A case of primary hepatic lymphoma and a review of literature

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SUMMARY

Introduction Primary hepatic lymphoma (PHL) is a rare disease and represents lymphoproliferative disorder confined to the liver parenchyma. This condition is difficult to distinguish from other liver diseases. Histopathology is essential and confirms the diagnosis. Treatment options for PHL include surgery, chemotherapy, radiation, or combinations of these modalities. The objective of this report is to present a case of PHL and to discuss disease features and treatment options in order to facilitate diagnostics and therapy.

Case outline A 72-year-old female was presented with abdominal pain, nausea, weight loss, and fatigue. Computed tomography (CT) revealed hypoattenuating solitary lesion in liver segment VIII. The detected liver lesion showed elevated 2-[fluorine 18] fluoro-2-deoxy-D-glucose uptake on positron emission tomography/CT examination. Extrahepatic disease was not detected. The tumor board opted for surgery, and atypical resection of liver segments VII and VIII was performed. Pathohistological examination of the resected tumor demonstrated liver infiltration with non-Hodgkin's lymphoma, diffuse large B-cell type. Postoperative recovery was complicated by fluid collections in the right subphrenic space, successfully managed by percutaneous drainage. Subsequently, the patient was treated with chemotherapy and attained a complete remission documented by negative CT findings.

Conclusion PHL can easily be misdiagnosed as another more frequent primary liver tumor due to its non-specific clinical manifestations, laboratory and imaging findings, and therefore should be considered in the differential diagnosis of a hepatic lesion.

Keywords: chemotherapy; drainage; liver; operative; tumor

INTRODUCTION

Primary hepatic lymphoma (PHL) is a lymphoproliferative disorder confined to the liver without any evidence of involvement of the spleen, lymph nodes, bone marrow, or other lymphoid structures [1]. PHL is a rare disease and accounts for 0.4% of all extranodal lymphoma and 0.016% of all non-Hodgkin’s lymphoma (NHL) [2]. PHL of diffuse large B-cell lymphoma (PHL-DLBCL) is more infrequent [3]. PHL typically occurs in middle-aged men, and the presenting symptoms, blood investigations, and imaging findings are usually nonspecific [1]. This condition is difficult to distinguish from primary liver cancer, liver metastases, granulomatous pseudotumor, and other liver diseases; therefore, it is easily misdiagnosed [3]. Histopathology is mandatory and confirms the diagnosis.

A patient with PHL is presented. A better understanding of the disease will facilitate diagnostics and therapy. We contribute our experience to the pool of data. Written informed consent was obtained from the patient for publication of this case report and accompanying images.
only in liver segment VIII without pathological elevation in other organs (Figure 1). On esophagogastroduodenoscopy atrophic gastritis was present. Colonoscopy detected ano-rectal polyps and enlarged hemorrhoidal nodes. A barium enema study revealed diverticulosis of the descendent and sigmoid colon. Extrahepatic disease was not detected.

The multidisciplinary tumor board opted for surgery and atypical resection of liver segments VII and VIII was performed. Lymphatic nodes in the hepatoduodenal liga-ment were dissected for frozen section analysis and proved to be benign.

Pathohistological examination of resected tumor revealed hepatic tissue with large nodular, tumorous, lymphoid infiltrates and numerous confluent necrotic fields, without tumor cells on the resection margin.

Immunohistochemical staining showed that 90% of tumor cells had positive reaction for CD 20, CD79a, bcl 6, MUM 1, and Ki 67. These histological and immunohistochemical findings demonstrated liver infiltration with DLBCL (Figure 2).

Three weeks after the hospital discharge, the patient was presented with abdominal pain, nausea, and vomiting and was promptly readmitted. Routine blood and biochemistry examination revealed elevated inflammatory markers and abdominal CT demonstrated pleural effusion, 150 × 97 × 103 mm fluid collection in the right subphrenic space with a mean attenuation value of 22 HU and viscous fluid collection in segment VI of the right liver lobe, containing gas inclusions, 95 × 57 × 110 mm in size (Figure 3).

The patient was referred to the interventional radiology department for percutane-ous drainage of the fluid collection at the liver resection site. Ultrasound guided initial puncture of the right subphrenic fluid collection was performed and specimen of viscous yellow fluid was sent for microbiological analysis followed by the placement of 10.2 Fr percutaneous drainage catheter in collection. Enterobacter spp. were isolated from the specimen and antibiotic therapy was initiated according to the antibiogram. Control CT scan of the ab-domen revealed resolution of the subphrenic collection around the tip of the pigtail catheter. On follow-up ultrasound examination, no fluid collection was detected and the patient was referred to the department of hematology for further treatment.

