Primary hepatic vascular tumours. A clinicopathologic study of 10 cases

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Abstract

Background : **Primary hepatic vascular neoplasms constitute a heterogeneous group of neoplasms with characteristic histology and variable tumour biology.**

Aim : **To provide an updated overview on clinicopathological features, treatment and outcome of primary hepatic vascular tumours.**

Patients and methods : **In our retrospective study, we reviewed 10 cases of primary hepatic vascular tumours that were diagnosed at the pathology department of Mongi Slim hospital over a thirteen-year period (2000-2012). Relevant clinical information and microscopic slides were available in all cases and were retrospectively reviewed.**

Results : **Our study group included 4 men and 6 women (sex ratio M/F = 0,66) aged between 23 and 78 years (mean = 55,5 years). Based on imaging studies, preoperative diagnosis of hemangioma was accurately made in only three cases. Three cases were misdiagnosed preoperatively as having hydatid cyst and four cases of hemangiomas were misdiagnosed preoperatively as liver metastases. All our patients underwent surgical resection of the tumour. Histopathological examination of the surgical specimen established the diagnosis of angiosarcoma in one case, cavernous hemangioma in 8 cases and sclerosing hemangioma in one case.**

Conclusion : **Hepatic tumours are increasingly detected incidentally due to widespread use of modern abdominal imaging techniques. Therefore, reliable noninvasive characterization and differentiation of such liver tumours is of major importance for clinical practice. Definitive diagnosis is based on histopathologic examination.** (Acta gastroenterol. belg., **2014**, 77, **347-352**).

Key words : liver, tumour, vascular, hemangioma, angiosarcoma.

Introduction

Primary mesenchymal tumours of the liver are by far less common than epithelial neoplasms. They are dominated by vascular tumours. Primary hepatic vascular neoplasms constitute a heterogeneous group of neoplasms with characteristic histology and variable tumour biology. Cavernous hemangioma is the most common benign hepatic neoplasm with a reported incidence of up to 20% (1). While primary hepatic angiosarcoma accounts for only 2% of primary hepatic tumours, it is the most common malignant mesenchymal tumour of the liver (2,3). In this paper, we report our experience with primary hepatic vascular tumours over the past 13 years. Our aim was to analyze epidemiological characteristics, clinical symptoms, radiological features, treatment and outcomes of 10 patients who were surgically treated at our institution. Our results are analyzed in comparison to a review of the literature.

Patients and methods

We undertook a retrospective study of 10 patients who were operated on for hepatic vascular tumour at the general surgery department of Mongi Slim hospital of Tunis between January 2000 and December 2012. The cases were retrieved from the files of the registry of surgery of the same hospital. Clinical records and microscopic slides of each patient were available for review in all cases. Clinical data, radiological investigations, treatment and outcome were retrospectively analyzed. All patients underwent imaging evaluation during the preoperative period. All specimens were surgically obtained. Tissues were fixed in 10% phosphate buffered formaldehyde, embedded in paraffin and sections were prepared for routine light microscopy after staining with hematoxylin and eosin. Immunohistochemical analysis was performed using the avidin-biotin complex technique with antibodies against CD 34. Patient confidentiality was maintained.

Results

Clinical findings

Our study group included 4 male and 6 female patients (sex-ratio M/F = 0,66) between 23 and 78 years of age (mean = 55,5 years). There were nine cases of hemangiomas that comprised 4 male and 5 female patients (sex-ratio = 0,8) with a mean age of 55,7. There was only one case of angiosarcoma that occurred in a 53-year-old patient. The delay from onset of symptoms to diagnosis ranged between 5 days and one year. Past medical history of the patients was significant for hypertension (n = 3), rectal adenocarcinoma (n = 2), gastric adenocarcinoma (n = 1), pancreatic neuroendocrine tumour (n = 1), diabetes (n = 2), asthma (n = 1) and tuberculosis (n = 1). One patient had no significant past medical history. The presenting clinical symptoms were dominated by abdominal pain in 7 cases (one case of angiosarcoma and 6 cases of hemangioma), fever in 3 cases (one case of angiosarcoma and two cases of hemangioma), altered general health and weight loss in two cases (one case of angiosarcoma

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and one case of hemangioma) while vomiting was present in two cases (one case of angiosarcoma and one case of hemangioma). Three cases of hemangiomas were fortuitously discovered.

