BENIGN MULTIPLE ADENOMATOSIS OF THE LIVER - A CASE REPORT

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Abstract:
Hepatic adenomatosis is a benign neoplasm with presence of multiple adenomas in the liver (more than 10 adenomas in one study and more than 4 in another). The potential for spontaneous bleeding, rupture and malignant transformation are more common in hepatic adenomatosis. This case report describes a 32 year old woman with multiple hepatic adenomas associated with rupture and hemorrhage. The histologic characters, complications and differential diagnosis of hepatocellular adenoma are discussed.

Keyword:
Hepatic adenomatosis, rupture, hemorrhage

CASE REPORT – A 32 year old woman presented with complaints of sudden onset right hypochondrial pain, vomiting and fever for 5 days. There was no past history of steroid and oral contraceptive pill intake. She is not a known diabetic and there was no history of previous trauma. On palpation, hepatomegaly and right hypochondriac tenderness was present. Liver function tests were normal. Viral markers were negative. Alpha fetoprotein level were within normal limits (2 IU/L). Ultrasound abdomen showed 8 cm x 6.2 cm hyperechoic soft tissue mass in segment 7 of the liver which appeared ruptured causing focal subcapsular hematoma. Another hypoechoic soft tissue mass measuring 10 cm x 6.2 cm x 5 cm projecting from segment 6 was also found. Right hepatectomy was done. GROSS: Received hepatectomy specimen measuring 20 cm x 10 cm x 7 cm. External surface (Figure 1) showed large pedunculated yellowish mass of size 10 cm x 6 cm bulging from the surface. Cut section (Figure 2) showed grey to yellowish mass of size 8 cm x 6 cm with large areas of hemorrhage and showed multiple well circumscribed small yellowish nodules each measuring 1-2 cm.
FIGURE 1: Hepatectomy specimen shows large pedunculated yellowish mass bulging from the surface and another large grey brown to yellowish mass with hemorrhage.

FIGURE 2: Cut section shows multiple well circumscribed yellowish nodules.

FIGURE 3: 10x View shows well circumscribed neoplasm, neoplastic cells in cords and sheets without any portal tracts or central vein or bile ducts within the tumour.

FIGURE 4: 40X View shows neoplastic cells which are large polygonal with abundant clear cytoplasm with small round nuclei without atypia. Diagnosis of Benign multiple adenomatosis of the liver was made.

**MICROSCOPY:**
Sections from all nodules (Figure 3) showed well circumscribed neoplasm composed of hepatocytes arranged in 2-3 cell thick cords and sheets without any portal triads or central veins or bile ducts within the tumour. Neoplastic cells (Figure 4) are large polygonal with abundant clear cytoplasm, small round uniform normochromatric nucleus without any pleomorphism or mitosis. Adjacent liver parenchyma appeared normal. Malignant changes are not observed.

