

PRIMARY LIVER LYMPHOMA

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Lymphomatous involvement of liver is common in lymphoma, but primary non Hodgkin's liver lymphoma is a rare entity. We present a case report of a middle aged male who was diagnosed with primary liver lymphoma after a long and exhaustive work up. Symptoms initially improved with chemotherapy but presented fifteen months later with central nervous system and vertebral dissemination. Primary liver lymphoma, even though rare should be kept in differentials of multiple space occupying lesions of liver with no evidence of vascular invasion, especially if there is no associated lymphadenopathy or spleen involvement.

Key-words: Liver neoplasms, diagnosis – Lymphoma, diagnosis.

Case report

A 45 year-old-male presented with history of off and on fever for the past 2 weeks, malaise and progressive abdominal distension for the past six months. His previous medical history was otherwise normal.

On examination, patient was alert and oriented; there was no evidence of pallor or yellowish discoloration of eyes. Per abdomen examination revealed hepatomegaly with firm nodules palpable on it. Overlying skin was normal with no evidence of local rise of temperature. There was no palpable superficial lymphadenopathy or splenomegaly. Haematological and blood chemistry tests (RFT, ESR) were within normal limits. Surprisingly, liver enzymes were also within normal limit. Serology was negative for HIV and hepatitis B and C viruses.

He was referred to radiology section for Computed Tomography (CT) whole abdomen. CT showed multiple well defined, hypodense nodular masses distributed in both lobes of liver. After administration of contrast, masses showed homogenous, mild enhancement (Fig. 1). There was evidence of displacement of vessels by masses in both lobes, which were distributed in subcapsular location. No evidence of dilated biliary channels, vascular invasion or thrombosis was seen. Also, splenomegaly and retroperitoneal lymphadenopathy was notably absent. A list of space occupying lesions of liver including metastasis, haemangioma, and lymphoma was considered in the differential diagnosis.

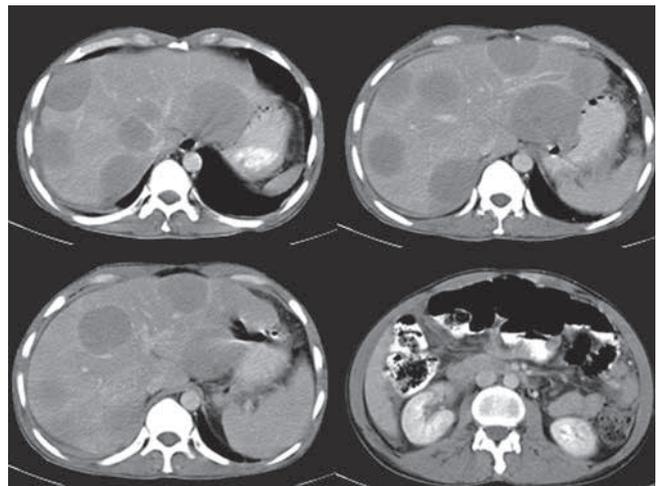


Fig. 1. – Axial CECT of the abdomen in portal venous phase shows multiple well defined hypodense mildly enhancing nodules distributed in both lobes of liver displacing vessels with no evidence of vascular invasion or thrombosis and biliary dilatation. No splenomegaly nor lymphadenopathy is noted.

Alpha-feto protein (AFP) and carcinoembryonic antigen (CEA) were also not elevated. Patient was advised biopsy to determine the nature of the lesions. FNA biopsy showed, monomorphic population of atypical lymphoid cells having hyperchromatic nuclei with fine opened up chromatin and scant cytoplasm (Fig. 2). Histopathology confirmed it to be large B-cell lymphoma. Further workup with CECT neck and chest did not revealed presence of mediastinal or cervical lymphadenopathy at any other site. Whole body fluorodeoxyglucose positron emission tomography (FDG-PET) and Ga-scintigraphy were performed which did not show any other lesion. To confirm the

myeloproliferative disorder, bone marrow biopsy was also performed which did not showed any abnormality.