Radiological findings and localization of hepatic vascular tumours :

Diagnostic imaging techniques included CT scan in 6 cases, ultrasonography in 7 cases and MRI in 2 cases. Based on imaging findings, preoperative diagnosis of hemangiomas was accurately made in only 3 cases (30%). Three cases (2 hemangiomas, 1 angiosarcoma) were misdiagnosed preoperatively as having hydatid cyst and four cases

of hemangiomas were misdiagnosed preoperatively as liver metastases. On CT scan, Hepatic angiosarcoma presented as a cystic mass of segment VIII with calcification and subcapsular collection. Ultrasonography demonstrated hyperechogenic, homogeneous lesions in all cases of hemangiomas. On CT scan, cavernous hemangiomas presented as slightly hypodense lesions without injection (n = 5) and as an isodense lesion in only one case. Hemangioma was solitary in 8 patients and multiple in only one case. The sites of solitary hemangiomas were segment II (n = 2), segment III (n = 1), segment IV (n = 2) and segment VII (n = 3). One case of multiple hemangiomas involved segments IV, V, VI and VII.

Treatment

All patients underwent surgical excision of the tumour. Postoperatively, no patient had received adjuvant therapy.

Pathologic findings

Hemangiomas ranged in size from 1 to 10 cm (mean = 4 cm), while angiosarcoma measured 14 cm in diameter. On cut section, all hemangiomas had a spongy hemorrhagic appearance, while angiosarcoma presented as an ill-defined heterogeneous focally cystic mass with hemorrhagic foci. Histopathological examination of the surgical specimen revealed cavernous hemangioma in 8 cases and sclerosing hemangioma in one case. Immunohistochemical study using the avidin-biotin complex technique with antibodies against CD 34 was performed in only one case and confirmed the diagnosis of hepatic angiosarcoma.

Operative morbidity and postoperative complications

One of our patients with hepatic angiosarcoma died on postoperative day 1 due to septic shock. There were no other postoperative complications.

Follow-up and evolution

Clinical data regarding follow-up was incomplete in 3 of the medical records. The follow-up period ranged between 7 months and 3 years. Five patients were lost to follow-up. One patient with hepatic angiosarcoma died on postoperative day 1. There were no postoperative sequels.

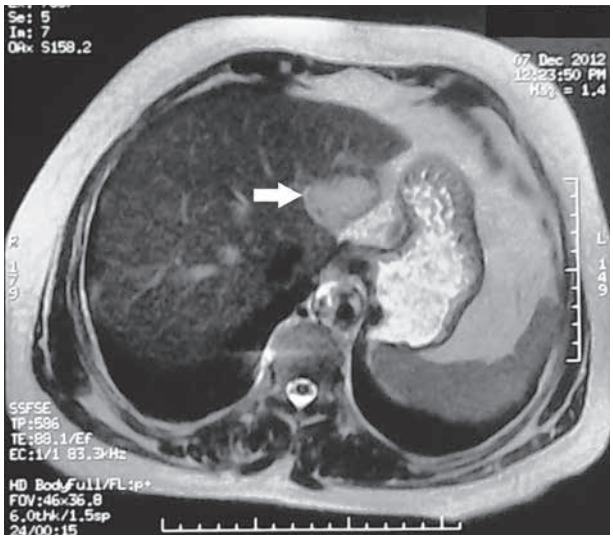

Fig. 1. — MRI demonstrating a homogeneous lesion measuring 58 mm in diameter with low intensity signal on T1 weighted image (arrow).

Discussion

Hepatic angiosarcoma

Epidemiology

Hepatic angiosarcoma ranks as the third place in the list of most common primary liver malignancies (4). The estimated incidence of angiosarcoma was about 0.14–0.25/1,000,000 in the USA (5). Hepatic angiosarcoma is frequently associated with several environmental carcinogens such as thorothrast, vinyl chloride, monomer, radium, pesticides, external radiation, cyclophosphamid, arsenical compounds, use of androgenic/anabolic steroids and iron (hemochromatosis) (6,7). However, the majority of hepatic angiosarcomas, are unrelated to the above agents as it was the case in our patient. Peak age incidence is in the sixth and seventh decades of life with a male to female ratio of 3/1 (6). Our female patient was 53 years old.

Clinical features

The presenting symptoms of hepatic angiosarcoma are non-specific and include right upper quadrant abdominal pain, anemia, fever, weight loss, malaise and abdominal mass. Our patient presented with fever, abdominal pain, weight loss and altered general health. Physical findings include ascites, hepatomegaly, jaundice and acute abdominal bleeding. Laboratory investigations are non-specific. In our patient, physical examination revealed hepatomegaly that was tender on palpation.

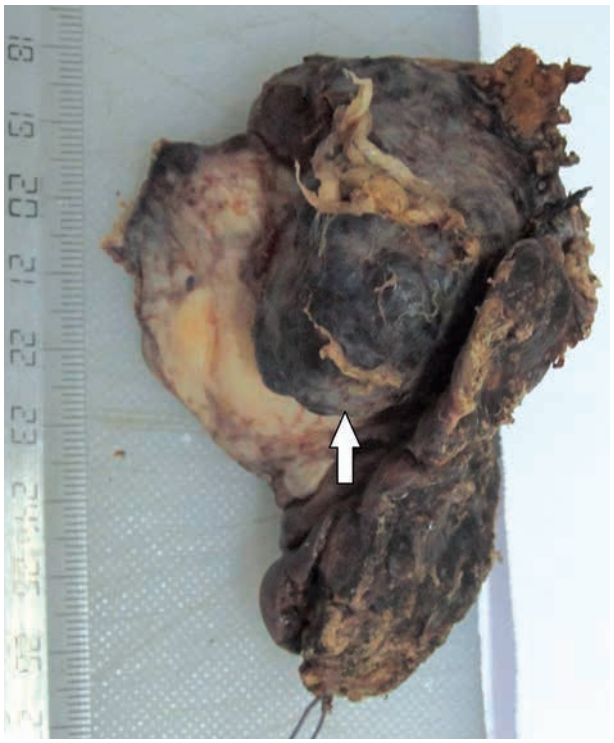

Fig. 2. — Macroscopic findings : A brown tumour protruding under the hepatic capsule.

Imaging features

It is difficult to make a diagnosis of hepatic angiosarcoma preoperatively using only imaging techniques such as CT and MRI because the imaging findings vary widely. On CT scan, most lesions are hypoattenuating but some appear hyperdense on unenhanced CT. On contrast-enhanced CT, angiosarcoma may show a variety of findings. In our patient, CT scan demonstrated a cystic mass of segment VIII with calcification and subcapsular collection. MRI also shows non-specific pattern (3). However, on T1-weighted images, tumours often contain irregular areas of high signal intensity suggesting hemorrhage and on T2-weighted images, tumours often show heterogeneous architecture (3). MRI was not performed in our patient.

Treatment

The first choice of treatment for hepatic angiosarcoma is liver resection but the reported percentage of patients who undergo resection is only 20% (9). In our case, based on imaging findings preoperative diagnosis was hydatid cyst and the patient underwent hepatic segmental resection. Due to the often difficult differential diagnosis, the scarcity of malignant vascular lesions and scattered transplant experience worldwide, the value of orthotopic liver transplantation in the treatment of these vascular diseases still remains questionable (6). The effects of systemic chemotherapy and radiation therapy is also poor (9).

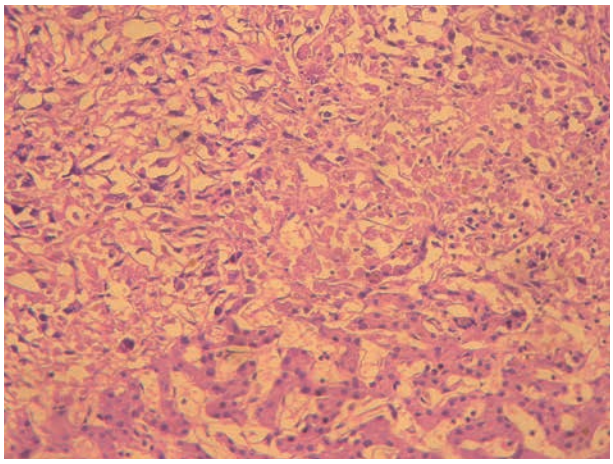

Fig. 3. — Hepatic angiosarcoma : irregular vascular channels lined by atypical endothelial cells. (Hematoxylin and eosin, magnification ×20).

