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Primary Hepatic Leiomyosarcoma Report of a rare case with review of literature

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ABSTRACT

Primary hepatic leiomyosarcoma is an extremely rare tumor with a dismal prognosis and difficulty in diagnosis. We present a 36-year-old female who presented with complaints of pain in right hypochondrium and epigastric region. Real-time ultrasonography revealed an enlarged liver with multiple hypoechoic lesions of varying sizes in both the lobes of the liver. USG guided core biopsy from the lesion showed an infiltrating malignant spindle cell neoplasm positive for smooth muscle actin and caldesmon-H confirming the diagnosis of leiomyosarcoma. It is vital to diagnose these lesions even on limited biopsies as early diagnosis can reduce hospital and operative morbidity and mortality rates in the patients.

Keywords: Primary hepatic Leiomyosarcoma, small biopsy, immunohistochemistry.

Primary hepatic leiomyosarcoma (PHL) is an exceedingly rare tumor with less than 50 cases reported in the English literature and only 4 cases were reported in premenopausal women [1, 2]. The etiologies of this disease are still not well-known, unlike hepatocellular carcinoma (HCC) which is the most common histology of primary hepatic malignancy and closely associated with infection of viral hepatitis, alcoholism, and liver cirrhosis. The clinical presentations of PHL are usually non-specific such as abdominal pain and weight loss [2]. Early diagnosis is difficult owing to its rarity and nonspecific clinical presentation and conventional imaging. Metastatic hepatic leiomyosarcomas from the gastrointestinal tract, uterus, and retroperitoneum are more common than a PHL [3]. Primary Hepatic Sarcoma has a wide diversity of histological types. Leiomyosarcoma and angiosarcoma are the most common histological types [4].

Undifferentiated sarcoma most often occurs in childhood but is also common in adults. The histological nomenclature for undifferentiated sarcoma was not uniform before 1978. The names were mesenchymoma, primary sarcoma of liver, fibromyxosarcoma, and malignant mesenchymoma. The clinical outcomes and treatment are quite different in each type of histology. The aggressive surgical approach seems to be the only effective treatment to achieve possible long-term survival for Primary Hepatic Sarcomas [5]. In time diagnosis of the lesion is essential for proper management of this rare malignancy.

CASE REPORT

A 36-year-old female was referred to our hospital with chief complaints of intermittent pain in right side of the abdomen of 2 months duration. She had no history of drug or alcohol abuse. She had no history of liver diseases or

other chronic diseases. She had completed her family, underwent tubectomy 10 years back. Her past medical history, family history, and menstrual history were unremarkable. Physical examination revealed mild pallor, no icterus and no palpable mass per abdomen. No hepatosplenomegaly was noted.

Laboratory investigations showed normal blood counts, coagulation parameters, and liver function tests, with negative results for hepatitis B surface antigen, hepatitis C virus, and Human immunodeficiency virus. Upper gastrointestinal endoscopy and colonoscopy showed normal study (**Fig. 1A, 1B**). Real-time ultrasonography examination in various planes revealed an enlarged liver with multiple hypoechoic lesions of varying sizes in both lobes of the liver with the largest lesion measuring 5.1 x 5.1 cm in the left lobe. Left kidney showed a cortical cyst in upper pole measuring 3.7 x 3.0 cm. Mild ascites was noted. Rest organs were normal in size and echotexture (**Fig. 2**).

Ultrasonography-guided biopsy from the liver lesion was performed. Light microscopy of the small biopsy revealed multiple cores of liver parenchyma harboring an infiltrating spindle cell neoplasm arranged in fascicles and bundles. The individual cell had elongated hyperchromatic nucleus with blunt edges, inconspicuous nucleoli and eosinophilic cytoplasm with perinuclear halo (**Fig. 3**). Atypical mitotic figures were discerned. On immunohistochemistry tumor cells were positive for smooth muscle actin (SMA) and Caldesmon-h, negative for desmin, CD117, DOG1 and CD34 (**Fig. 4, 5**). The final diagnosis of primary leiomyosarcoma of the liver was made. The patient is planned for a surgery.

DISCUSSION

Primary mesenchymal tumors of the liver account for 1-2% of all primary malignant tumors of the liver with angiosarcoma and leiomyosarcoma being the most common among all of them [1, 2]. Primary hepatic leiomyosarcoma (PHL) is an exceedingly rare tumor. The reported cases in literature were summarized in a table by shivathirthan et al [6] which is later on updated (Table 1). Excluding a metastatic tumor is essential for diagnosing a primary lesion. In the present case, metastatic spindle cell lesions were excluded on imaging as well as on IHC.