Final diagnosis of primary liver Non Hodgkin's lymphoma was made and the patient underwent treatment which included cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) regimen. Patient showed improvement of symptoms at 12 months follow up period, but presented again after 15 months of initial diagnosis with complains of paraplegia of acute onset. There was sensory loss up to T4 level, 0/5 weakness in B/L lower limbs, plantar were B/L flexors. He was immediately taken for MRI dorsal spine. MRI showed multiple altered signal intensity lesions within the substance of cord at lower cervical and upper dorsal levels and vertebral bodies suggestive of secondary spread. He was given high dose methotrexate, but during the hospital stay patient developed respiratory complications and unfortunately could not be revived.

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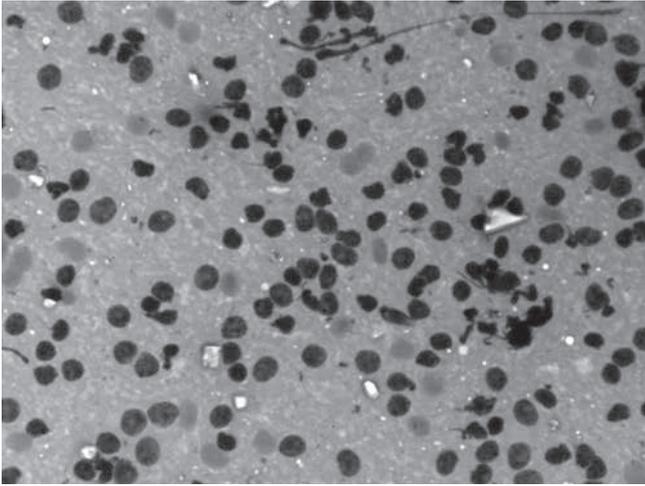


Fig. 2. — Fine needle aspirate smear, showing monomorphic population of atypical lymphoid cells having hyperchromatic nuclei with fine opened up chromatin & scant cytoplasm consistent with diffuse large B-cell lymphoma (H&E, 40x).

Discussion

Liver involvement by secondary Non Hodgkin's lymphoma is relatively common. Primary liver lymphoma (PLL) is extremely rare. Among all extra nodal lymphomas, PLL constitutes < 1% of all cases (1,2).

Lei KI proposed the following criteria for the diagnosis of PLL: at the time of diagnosis, symptoms are mainly attributable to liver involvement, absence of clinically palpable lymphadenopathy and no radiological evidence of distant lymphadenopathy, and peripheral blood smear shows no evidence of leukemic cells (2).

Due to its rare occurrence, aetiology is poorly understood. However, association between PLL and hepatitis C has been reported (3, 4, 5). Higher incidence is seen in immunocompromised patients (6). HBV and chronic hepatitis have also been implicated (7) but some disagree (8). PLL typically occurs in middle aged males as seen in our case. There is 2:1 male predominance reported (2, 9). Presentation is usually with complains of abdominal pain, distension, fever and weight loss (8).

On Ultrasonography (USG), PLL typically appears as multiple hypoechoic masses in both lobes of liver. CT features are multiple, well defined hypodense lesions with no evidence of vascular or biliary channels invasion. On administration of contrast, mild homogenous or peripheral contrast enhancement is seen. However, a significant number may not show any enhancement and can be detect-

ed even on non-contrast scans (9). On MRI, they are moderately low in signal intensity on T1W sequence and mild to moderately hyperintense on T2W sequence and shows rim or no enhancement or contrast agent accumulation in the hepatobiliary phase (9-11). They are of high signal intensity on diffusion-weighted imaging (DWI). However, these lesions demonstrate a very low apparent diffusion coefficient (11).

These lesions cannot be differentiated from lesions of lymphoma with secondary liver involvement. However, lymphadenopathy and lesions in other organs/site helps to differentiate them. Liver is second only to regional lymph nodes as a site for metastatic disease. Metastasis also presents with multiple lesions in both lobes of liver, but enhancement pattern helps to differentiate them from lymphomatous deposits. The metastatic deposits may show hyperenhancement which is unlikely in lymphomatous lesions. Rim enhancement may present a diagnostic difficulty. Lymphomatous deposits displace vessels whereas metastatic lesions invade them. Haemangioma is the most common benign lesion of liver, atypical hemangioma are hypoechoic on USG, but have a characteristic 'centripetal fill in' on the delayed post contrast scans which helps to confirm the diagnosis.