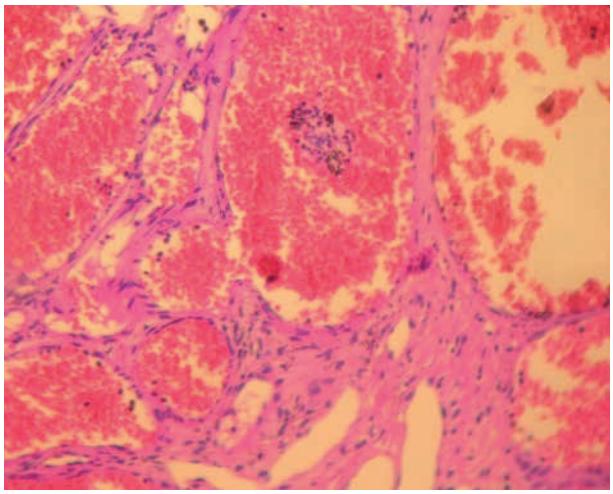

Fig. 4. — Cavernous hemangioma : variable-sized vascular channels lined by a single layer of flat endothelial cells separated by fibrous septa. (Hematoxylin and eosin, magnification × 40).

Pathological characteristics

The diagnosis, especially of diffuse hepatic angiosarcoma, can be extremely difficult. Liver biopsy has been reported as treacherous and non-diagnostic (8). In some instances, even if liver biopsy results are suspicious for angiosarcoma, determining whether the liver or the other organ is the site of the primary lesion is difficult. In our patient, a diagnosis of primary hepatic angiosarcoma was made on surgical specimen and there were no affected organs with findings suggestive of primary soft-tissue angiosarcoma.

Macroscopic findings

Macroscopically, hepatic angiosarcoma appears as an ill-defined spongic haemorrhagic nodule that involves the whole liver. Hepatic angiosarcoma can present four

types of growth patterns : multiple nodules, large dominant mass, mixed patterns of multiple nodules and dominant mass and more rarely diffusely infiltrating macronodular tumour (6). In our case, angiosarcoma presented as an ill-defined heterogeneous focally cystic mass with hemorrhagic foci.

Microscopic findings

Microscopically, angiosarcomas can show solid and pseudopapillary patterns with formation of irregular vascular channels lined by variably atypical endothelial cells that often show multilayering and mitotic activity as it was the case in our patient (10). Cases associated with thorothrast often contain portal fibrosis with granules of thorothrast present in these areas.

Prognosis and outcome

At the moment of diagnosis, extrahepatic metastases are present in 20-40% of patients ; the most common sites of metastases are lung, spleen, bone and adrenal (6). Prognosis is poor and most patients die within one year (6,9). Our patient died on postoperative day 1 due to septic shock.

Hepatic cavernous hemangioma

Epidemiology

Hemangiomas are the most common primary liver tumour, with a prevalence in the general population estimated to range between 0.4% and 7.3% (11). These vascular tumours have an unknown etiology ; however, some studies have suggested a possible relationship with the intake of steroid hormones (11). They are more frequently found in women, usually in the fifth decade, being rare in children. In our series, there was a slight female predominance in hemangiomas with a sex-ratio M/F = 0,8 and a mean age of 55,7 years.

Clinical features

Most hemangiomas are small (less than 4 cm), solitary (90%), asymptomatic and diagnosed in adults on incidental medical check-up. The vast majority of hemangiomas remain stable in size (12,13). Tumours greater than 4 cm in diameter are called giant hemangiomas. In our series, hemangiomas ranged in size from 1 to 10 cm (mean = 4 cm). Hemangiomas are symptomatic only when they are more than 4 cm in size, leading to pain or a mass syndrome. In our series, three cases of hemangiomas were incidentally discovered during check-up for unrelated disease.

Imaging findings

MRI with vascular reconstruction is the best noninvasive diagnostic study ; spiral CT remains a very valuable alternative. Ultrasonography reveals, a hyperechogenic, homogenous lesion presenting a posterior acoustic enhancement (14). In unenhanced CT, the density of the lesion is the same as that of the vessels. In MRI, the lesion presents an homogenous and high intensity signal on T2-weighted images, a low intensity signal on T1-weighted images (14).

Treatment

The therapeutic algorithm for the management of giant hemangiomas is still not well standardized. Surgical resection is considered the definitive treatment ; however, its indications are quite restricted and resection must, indeed, be reserved for situations such as incapacitating pain, compression of adjacent organs, diagnostic uncertainty, and the extremely rare Kasabach-Merritt syndrome. Surgery should be avoided even in the presence of symptoms like pain, which should be treated with analgesics, because liver resection presents higher morbidity and mortality rates when compared to the natural course of the disease (12).