**DISCUSSION:**
Hepatic adenoma is a rare, primary benign neoplasm of liver with uncertain origin. The incidence of hepatic adenoma is 3 to 4 case per 100000 in long term oral contraceptive user, but only 1 per million in non users\(^1\).
Hepatic adenoma is usually solitary, occurring in young women around 15-40 years undergoing long term estrogen therapy. It also occurs in individuals receiving anabolic steroids and in patients with glycogen storage disease. Most are asymptomatic, unless there is hemorrhage, which occurs in a minority of patients. Hepatic adenomatosis is a rare condition which was first recognised as a separate and distinct entity from hepatic adenoma by Flejou et al. in 1985 and defined as presence of >10 adenomas within an otherwise normal liver. Yoshidome et al. and Riberio et al. revised the criteria and defined as more than 5 adenomas or more than 4 adenomas respectively. Our case revealed 8 adenomas in a background of normal liver architecture. Hepatic adenomatosis is usually diagnosed in the fourth decade with a mean age of 32 years. It was first reported to affect both sexes with no relation to steroid intake or glycogen storage disease. Chiche et al. study showed female preponderance (74%) and association with steroid intake (46%). Yoshidome et al. study also showed female preponderance (63%) but there is no association with steroid intake or glycogen storage disease. Our case was reported in a non diabetic, 32 year old female without any history of steroid intake. Hepatic adenomatosis patients may be completely asymptomatic and are diagnosed incidentally by imaging studies. But most of the patients present with abdominal pain due to hepatomegaly, intratumoral hemorrhage, necrosis, intraperitoneal bleeding due to spontaneous rupture. Our patient presented with sudden onset right hypochondrial pain without any history of trauma. Spontaneous rupture and hemorrhage have caused abdominal pain. On gross examination hepatic adenomatosis shows multiple bulging well circumscribed typically unencapsulated soft nodules more than 4 to 10 in number. Size of the nodules varies from 2 cm to 10 cm and even measures up to 30 cm in diameter. Cut section of nodules show varying shades of yellow to tan brown mass depending upon the amount of fat content. There may be areas of necrosis or hemorrhage. Evidence of cirrhosis is typically absent and these nodules usually arises in a background of normal liver. Our case revealed 8 well circumscribed yellow nodules varying in size from 1 cm to 10 cm in a background of non cirrhotic and normal liver. Histopathological examination is needed to confirm the diagnosis of hepatic adenomatosis. On microscopy, both adenoma and adenomatosis are composed of relatively uniform population of hepatocytes arranged in one to three cell thick plates. The tumour cells are usually larger and paler than non tumour hepatocytes in the surrounding tissue due to increased cytoplasmic glycogen or fat. The cytoplasm may be clear or eosinophilic. The nuclei of tumour cells are typically uniform and regular with a normal nuclear cytoplasmic ratio. Nucleoli are seldom prominent. Mitotic figures are absent or extremely rare. Portal triads or central veins or bile ducts are typically absent within the tumour. Intracellular and canalicular bile may be seen. Histopathological examination of our case has correlated with other studies like Flejou et al., Wesley et al. The histopathological differential diagnosis of hepatic adenomatosis includes multiple liver lesions like metastatic disease, multifocal hepatocellular carcinoma, multiple focal nodular hyperplasia, nodular regenerative hyperplasia.
Hepatocellular carcinoma has liver cell plates >3 cell thick with tumour cells showing significant nuclear pleomorphism with increased nuclear cytoplasmic ratio with prominent nucleoli, vascular invasion and increased mitosis. Hepatocellular carcinoma usually arises in the background of underlying liver disease. like cirrhosis and alpha fetoprotein level (AFP) is usually elevated (5)(7). Our case has normal AFP level, <3 cell thick liver plates, no nuclear atypia and developed in a background of non cirrhotic and normal liver. Focal nodular hyperplasia shows central stellate scar on gross examination, nodular growth pattern of benign hepatocytes surrounded by fibrous septae with bile ductular reaction on microscopy (5)(7). Absence of fibrous septae and bile ductules in our case favours adenomatosis. Nodular regenerative hyperplasia is characterized by diffuse hyperplastic nodules of varying sizes with central portal tracts, with no intervening fibrous septae (5)(7). Absence of portal tracts in our case favours adenomatosis. Hepatic adenomatosis is a benign neoplasm but patients may rarely develop fatal complications like hypovolemic shock due to rupture with intraperitoneal hemorrhage. Intraportal or intratumoral hemorrhage are more common in patients with liver adenomatosis than in patients with solitary hepatic adenoma. The reported incidence of spontaneous bleeding in hepatic adenomatosis is 40-62.5% (3)(5). Malignant transformation to hepatocellular carcinoma in adenomatosis can occur in 6-10% of cases (3)(6). Our patient presented with spontaneous rupture and hemorrhage. The management of hepatic adenomatosis is usually surgical resection in symptomatic patients and larger adenoma >5 cm because of the low but grave risk of hemorrhage and malignant transformation. Close follow up with yearly imaging of liver and measurement of AFP level is recommended in asymptomatic patients with smaller adenoma <5 cm. Orthotopic liver transplantation can be done in patients who have progressive symptoms after partial resection or in whom carcinoma is suspected (5)(8).

CONCLUSION:
This case is reported because of its rarity and to highlight the importance of Hepatic adenomatosis which has potentially lethal complication of hemorrhage.

REFERENCES:
