Mesenchymal Hamartoma of the Liver and Spleen-A Rare Pseudotumour in Adults

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1. Abstract

Hepatic mesenchymal hamartoma is the third most common liver neoplasm of the pediatric age group, rarely diagnosed in adults, with under 50 cases having been reported so far. Mesenchymal hamartoma of the spleen is a very rare vascular lesion, documented in less than 200 cases since 1861 when it was first described by Karl von Rokitansky.

1.1. Aim: The aim of this paper is to discuss the differential diagnosis of these tumour-like lesions and the association between them, especially considering their rarity.

1.2. Methods: We present a case of multifocal mesenchymal hamartoma of the liver and spleen in a 51-year-old female patient. The hepatic tumour appears as a macro nodular lesion involving the interface between segments V and VIII [30x28mm], showing central scarring upon MRI imaging and suggesting the diagnosis of focal nodular hyperplasia. Moreover, a sub capsular splenic cystic mass was also revealed, involving the sub diaphragmatic surface of the organ [15x10mm].

1.3. Results: The histological examination of the hepatic tumour revealed a myxoid stromal proliferation, composed of stellate and fibroblastoid cells, bile ducts with inconspicuous lumina, small vascular structures and chronic non-specific inflammatory infiltrate. On microscopic examination, the splenic lesion exhibited nodular collagenous fibrosis, radial septa and large hyalinized areas.

1.4. Conclusion: A key aspect in the effective treatment of patients diagnosed with mesenchymal hamartomas is surgery with negative margins. The peculiarity of this case consisted of the incidental finding of multiple liver tumours, the incidental finding of the splenic mass, and the rarity of this particular association in adults.

2. Introduction

Hepatic mesenchymal hamartoma [HMH] is considered a ductal plate malformation arising from isolated mesodermal rests in the normal portal triad architectural elements [1]. These rare benign lesions usually occur in the pediatric age group patients and 80% of them are diagnosed within the first 2 years of age [2,3]. HMH represents 8% of all tumours of the liver and frequently presents as an enlarging mass in the liver of young children [4,5]. However, only less than 200 cases have been reported in the literature so far [1-6]. This benign tumour is a very uncommon neoplasm of the adult with only 5% of the cases reported in patients older than 5 years of age [7]. A tendency of arising in the right hepatic lobe has also been described for this lesion [75% of cases] [7, 8, 9]. Although the first case of HMH was reported by Marsh in 1903, the term was established by Edmonds later in 1956 [5]. Splenic
hamartoma also called splenoma] is a very rare vascular lesion which can be discovered incidentally in adults, as it usually remains asymptomatic [6]. Fewer than 200 cases of such splenic tumours have been identified since 1861, when the first case was described by Karl von Rokitansky [6]. The aim of this paper is to discuss the differential diagnosis of these tumour-like lesions and the association between them, especially considering their rarity.

3. Materials and Methods
A 51-year-old female, with a history of three colonic tubulovillous adenomas with low-grade dysplasia which had been surgically removed the previous year, was referred to Fundeni Clinical Institute after a CT scan revealed the presence of four hepatic nodules and of a splenic cystic lesion. Upon clinical examination, the patient was found afebrile and anicteric. Initial blood tests showed normal bilirubin, AST and ALT levels. Tumoral and viral markers were also in the normal range. Later on, Magnetic Resonance Imaging in hepatic incidence was performed and the results came back as follows: four right hepatic lobe lesions-one nodular lesion in glandular segment V [26x14mm] [Figure 1] and two nodules occupying the peripheral and paracaval regions of segment VII [Figure 3] measuring 15x13mm and 9x12mm respectively. These radiological findings were presumed to be hemangiomas. A large multinodular tumour-like lesion [30x28mm] involving the hepatic segments VIII and V was also identified [Figure 2]. The radiological aspect of the fourth liver mass [central scarring] suggested focal nodular hyperplasia. Subsequent laparotomy revealed a subcapsular splenic mass [15x10mm], involving the diaphragmatic surface of the organ [Figure 4]. Eventually, fragments of the hepatic nodules were submitted to our laboratory as the intraoperative frozen sections and the histological examination of the specimens showed a benign mesenchymal proliferation. The splenic tumour was surgically removed. In order to clarify the diagnosis, the surgical resection specimens were examined in our pathology department.