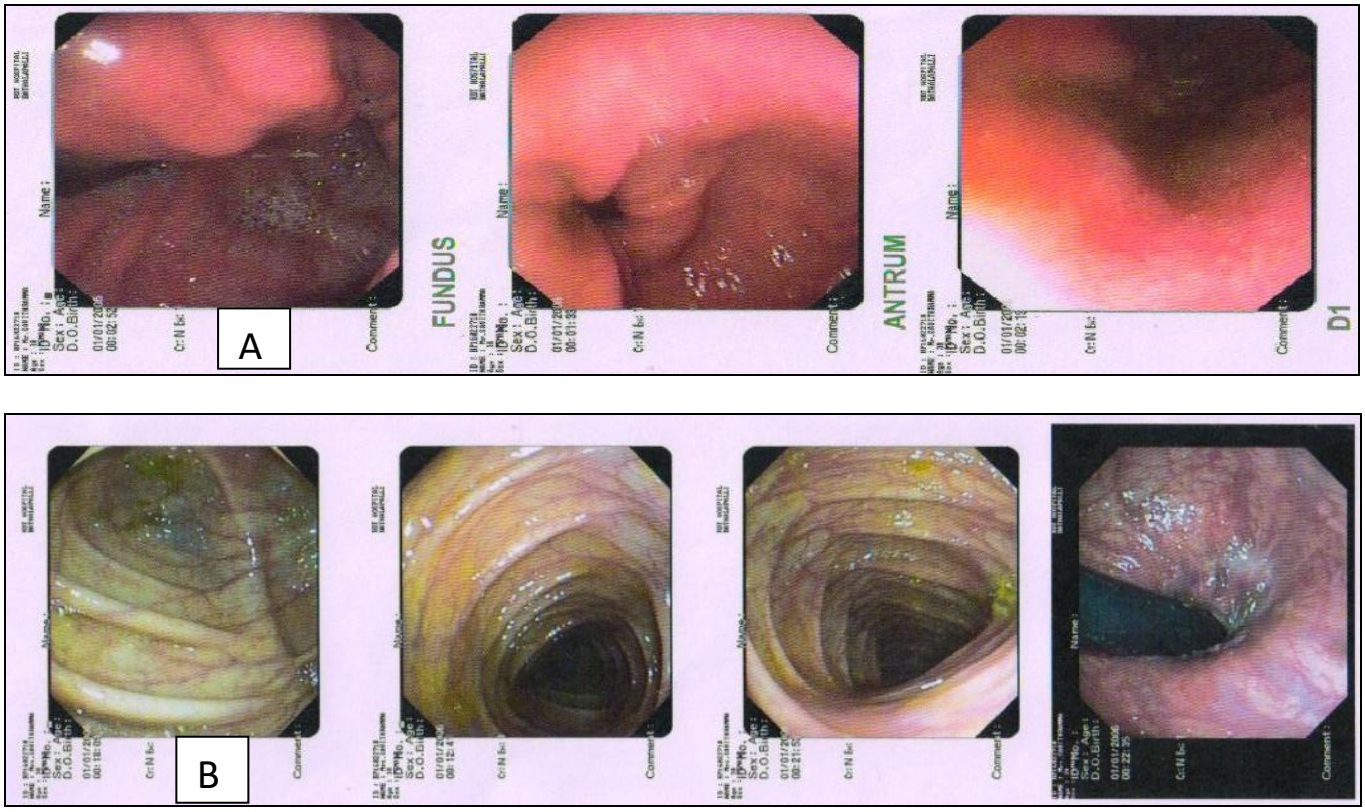

Figure no. 1: A) UGI endoscopy: Normal study, B) Colonoscopy: Normal study

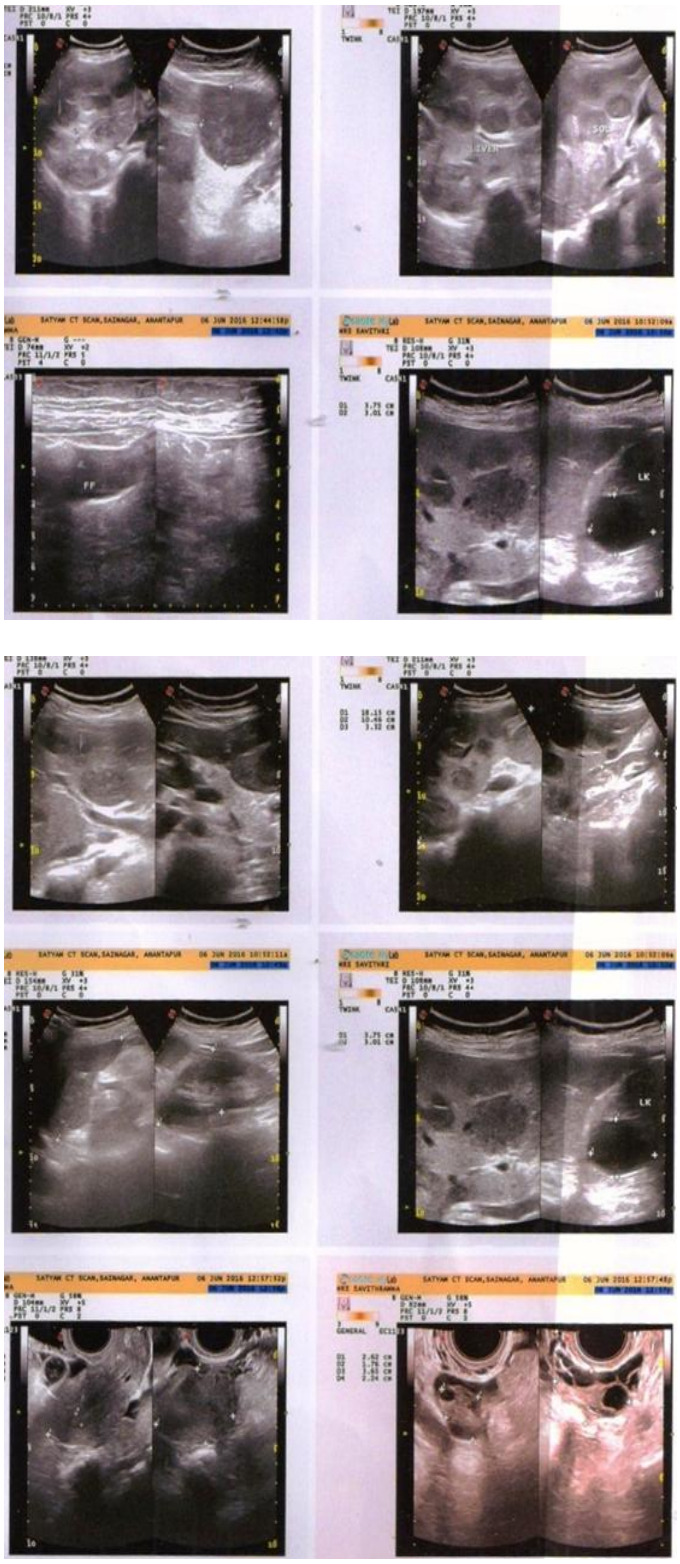

Figure no. 2: Real-time ultrasonography: Hepatomegaly with multiple hypoechoic lesions of varying sizes in both lobes of liver and largest measuring 5.1x5.1cms.Left renal cortical cyst is noted in upper pole measuring 3.7x3.0cms

