A rare clinical entity misdiagnosed as a tumor: Peliosis hepatis

Yanlışlıkla tümör tanısi konmuş nadir bir klinik durum: Peliosis hepatis

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Peliosis hepatis (PH) is a rare condition characterized by the presence of cystic, blood filled cavities within the hepatic parenchyma. Regardless of the reason, surgery should be performed under meticulous control of hemorrhage, if it is thought to be unavoidable. In this case report, ominous results of clinically misdiagnosed PH have been presented. PH should be kept on mind in all patients with hepatic mass, especially presented by sudden onset distention of the abdomen. Every effort should be done for the differential diagnosis with other cystic conditions like hydatid cyst in endemic areas.

Key Words: Hemorrhage; liver; Peliosis hepatis.


Anahtar Sözcüklər: Kanamalı karaciğer, Peliosis hepatis.

CASE REPORT

Forty three-years-old male was admitted to clinic with a huge cystic lesion almost occupying the whole right lobe of the liver (23 x 18 x 13 cm). His physical examination was significant for shortness of breath, right pleural effusion and a huge palpable mass on right upper abdomen. In his past medical history, he had been admitted to surgery clinic 5 months before in rural area with a right upper abdominal discomfort lasting for two months. Serology had been reported negative for hydatid cyst and ultrasound revealed a cystic lesion (16 x 14 cm) in the right liver lobe. Laparotomy had been performed and a septated cyst was found. According to previous clinical discharge report it was full of clear fluid. The cyst was unroofed and a biopsy specimen was taken from the wall. Pathological interpretation was reported as a “simple cyst”.

Both of shortness of breath and hypotension has worsened patient’s clinical condition and he has been scheduled for right hepatic lobectomy as an emergency case. In surgery no cleavage could be detected between diaphragm and the liver due to dense adhe-
sion. In order to have a control on suprahepatic IVC, we attempted to perform mobilization of the right liver which ended with rupture of multiple blood filled cysts. The liver was enlarged with these cysts and implied spontaneous hemorrhage into the cysts. To avoid massive blood loss Pringle maneuver was performed. However, without control on suprahepatic IVC, Pringle maneuver alone could not prevent massive blood loss and subsequent multiple transfusions. Right hepatic lobectomy was performed and the patient has been sent to ICU. Following a stormy postoperative course, the patient died three days after the operation with multiorgan failure. On pathologic examination, a multicystic blood filled lesion was determined. The sizes of the cysts were ranging from 0.5 to 4 cm. On microscopic examination, the hepatic parenchyma was replaced with multiple cystic cavities filled with erythrocytes and lined by flattened endothelium like cells in some areas. In most areas the cavities had no lining and occasionally had fibrosis and mixoid areas on their walls. Irregular hepatic parenchyma showing sinusoidal dilatation could be observed between the cysts. The lesion was diagnosed as PH.

**DISCUSSION**

Peliosis hepatitis may have no obvious etiology (25-50%)\(^9\). But the diversity of etiologies detected (or suspected) should alert the surgeon to make correct diagnosis and to prepare himself for correct operation (Table 1).\(^4\)

Bagheri & Boyer suggested the pathogenesis of PH as following: PH begins with focal cell necrosis that ultimately destroys the reticulum framework allowing the cyst to form from the inflow of the blood coming from the adjacent sinusoids.\(^5\) Beyond the histopathologic appearances reported, in 1964 Yannoff & Rawson classified PH into two histological pattern; parenchymal and phlebectatic. The former has blood filled spaces with no endothelial lining and is usually associated with hemorrhagic necrosis and the latter has spaces with endothelial lining that is aneurysmal dilatation of the central vein.\(^6,7\) This distinction has been abandoned as both patterns can be seen in the same liver and probably represents different stages of the same disease.\(^8\) The cysts show no zonal predominance and may communicate with the sinusoids (which may be dilated). Hepatocellular necrosis may be present. Electron microscopy studies\(^9\) showed marked dilatation regarding both the spaces of Disse and the sinusoidal lining with large communication between each other.