Figure 1: MRI scan notable for hepatomegaly and a nodular mass involving segment V of the liver.
Figure 2: Hepatic nodule involving segment V of the liver.

Figure 3: Hepatic nodule involving segment VII of the liver.
4. Results
Grossly, the largest hepatic tumour-like lesion enclosed a round, well-circumscribed, encapsulated solid mass, measuring 3 cm in diameter. On the cut surface, we identified white-brown colored multiple cystic cavities. Specimen samples were fixed with 10% buffered formalin for 24 hours, processed by conventional histopathological methods and examined by two different pathologists in our department. Light microscopic examination revealed a benign proliferation composed of mesenchymal components, comprising cells with irregular morphology, such as stellate and fibroblastoid, disorganized bile ducts with inconspicuous lumina and small vascular channels, in a fibro-myxoid stroma. The presence of nonspecific chronic inflammation was noted, as variable amounts of lymphocytes and plasma cells focally infiltrated the tumoral mass [Figure 5,6 and 7]. The gross examination of the splenic tumour also spotted a nodular, encapsulated, white-brown mass with small cystic cavities on cut surface. Histopathological examination revealed nodular collagenous fibrosis with radial septa and large areas of hyalinization [Figure 8]. An immune histochemical panel was also performed, using the standard procedure. The tissue section was deparafinnized and then rehydrated before applying the primary antibody. Enzyme-conjugated secondary antibodies were then applied so that specific staining can be visualized after adding the enzyme-specific substrate.

Cytokeratin 19 [Figure 10], Cytokeratin 8/18 and Epithelial Membrane Antigen [EMA] were negative, whereas the stromal cells stained weakly positive for alpha-fetoprotein [Figure 9] and negative for CD 34 [Figure 11]. A proliferation index [Ki67] of 2% was noted [Figure 12], thus confirming the benign nature of the tumour and also the diagnosis of mesenchymal hepatic hamartoma. The final pathology report established the diagnosis of multifocal mesenchymal hamartoma of liver and spleen. The postoperative evolution was favorable and the patient was released three days later. The patient is recurrence-free four years after diagnosis.
Figure 5: Hepatic Mesenchymal Hamartoma, HE, 4X (mesenchymal myxoid stroma with bile ducts, small vascular structures and a chronic inflammatory reaction)

Figure 6: Hepatic Mesenchymal Hamartoma, HE, 10X
Figure 7: Hepatic Mesenchymal Hamartoma, HE, 10x (bile ducts and small vessels set in a mesenchymal stroma)

Figure 8: Splenic Hamartoma, HE, 20x (collagenous fibrosis and large areas of hyalinization with radial septa)

Figure 9: Weak positive AFP stromal staining, 20X
Figure 10: Negative CK19 staining, 10X.

Figure 11: Diffuse vascular endothelial CD34 staining, 20X.