Bone marrow biopsy did not reveal lymphoma infil-tra tion. Complete blood test excluded leukemic cells in the peripheral blood. Due to reduced left ventricular function (EF 55%), the lymphoma board decided to treat the patient with a R-miniCHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, prednisone) low-dose chemotherapy protocol. She was given eight cycles of R-miniCHOP at three-week intervals. During the course
PHL is an extra-nodal lymphoma of the liver without involvement of any other organ (lymph node, spleen, etc.) [4]. The most common presenting symptom in PHL is abdominal pain, occurring in more than 40% of patients. The B-symptoms of fever and weight loss occur in about one-third of the patients. Jaundice is seen in less than 20% of patients [5]. Our patient’s clinical presentation included abdominal pain, nausea, weight loss, fatigue and were consistent with that of primary hepatic NHL.

Preexisting liver disease, such as chronic liver cirrhosis secondary to hepatitis B virus, hepatitis C virus, or hemochromatosis, is present in less than 9% of the patients [6]. In rare circumstances, progressive hepatitis and acute hepatic failure with rapid progression and poor prognosis may occur [7, 8].

The presented patient was diagnosed with NHL by pathohistological examination of the resected tumor. The pathological type was DLBCL. The involvement of other sites was excluded by lymph node examination, radiologic examinations (ultrasound, CT, PET/CT, barium enema), and endoscopic examination (esophagastroduodenoscopy, colonoscopy).

Most PHL patients show a two- to three-fold increase in alanine aminotransferase and aspartate aminotransferase levels, with an increase in bilirubin and high-density lipoprotein levels. However, AFP and CEA levels are usually normal, in contrast to those in primary liver cancer and liver metastases [3]. The presented patient had normal liver enzyme and bilirubin values. Tumor markers (CEA, CA19-9, AFP) were not elevated.

The exact incidence and prevalence of PHL is not known. PHL is rare and comprises 0.4% of all cases of extra nodal NHL and 0.016% of all cases of NHL [2]. The male-to-female ratio is 1.9:1 [9]. The patient in this report was a 72-year-old female, although PHL is more common in males of around 50 years old.

Although PHL is rare, persistent inflammatory processes associated with HCV infection or autoimmune disease may play independent roles in the lymphomagenesis of hepatic B cells [10]. The presented patient was negative for HIV, AIDS, HBV, HCV, and EBV and did not have any autoimmune disease.

There are three radiological presentations of PHL: 1) a solitary lesion, 2) multiple lesions within the liver, and 3) diffuse hepatic infiltration. The most common presentation is a solitary lesion. The initial radiologic test is usually an ultrasound that demonstrates a large, solitary hypoechoic lesion or multiple hypoechoic lesions resembling metastasis [11]. On CT scans, PHL lesions appear as hypoattenuating lesions and may have a central area of low intensity indicating necrosis. Following the administration of intravenous contrast, 50% of PHL lesions do not enhance, 33% show patchy enhancement, and 16% show a ring of enhancement [11]. CT scan of this patient revealed a hypoattenuating lesion in liver segment VIII on non-enhanced scans, with rim-enhancement in the arterial phase, conceding with 16% ring enhancement as described in literature.

Due to the rarity of this disease entity and its nonspecific clinical presentation and laboratory and radiologic features, a definite clinical diagnosis of PHL is difficult. PHL may be confused with hepatitis, primary hepatic tumors, hepatic metastases from gastrointestinal carcinoma, and systemic lymphoma with secondary hepatic involvement [12].

Percutaneous liver biopsy is the most valuable tool for the diagnosis of PHL. The transjugular approach is an alternative when a discrete mass is not visible on imaging for percutaneous liver biopsy [13]. A liver biopsy was not done because the liver lesion appeared malignant on radiological assessment and in order to avoid the risk of tumor seeding in resectable patient. Similar scenarios are described in the literature, where patients, incorrectly diagnosed as PHL, were operated on for other diagnosis.

Treatment options for PHL include surgery, chemotherapy, radiation, or combinations of these modalities. It has been suggested that, for low-volume localized PHL, surgical resection, alone or in combination with chemotherapy, might be a treatment of choice. Lei [6] described 10 patients treated with curative intent surgery who had a median survival of 22 months, ranging 1.5–120 months. Avlonitis and Linos [5], in a large review of the literature, showed similar results that patients treated by surgery and followed by chemotherapy have better survival rates, with median survival of 15.3 months (range: 0–123.6 months). The current indications for surgery, based on the available data from the literature, include localised disease that can be completely resected [5].
R-CHOP chemotherapy regimen is the standard treatment for patients with DLBCL. There are reported cases of complete response to R-CHOP alone in patients with PHL-DLBCL [14, 15]. Whether systemic chemotherapy alone will give results comparable to surgery in resectable cases is currently unclear [16].

In conclusion, PHL is a rare disease and can be misdiagnosed as another more frequent primary liver tumor due to its non-specific clinical presentation, laboratory and imaging findings, and therefore should be considered in the differential diagnosis of a hepatic lesion. Pathohistological analysis is essential for definite diagnosis, determining PHL subtype and the extent of involvement of surrounding tissue. There is no consensus on the optimal treatment for PHL and the prognosis is variable. All complications during treatment should be diagnosed on time and properly managed. Further prospective studies are mandatory for providing treatment guidelines.

Conflict of interest: None declared.

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