Blood filled cavities in PH may range from less than 1 cm to several centimeters and are not restricted to the liver. Foci have been reported in lung\(^10\) and reticuloendothelial system including the spleen, lymph nodes and bone marrow.\(^11\) PH may present as hepatomegaly,\(^12\) portal hypertension with esophageal varices and ascites,\(^12\) liver failure or as hemoperitoneum with shock\(^13\) secondary to intraperitoneal rupture. The cavity size appears to be predictive of the clinical manifestation.\(^14\) Degott et al.\(^12\) classified PH into two forms depending on the size and extent of liver involvement: major and minor form. Only

**Table 1.** Associated conditions reported within Peliosis hepatitis and related literature

<table>
<thead>
<tr>
<th>Drugs and chemicals</th>
<th>Androgenic-anabolic steroids(^2)</th>
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<tbody>
<tr>
<td></td>
<td>Tamoxifen(^24)</td>
</tr>
<tr>
<td></td>
<td>Contraceptive steroids(^33)</td>
</tr>
<tr>
<td></td>
<td>Azathiopurine(^9)</td>
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<tr>
<td></td>
<td>Corticosteroids(^5)</td>
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<tr>
<td></td>
<td>Arsenic(^90)</td>
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<td></td>
<td>Thorium dioxide(^27,30)</td>
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<tr>
<td></td>
<td>Vinyl chloride(^30)</td>
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<tr>
<td></td>
<td>Copper sulfate(^28)</td>
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<tr>
<td></td>
<td>Toxic oil syndrome(^18)</td>
</tr>
<tr>
<td>Bacterial infections</td>
<td>Endocarditis(^28)</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis(^10)</td>
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<td></td>
<td>Leprosy(^12)</td>
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<tr>
<td>Monoclonal gammopathies</td>
<td>Multipl myeloma(^4)</td>
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<tr>
<td></td>
<td>Waldenström macroglobulinemia(^4)</td>
</tr>
<tr>
<td>Malignancies</td>
<td>Malignant tumors(^34)</td>
</tr>
<tr>
<td></td>
<td>Hodgkin’s disease(^9)</td>
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<tr>
<td>Other conditions</td>
<td>Cardiac &amp; renal transplantation(^9,18,19)</td>
</tr>
<tr>
<td></td>
<td>Chronic hemodialysis(^16,18)</td>
</tr>
<tr>
<td></td>
<td>Diabetes(^15)</td>
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<td></td>
<td>Acquired immunodeficiency syndrome(^9,11)</td>
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<td></td>
<td>Sprue(^24)</td>
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<td>Necrotizing vasculitis(^10)</td>
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patients with major Peliosis had hepatomegaly and signs of portal hypertension.

Hepatocellular necrosis as an etiology was raised by Bagheri & Boyer[9] who noted foci of necrosis next to the peliotic cavities. They suggested that necrosis destroyed the reticulum framework allowing inflow of blood with subsequent cyst formation. Experimental Peliosis induced by lasiocarpine in mice shows hepatocyte necrosis before cavity development.[15]

Numerous theories have been proposed for the etiology of PH. Earlier theories which were summarized by Zak[11] include a) congenital malformation, b) vascular varicosities with or without prior angetis, c) ruptured vessels with or without prior inflammation, d) hemorrhage preceded by focal hepatocyte necrosis and e) a combination of inflamed vessels that bulging into the necrotic parenchyma.

Zafrani et al.[9] have suggested three possible etiologies that include a) outflow obstruction at the sinusoidal hepatic venule junction, b) a toxic effect of a substance on the sinusoidal wall and c) hepatocellular necrosis leading to cyst formation.