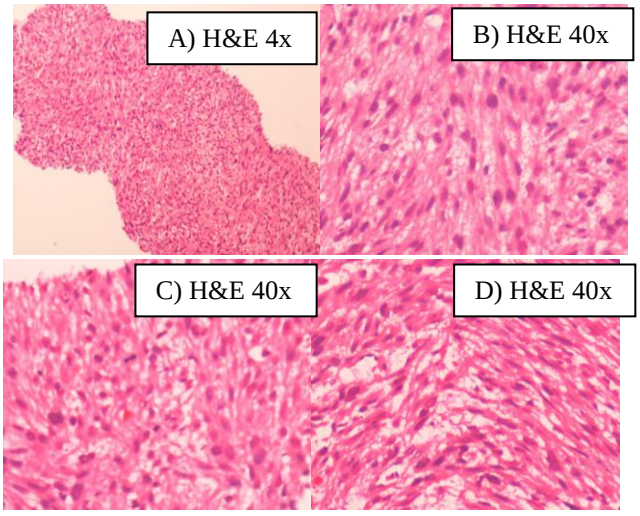

Figure 3 - A) H&E, 4x: Needle core biopsy show an infiltrating tumor arranged in bundles and fascicles. B) H&E, 40x: Section shows spindle shaped cells with elongated nucleus with blunt end exhibiting nuclear pleomorphism. C) H&E, 40x: Section shows neoplastic cells with atypical mitotic figures. D) H&E, 40x: Section shows neoplastic cell bundles with paranuclear vacuolation

