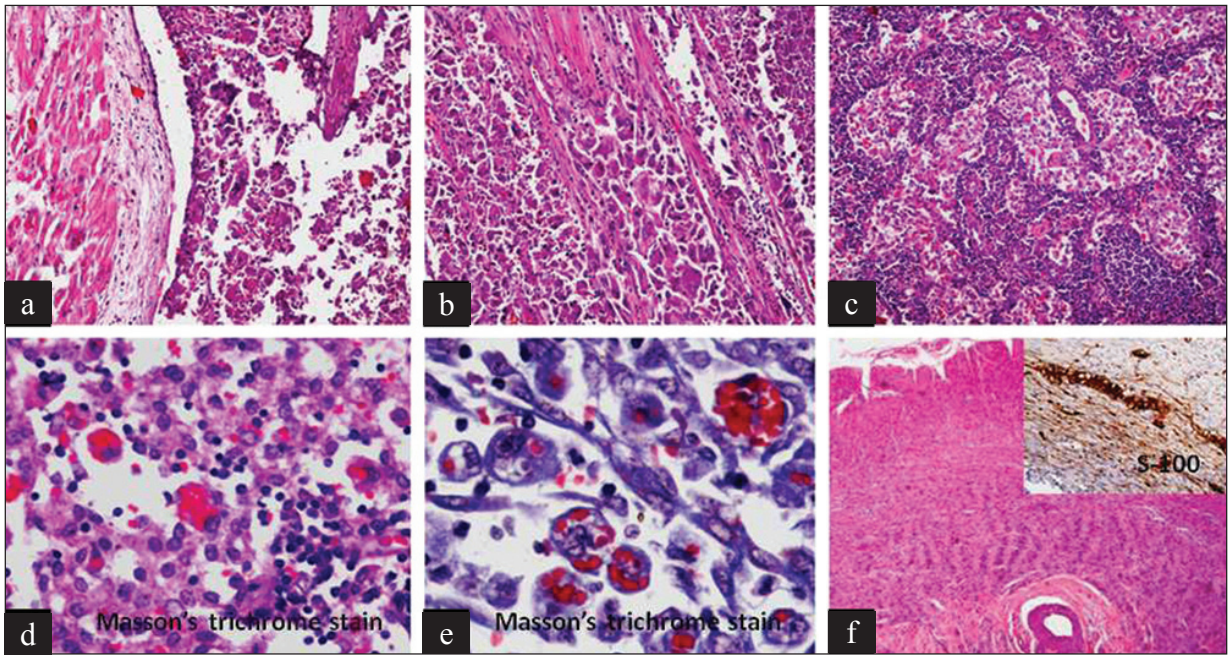

Figure 3: Photomicrographs show tumor in the atrial cavity, as well as focal endomyocardium infiltration (a and b; a, H and E, ×40). The lymph node shows marked sinus histiocytosis (c; H and E, ×40) and evidence of hemophagocytosis (d and e; d, H and E, ×200; e, Masson's trichrome, ×200). Appendicular neuroma with verrocay bodies and positivity for S-100 immunostain (f; H and E, ×40; inset-IHC, S-100 stain, ×40)

effusion and fibrous adhesions were seen on both pleural and pericardial surfaces. Minimal ascites was also present.

Histological examination showed a tumor, where the tumor cells were arranged in nodules with thick and thin fibrous septae in between the nodules along with areas of necrosis and hemorrhage. The tumor cells were large, pleomorphic, predominantly polygonal in shape with abundant eosinophilic cytoplasm and single to multiple pleomorphic vesicular nuclei with prominent nucleoli. Bizarre nuclei and atypical mitosis were also noted. Numerous tumor giant cells were seen distributed throughout the lesion, having multiple pleomorphic nuclei with remnants of phagocytosed neutrophils and cell debris in the cytoplasm [Figure 2]. Immunohistochemistry for cytokeratin, vimentin, and alpha-feto protein were positive in tumor cells while CD68 and alfa-1-anti-chymotrypsin were negative. Sections from the IVC, right atrium, and embolus in the right bronchial artery all showed tumors with similar histomorphology [Figures 3a and b].

The rest of the liver showed features suggestive of cirrhosis with regeneration and marked cholestasis. There were also areas of central hemorrhagic infarct in the regenerative nodules. These features were suggestive of hepatic venous outflow obstruction. Sections from the spleen showed capillarization and dilatation of sinusoids, suggestive of chronic passive venous congestion. Porta hepatis and mesenteric lymph nodes as well as spleen showed sinus histiocytosis with evidence of microscopic hemophagocytosis [Figure 3c-e]. Sections from the appendix, incidentally, showed features suggestive of an appendicular neuroma [Figure 3f].

DISCUSSION

Anthony (1973) first described the pleomorphic giant cell-rich variant of hepatocellular carcinoma (PG-HCC) and there are only a few published reports in the English literature.[1] Vascular invasion and spread through the inferior or superior vena cava and portal veins are common in HCC. Extension into the right cavity, though an unusual finding, has been reported. In a study by Thiefin (1987) on 439 cases of HCCs, 48 patients showed extension into the IVC (10.9%) and 18 showed extension into the right atrium (4.1%).[2] In a similar study on 282 Ugandan patients, 9 showed IVC extension (3.1%), 14 showed hepatic vein extension (4.9%), and 33 showed portal vein extension (11.7%).[3] Our case deteriorated rapidly with an interval between the onset of symptoms and death being less than 1 month. The involvement of the right atrium and both the vena cavae explains the hypotension and shock with which the patient presented to the casualty.

Histopathological examination of both the tumor masses in the index case revealed a HCC along with numerous pleomorphic multinucleated giant cells. In a HCC, if giant cells are seen, the differentials considered are either a PG-HCC or osteoclast-like giant cell-rich HCC. When tumor giant cells predominate in the tumor, it is called a PG-HCC. It should be noted that though the occurrence of an occasional tumor giant cells is known in a conventional HCC, giant cell-rich HCCs are rare. Out of the 282 African patients mentioned previously, 30 (10.6%) were found to have tumors rich in giant cells. In these tumors, the cells were arranged in solid sheets containing multiple bizarre nuclei. There was no evidence of glycogen or bile in the cytoplasm and mitosis was relatively infrequent.[3] The giant cells of PG-HCC differ morphologically from the osteoclast-like giant cells, where in the latter the multinucleated giant cells show monomorphic, bland nuclei with a uniform distribution among the mononuclear stromal cells. In our case, there was a few giant cells showing monomorphic, bland nuclei, but uniform stromal distribution was lacking and the majority of the giant cells in fact were tumor giant cells.[3] Giant cells can also be seen in the sarcomatoid variant of HCC, but the features of sarcomatoid HCC were not present in our case.

Almost all the cases of osteoclast-rich HCC reported previously had a rapidly deteriorating clinical course. Though the outcome of PG- HCCs is exactly not known, the median survival in such cases was not found to be more than 35 days in the literature.[4]

Lymph nodes excised from the porta hepatis from the index case, showed sinus histiocytosis with extensive hemophagocytosis [Figures 3c-e]. Among the various malignancies associated with HPS, HCC to the best of our knowledge has only been reported once to be associated with it.[5] HPS is characterized by the rapid deterioration of the clinical course with multiorgan failure due to an excessive release of cytokines. Hence coexistence of HPS with a PG-HCC may contribute to the aggressive deteriorating behavior of this tumor.

PG-HCC is a rare variant of HCC with a possible atypical clinical presentation and an aggressive clinical course. Atypical clinical presentation and association with other ailments like hemophagocytosis may add to the fatality of the disease.

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