Figure 12: Ki67 nuclear positivity (2%), 40X.
5. Discussion

To our knowledge, the case described was the first one of an adult developing multifocal hepatic mesenchymal hamartoma and mesenchymal hamartoma of the spleen. These tumour-like lesions pose a diagnostic challenge for pathologists, especially because they are exceptionally rare neoplastic lesions in adult patients [7]. The differential diagnosis of the hepatic mesenchymal hamartoma implies other benign hepatic neoplasms such as focal nodular hyperplasia, bile duct adenoma and hemangiomia, as well as malignant tumours [8,9]. Furthermore, differential diagnosis of mesenchymal hamartoma of the spleen implies both benign and malignant vascular lesions such as hemangiomia, hemangoendothelioma and angiosarcoma [6]. Nodular hepatic hyperplasia is the second most common liver tumour, occurring frequently in reproductive age women [10]. On microscopic examination, it displays all the features of the normal hepatic parenchyma, albeit with an anomalous organization [11]. Hepatic cystadenoma should be taken into consideration, as it microscopically presents as a three-layered, often mucin-producing cystic proliferation [11,12]. Malignant tumours of the liver are important entities that should be considered in the differential diagnosis of hepatic mesenchymal hamartoma, as this lesion often involves a possible association with undifferentiated hepatic embryonal sarcoma, which has been demonstrated throughout various studies [12]. Malignant transformation of HMH has been well documented in patients who have undergone surgical resection, even multiple years after the procedure [12]. Undifferentiated embryonal sarcoma is a malignant lesion with an overall low incidence [12,13]. There are several histological findings which are highly suggestive for this diagnosis, such as stellate cells with inconspicuous nucleoli, multinucleated giant cells, and hyaline globules [13]. Although the differential diagnosis can usually be made on the hematoxylin and eosin stain, the proliferative index Ki 67 can be very useful [13]. In our patient’s case, the lack of significant histological atypia and a Ki 67 expression of 2% helped rule out the diagnosis. Hemangiomia, as well as its malignant counterpart, should also be taken into consideration when dealing with this type of hepatic tumour [14]. However, hemangiomia can be quite easily distinguished from HMH by way of its prominent vascular structures, most of the time consisting of “back to back” capillaries lined by benign endothelial cells [14,15]. Other malignant neoplasms of the liver which may bear a resemblance to hepatic mesenchymal hamartoma are hepatoblastoma and angiosarcoma [15]. Elevated alpha-fetoprotein levels mandate a differential diagnosis with hepatoblastoma, using radiological investigations and histopathological examination, as this malignancy also occurs in young patients [15,16]. On microscopic examination, the tumour exhibits both epithelial and mesenchymal components in variable proportion, with immature liver cells resembling fetal or embryonal hepatocytes [16]. Hepatoblastoma may be associated with various genetic disorders [familial colonic polyposis, Li Fraumeni and Beckwith-Wiedemann syndromes] as well as with low birth weight [16]. The histopathological findings and the genetic susceptibility of this rare hepatic lesion help rule out the diagnosis of hepatoblastoma [16-17]. Angiosarcoma is usually composed of infiltrative anastomosing blood filled channels lined by pleomorphic cells with eosinophilic cytoplasm [17]. In our patient’s case, both the HE stain and the immune histochemical examination ruled out the diagnosis.

The incidental finding of the cystic tumour-like lesion of the spleen in the same adult patient is highly uncommon [6,18,19]. In the face of such a rare histopathological finding, several vascular lesions were considered. First of all, hemangiomia is the most common benign splenic tumour which is microscopically composed of vascular channels lined by endothelial cells that show no histological atypia [18]. Its malignant counterpart displays abnormal multilayered vascular spaces with variable degrees of cytological atypia, brisk mitotic activity and necrotic foci [19]. Clinically, the presence of such a splenic mass is usually accompanied by abdominal pain, but in our patient’s case it was an incidental finding.

A key aspect in the effective treatment of patients diagnosed with mesenchymal hamartoma is surgical excision with negative resection margins, in order to avoid a later recurrence and malignant transformation [2-6]. Currently, the gold standard for the treatment of mesenchymal hamartomas is complete surgical resection, but liver transplantation has also been reported in a 17-month-old female patient [3].

6. Conclusion

The peculiarity of this case consisted of the incidental finding of multiple liver tumours, the incidental finding of the splenic mass and the rarity of this particular association in adults. This unusual association between hepatic and splenic mesenchymal hamartomas needs further studies in order to assess a syndromic involvement. This particularly rare hepatic pseudotumour requires a good interdisciplinary collaboration between radiologists, surgeons and pathologists especially in oncologic patients, prone to liver metastasis.

References

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