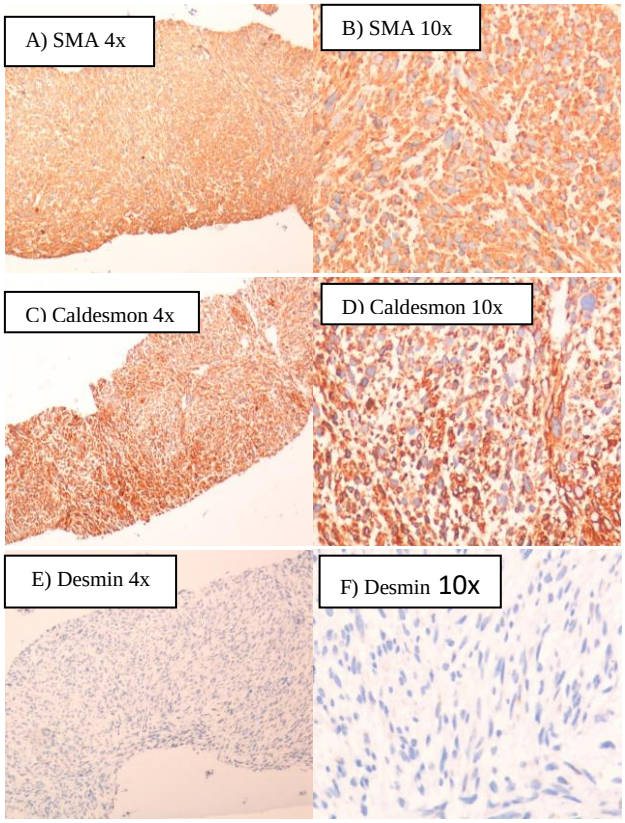

Figure 4 - A & B) SMA 4x & 10x: positive, C & D) Caldesmon H, 4x & 10x: positive, E & F) desmin, 4x & 10x: negative