Arterial embolization

Several reports and studies have highlighted the importance of transarterial embolization in treating symptomatic hemangiomas, ruptured hemangiomas and diffuse hemangiomatosis (15,16). Embolic material used for this purpose include polyvinyl alcohol, gelfoam, steel coils and isobutyl cyanoacrylate. The long-term success rate of embolization (without subsequent surgical resection) is not well studied.

Surgical ligation of feeding vessels

Transhepatic compression sutures using polytetrafluoroethylene pledgets and selective ligation of large feeding vessels have been described. In one case, this technique successfully reduced intratumoral shunting that otherwise would have led to intractable cardiac failure (17).

Radiofrequency ablation

Both percutaneous and laparoscopic radiofrequency ablation have been used successfully to improve abdominal pain in small numbers of patients with symptomatic hepatic hemangiomas (18).

Hepatic irradiation

Hepatic irradiation with a dose of 15-30 Gy in 15-22 fractions over several weeks has been used to treat symptomatic hemangiomas. Tumour regression and symptom relief were noted in most patients, with minimal morbidity (19).

Orthotopic liver transplantation

This option is occasionally offered to symptomatic patients with large or diffuse lesions. Several cases have now been reported in the medical literature (20).

In our series, all patients underwent surgical excision of the tumour.

Pathological findings

Macroscopy

Macroscopically, cavernous haemangiomas are usually single and soft or fluctuant. When sectioned, they

Table 1. — **Distinctive radiological and pathological features between cavernous hemangioma and angiosarcoma (4,14)**

	Hepatic Angiosarcoma	Cavernous Hemangioma
Imaging		
Ultrasonography	Hyperechoic heterogeneous single or multiple nodules	Hyperechoic, homogenous lesion presenting a posterior acoustic enhancement.
CT scan	Most lesions are hypoattenuating but some appear hyperdense on unenhanced CT.	Typical hepatic hemangiomas are often hypodense on precontrast CT scan. In arterial phase there is peripheral enhancement in the lesion the central portion typically remaining hypodense. In the portal venous and delayed phases the enhancement is usually seen to progress centripetally
MRI	On T1-weighted images, tumours often contain irregular areas of high signal intensity suggesting hemorrhage and on T2-weighted images, tumours often show heterogeneous architecture.	Homogenous and high intensity signal on T2-weighted images, a low intensity signal on T1-weighted images and the absence of restriction of the apparent diffusion coefficient.
Pathological Features		
Macroscopy	ill-defined spongic hemorrhagic nodule.	Soft or fluctuant. When sectioned, they partially collapse owing to the escape of blood and have a sponge appearance.
Microscopy	Irregular vascular channels lined by variably atypical endothelial cells that often show multilayering and mitotic activity.	Varying sized blood-filled vascular channels lined by a single layer of flat endothelial cells and separated by fibrous septa of various thicknesses.

partially collapse owing to the escape of blood and have a sponge appearance (10).

Microscopy

Histologically, lesions are typically composed of varying sized blood-filled vascular channels lined by a single layer of flat endothelial cells and separated by fibrous septa of various thicknesses (10). Although grossly well-circumscribed, microscopic extension of dilated vascular spaces into adjacent hepatic parenchyma may be observed (10,21). Thrombi in various stages of organization with areas of infarction may be present and older lesions show dense fibrosis and calcification. In sclerosed hemangiomas, most or all of the vessels are occluded and sometimes are only demonstrable by stains for elastic tissue (10). Extremely rarely, diffuse and multiple lesions (diffuse hemangiomatosis) with progressive development do occur (1). In our series, there was only one case of multiple hemangiomas involving segments IV, V, VI and VII.

Prognosis and outcome

Cavernous hemangiomas are not known to undergo malignant change. Complications of hemangioma are rather uncommon ; they can include spontaneous bleeding and/or rupture, development of febrile syndrome and Kasabach-Merritt syndrome (12,13).

The main distinctive radiological and pathological features between hepatic angiosarcoma and cavernous hemangioma are summarized in table 1.

Conclusion

In summary, this retrospective study from Tunisia provides an overview on clinical symptoms, radiological features, treatment and outcome in 10 patients with primary hepatic vascular tumours. Histopathological diagnosis should be correlated with radiological findings to avoid error in diagnosis. Early diagnosis of angiosarcoma is crucial, because once patient become symptomatic, the disease progress is accelerated and treatment cannot be offered (2,3).

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