Peliosis hepatitis has been described in kidney recipients at variable frequencies ranging from 0% to 12%[16,17] and a possible relation to azathiopurine toxicity[12,18] has been suggested. Outflow obstruction was also suggested by Degott et al.[12] who believed that Peliosis was secondary to fibrous thickening of hepatic venules possibly due to azathiopurine in their renal transplantation patients. Also it had been noted that hyperplastic hepatocytes might prolapse into the terminal hepatic venules in anabolic steroid-induced Peliosis. However, neither Zafrani et al.[9] nor Nadell and Kosek[19] have observed such changes. The belief that toxic substances induce Peliosis is supported by finding increased endothelial cell permeability with numerous red blood cells in the space of Disse.[9]

Although PH and nodular regenerative hyperplasia are histologically different lesions they have several common causes. These similarities in their etiology might be related to similarities in their mechanisms; both lesions might be the consequences of disordered intrahepatic circulation.[4]

Bacillary PH is an uncommon but well recognized disease due to disseminated Bartonella infection occurring predominantly in immunocompromised individuals infected with HIV type 1.[20] Treatment of Bartonella infection has never been systematically studied. In general, oral administration of erythromycin (500 mg four times a day for 3 months) has been the first agent of choice.[21] It is important to note that after first dose of an appropriate antibiotic, patient may experience a Jarisch-Herxheimer reaction with the exacerbation of the systemic symptoms and fever.[22] Ahsan et al. speculate that the current practice of routine use of sulphonamides in post transplant patients for Pneumocystis carinii prophylaxis may account for relatively decreased incidence of this disease in these patients.[23] Whereas erythromycin is the first drug of choice, blood levels of cyclosporine and tacrolimus must be monitored closely due to drug interactions when the patient is receiving erythromycin treatment.[20]

Garcia-Tsao et al.[23] have demonstrated bacillary PH as a cause of acute anemia in a patient with AIDS which rapidly respond to zidovudine and ampicillin/sulbactam therapy. Bartonella bacilliformis was shown by silver stain (Dieterle) surrounding hepatocytes at the edge of the peliotic spaces and among the erythrocytes. Bartonella bacilliformis is probably the main reason of the development of PH and has a good response against ampicillin/sulbactam therapy but using zidovudine treatment before improvement. They also speculated that damage to sinusoidal endothelial cells could have been caused by the HIV virus itself also and that improvement was caused by treatment with zidovudine.

Patients with hypervitaminosis A show features of Peliosis[23] including dilatation of perisinusoidal spaces, extravasation of red blood cells between abnormal sinusoidal lumina and swelling of endothelial cells. The causative agent for Cutaneous Bacillary Angiomatosis and HIV-related PH is Rochalimaea henselae, a Rickettsia like organism[24] and Rochalimaea quintana.[25]

Peliosis is a rare pathologic finding in hematopathies including Hodgkin’s disease,[26] leukemia,[27] multiple myeloma,[28] and light chain disease.[29] Liote et al. described a case of hepatic AMM associated with Peliosis first[30] although one case of Peliosis of the spleen has been reported in AMM.[31] A relationship between AMM and sinusoidal endothelial cell proliferation can be suggested in
view of increased endothelial cell metabolic activity in myelosclerosis.\textsuperscript{[13]} Simon et al. reported the first case of PH in a patient with marasmus.\textsuperscript{[14]}

Zafrani et al. reported a case with focal hemorrhagic necrosis of the liver possibly related to oral contraceptives with large hepatic zones of decreased density at CT scan.\textsuperscript{[13]}

Diagnosis of PH requires a high degree of suspicion. Hepatic USG may disclose hyperechoic areas.\textsuperscript{[13]} Herrera et al.\textsuperscript{[14]} reported a case with a normal appearances on CT scan. Angiography,\textsuperscript{[13,15]} in PH shows multiple accumulations of contrast media that are most prominent during the parenchymal and venous phases. Helical CT shows multiple peripheral low-density regions with foci of spontaneous high density regions suggesting the presence of blood component. On MR imaging the multiple peripheral lesions were hypointense on T1 weighted and hyperintense on T2 weighted images with bright foci on all sequences suggesting subacute blood. Angiography shows no evidence of tumor or vascular malformations, multiple nodular vascular lesions filling in the parenchymal phase and persisting in the venous phase suggested blood filled cavities.\textsuperscript{[13]}

We believed that our patient is the first case of PH developing after a simple liver cyst. Whether the etiology PH in our patient was liver cyst alone or the operation has played a role in induction of PH development remained to be uncertain. The diagnosis is the real one when the definite one from the differential diagnosis can be found by the clinical presentation, laboratory findings and radiodiagnostics procedures.

REFERENCES