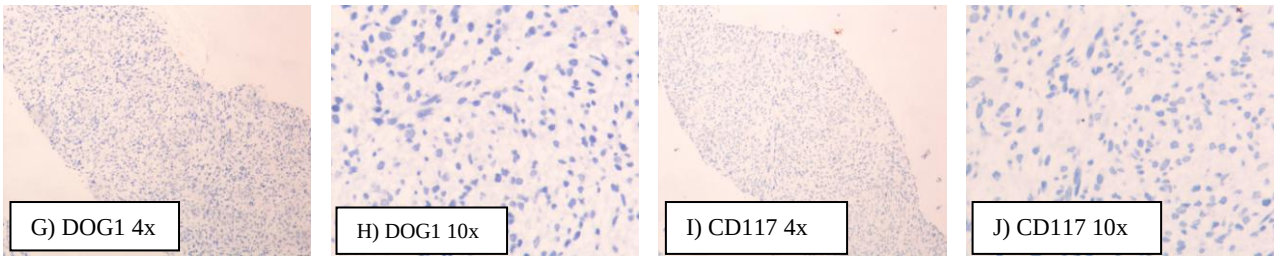

Figure 5 - G & H) DOG1, 4x & 10x: negative, I & J) CD117, 4x & 10x: negative

Table 1-Previously published cases on hepatic leiomyosarcoma

Author/year	Age	Treatment/risk factor	Follow-up
Wilson (1971)	49 F	Wedge resection	Died at 18 months
Fong (1974)	62M		Died at 20 months
Masur (1975)	62F	Chemotherapy	Autopsy diagnosis
Masur (1975)	66F	Lobectomy	Died at 49 months
Yoshikawa (1977)	58F	Wedge resection	Died at 11days post-op
Bloustein (1978)	12F	Trisegmentectomy, chemotherapy	NED at 6yrs
O'Leary (1982)	69M		Alive at 24 months
Chen (1983)	78M	Chemotherapy, radiation	Died at 10 months
Maki (1987)	86F	Surgery	NED at 5 months
Paraskevopoulos (1991)	62M	Lobectomy	NED at 5 months
Baur (1993)	69F	Surgery	Recurrence after 10years
Holloway (1996)	63M	Conservative	
Soyer (1996)	67F	Surgery	
Sato (2000)	62F		Autopsy diagnosis
Tsuji (2000)	68M	Hepatitis C	Autopsy diagnosis
Lordanidis (2002)	25M	Surgery	Died at 3 months
Fujita (2002)	33F	Prior renal transplant right posterior segmentectomy	NED at 24 months
Lee (2002)	64F	Right lobectomy and wedge resection of left lobe	NED at 24 months
Almogy (2004)	58F	Surgery and chemotherapy	Died at 4months
	63 F	Surgery and chemotherapy	Died at 12 months
Watanabe (2008)	63		Autopsy diagnosis
	49F		Autopsy diagnosis
Matthei (2009)	19F	Liver transplant	Died at 73 months
	64 F	Surgery	NED 181 months
	53 F	Surgery	Died 21 months
	55 M	Surgery	NED 133 months
	51 M	Liver transplant	NED 144 months
	59 M	Surgery	Died 45 months
	63 F	Surgery	NED 133 months
Giuliante (2009)	26 M	Righ lobectomy and wedge resection of segment	Died at 25 months
Liang (2009)	44 F	Liver transplant	Died 34 months
Shamseddine (2010)	25 F	Right lobectomy	Died 22 months
	39 M	Extended right lobectomy	Died 19 d
	30 M	Right lobectomy + chemotherapy	NED at 12 mo
Shivathirthan (2011)	67M	Extended left hepatectomy	NED at 9 months
Lin (2015)	39M	Right partial segmentectomy	Died at 33.7 months

Leiomyosarcomas in liver arise either from intrahepatic vascular structures, bile duct or ligament teres which differ in clinical presentation and prognosis [7]. PHL is reported in close association with acquired immunodeficiency syndrome (AIDS) [8], Epstein-Barr virus (EBV) [9], post-transplantation due to immunosuppression [10], and thorotrast exposure [11]. No association was seen in our patient.

The median age of presentation is 54 yrs with no sex predilection and most common presentation is a pain in right hypochondrium and hepatomegaly as seen in our patient [4, 11]. Other symptoms include loss of weight, vomiting, anorexia and jaundice. Liver function tests may be a variable and carcinoembryonic antigen, alpha-fetoprotein and other serological tests are usually normal. PHL being a hypovascular tumor does not enhance on imaging studies. Generally, a homogeneous hypoechoic or mixed-echoic patterns were seen in the tumors as was seen in our patient. A cystic variant of leiomyosarcoma may be misdiagnosed as hydatid cyst or liver abscess on imaging studies. Magnetic resonance imaging is more sensitive; however, it was not performed in our patient [12-13].

Our patient showed histological features of an infiltrating spindle cell tumor composed of intersecting bundles of spindle-shaped cells containing a hyperchromatic elongated nucleus with blunt ends and eosinophilic cytoplasm and paranuclear vacuoles and atypical mitotic figures. Smith et al [14] reported similar features. Immunohistochemistry is reported to be positive for desmin, vimentin, and SMA but negative for keratin, S-100 protein and neuron-specific enolase. The biopsy in our patient was positive for SMA and caldesmon-h and negative for all other metastatic differential diagnostic possibilities. Surgical resection followed by adjuvant chemotherapy is recommended in an empirical manner [2].

The mean survival of untreated intrahepatic leiomyosarcoma is about 10 months. With a combination of surgery and chemotherapy, the mean survival is 3.3 years. Liver transplant has been attempted sporadically in primary hepatic leiomyosarcoma but is not as well defined as in the setting of primary hepatic epithelioid hemangioendothelioma [14]. The outcome for liver transplant in primary hepatic leiomyosarcoma has been varied with all cases developing the recurrent or metastatic disease and only one case showing long-term survival after undergoing resection for local chest wall recurrence [15].

CONCLUSION

Primary leiomyosarcoma is a rare tumor with often delayed diagnosis and poor prognosis. Diagnosis of primary leiomyosarcoma of the liver is challenging owing to its nonspecific presenting symptoms, lack of serological markers and non-specific conventional imaging studies. This case highlights the diagnostic value of this rare tumor on small biopsy using IHC.

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