On histology, the most common subtype of PLL is diffuse large B-cell lymphoma, as was seen in our case (2, 4). A few cases of small lymphocytic, T cell, anaplastic, folli-



Fig. 3. — Sagittal MR T2W images show multiple hyperintense lesions in the cord at lower cervical and upper dorsal levels and vertebral bodies suggesting secondary spread.

cular (4, 8, 12) and other had been described.

PLL has been considered an aggressive disease with poor prognosis (8). Emile J.F. et al. suggested that prognosis depends on whether the disease is nodular or there is diffuse liver infiltration (13). They concluded that diffuse liver infiltration has a poor prognosis while lymphoma with nodular infiltration has a good prognosis with anthracycline based chemotherapy.

Treatment modalities include surgical resection, chemotherapy and radiotherapy alone or in combination. Page RD et al. noted favourable results with combination chemotherapy (5). CHOP regime is the standard treatment for patients with diffuse large B cell lymphoma. Rituximab (monoclonal antibody targeting CD 20) augments survival when used with CHOP regime in elderly patients with diffuse large B-cell lymphoma without significant increase in toxicity (14). Our patient also responded

well to CHOP regime with significant resolution of symptoms until he presented with again with acute onset paraplegia. He was given methotrexate for relapse but patient expired due to aspiration.

Teaching point

There are no specific radiological features which can confirm the diagnosis but diffusion weighted MRI and contrast pattern may suggest the diagnosis. PLL should be considered in the differential diagnosis of multiple well defined space occupying nodular lesions in liver with no evidence of vascular invasion or associated lymphadenopathy. Final confirmation comes from histopathological examination.

References

1. Freeman C., Berg J.W., Cutler S.J.: Occurrence and prognosis of extra-nodal lymphomas. *Cancer*, 1972, 29: 252-260.
2. Lei K.I.: Primary non-Hodgkin's lymphoma of the liver. *Leuk Lymphoma*, 1998, 29: 293-299.
3. Bronowicki J.P., Bineau C., Feugier P., et al.: Primary lymphoma of the liver: clinical-pathological features and relationship with HCV infection in French patients. *Hepatology*, 2003, 37: 781-787.
4. Page R.D., Romangura J.E., Osborne B., et al.: Primary hepatic lymphoma. Favourable outcome after combination chemotherapy. *Cancer*, 2001, 92: 2023-2029.
5. Agmon-Levin N., Berger I., Shtalrid M., et al.: Primary hepatic lymphoma: a case report and review of the literature. *Age Ageing*, 2004, 33: 637-640.
6. Avlonitis V.S., Linos D.: Primary hepatic lymphoma: a review. *Eur J Surg*, 1999, 165: 725-729.
7. Ohsawa M., Aozasa K., Horiuchi K., et al.: Malignant lymphoma of the liver. Report of five cases and review of the literature. *Dig Dis Sci*, 1992, 37: 1105-9.
8. Lei K.I.K., Chow J.H.S., Johnson P.J.: Aggressive primary hepatic lymphoma in Chinese patients. Presentation, pathologic features and outcome. *Cancer*, 1995, 76: 1336-1343.
9. Maher M.M., McDermott S.R., Fenlon H.M., et al.: Imaging of primary non-Hodgkin's lymphoma of the liver. *Clin Radiol*, 2001, 56: 295-301.
10. Steller E.J., van Leeuwen M.S., van Hillegersberg R., et al.: Primary lymphoma of the liver – A complex diagnosis. *World J Radiol*, 2012, 28, 4: 53-57.
11. Kaneko K., Nishie A., Arima F., et al.: A case of diffuse type of primary hepatic lymphoma mimicking diffuse hepatocellular carcinoma. *Ann Nucl Med*, 2011, 25: 303-307.
12. Gomyo H., Kagami Y., Kato H., et al.: Primary hepatic follicular lymphoma: a case report and discussion of chemotherapy and favorable outcomes. *J Clin Exp Hematop*, 2007, 47: 73-77.
13. Emile J.F., Azoulay D., Gornet J.M., et al.: Primary non-Hodgkins' lymphomas of the liver with nodular and diffuse patterns have different prognosis. *Ann Oncol*, 2001, 12: 1005-1010.
14. Coiffier B., Lepage E., Briere J., et al.: Chop chemotherapy plus rituximab compared with chop alone in elderly patients with diffuse large-B-cell lymphoma. *N Engl J Med*, 2002, 346: 235-242.