



Intra-Arterial Embolization in Benign Liver Tumors: Why is It Useful to Perform This?

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Introduction

Benign liver tumors occur frequently, and are often encountered incidentally as a consequence of the widespread use of imaging tests and often have a benign course. They are a heterogeneous group of lesions with different cellular origin. In most cases, they are accurately diagnosed by non-invasive radiologic imaging techniques. The most common benign hepatic tumors include cavernous hemangioma, focal nodular hyperplasia and hepatic adenoma. The majority is asymptomatic, but some cause hepatomegaly, right upper quadrant discomfort, or intraperitoneal hemorrhage and treatment is necessary only in a few of these specific circumstances [1].

These tumors are often identified initially on an abdominal ultrasound scan and following examinations, clinic history and laboratory test aim to suspect diagnosis. Further studies such as computed tomography and magnetic resonance imaging for tumor characterization are indicated. These studies are generally sufficient to establish a diagnosis of benign liver tumor but, however, if there was any doubt a biopsy would be indicated [2].

In patients with symptomatic tumors, the classic treatment has been resective surgery. When surgery is considered, it must be carefully planned, taking into account mortality and morbidity, surgical complications are to be considered as well as including intraoperative and postoperative bleeding [3]. The possibility of intra-arterial embolization is well established in cases of active bleeding, but is not well standardized as a presurgical option, although there are publications with regard in to this medical literature [4-6].

Recent advances now offer selective Trans catheter arterial embolization as an option in the management of these tumors. The aim of embolization should be: to control acute hemorrhage, to decrease bleeding during surgery and to control growth of the tumor in unresectable tumors [7].

All these invasive procedures are associated with risk and should only be considered after multidisciplinary team agreement. The team should have expertise in the management of benign liver lesion and should include a hepatologist, a hepatobiliary surgeon, diagnostic and interventional radiologist and pathologists. This experienced multidisciplinary team is mandatory for decision-making as emphasized in the Clinical Practice Guidelines [2].

Now we will describe the most important characteristics of each of them.

Hepatic Cavernous Hemangiomas

These are the most common benign tumors of the liver. They arise from the mesoderm and are composed of blood-filled cavernous spaces of varying size lined with a single layer of flat endothelial cells, which may be separated by fibrous septa of variable thickness. In infants, hemangiomas often regress spontaneously by the age of 2. In adults, 80% are in women and 40% can be multiple. When they are larger than 10 cm they are classified as giant cavernous hemangiomas, these can be symptomatic and present with pain or abdominal mass.

Intraabdominal hemorrhage is rarely described and the incidence of spontaneous bleeding is unknown, but large subcapsular lesions are thought to be at greater risk. However, large hemangiomas occasionally cause arteriovenous shunting sufficient to cause heart failure and sometimes consumption coagulopathy. In these cases, treatment may include high-dose corticosteroids, sometimes diuretics and digoxin to improve heart function, interferon alfa, surgical removal, selective hepatic artery embolization, and, rarely, liver transplantation [4,8].

Hemangiomas and giant hemangiomas are easily diagnosed on MRI, showing a fast filling based on strong hyperintensity on T2-weighted images and the persistent enhancement of delayed phase imaging, giant hemangiomas may show central heterogeneity due to thrombosis or fibrosis [9].

Interventional procedures should be performed only in cases of symptomatic hemangiomas, hemangiomas that grow progressively, and hemangioma bleeding or with high risk of bleeding. Recent advances now offer selective transcatheter arterial embolization to decrease bleeding during surgery and to treat unresectable tumors [7].

Focal Nodular Hyperplasia (FNH)

It is the second most common benign tumor of the liver. It is thought to be secondary to a proliferative response of hepatocytes. It is present in 3% of the population and is often found in women 30-50 years old, typically asymptomatic and has no malignant potential. This can rarely produce symptoms of pain or discomfort [1]. In most cases, they are solitary and smaller than 5 cm and can be multiple in 20-30% of cases and even associated with hemangioma in 20% of cases [10].

Identification of classic FNH by way of its "spoke-wheel" with a drainage vein from these spoke-wheels on arteriography or contrasted-enhanced ultrasound and central scar on cross-sectional imaging is relatively straightforward to diagnose. MRI has the highest sensitivity compared with ultrasound and CT and a specificity of almost 100% for the diagnosis [11].

For a typical lesion of FNH, follow-up is not necessary and the treatment is not recommended, but if the lesion is atypical or the patient is symptomatic, a biopsy of the tumor must be considered and the final decision can be managed by the multidisciplinary team [2]. Hepatic resection has been the traditional treatment in symptomatic patients, but surgical resection carries significant risks, and should only

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be reserved for exceptional cases [2]. In those cases in which surgical resection is essential, the preoperative intra-arterial embolization is an option supported mainly by the existence of isolated published cases of intralesion bleeding and rupture of tumor [12] and it may be a suitable and effective alternative in cases when resection can be is very difficult [7,13].

Hepatic Adenomas (HA)

They are uncommon benign epithelial liver tumors. They are approximately 10 times less common than FNH and are frequently diagnosed in women aged 35-40. In histopathologic analysis, hepatic adenomas contain well-differentiated hepatocytes lacking bile ducts or portal triads. Predisposing factors to adenoma formation include oral contraceptive use in female patients, anabolic steroid use in male patients, and glycogen storage disease. Adenomas due to contraceptive use often regress if the contraceptive is withdrawn. These lesions may present complications such as spontaneous bleeding (especially, patients with lesions >5 cm) [2]. Another complication is the possibility of malignant degeneration, but this is relatively rare. In practical terms, the course of HA diagnosed in women is more often benign, while adenomas diagnosed in men have a significantly higher incidence of malignancy [14].

Based on genomic analysis, there are four molecular subtypes of hepatic adenomas:

- 1.) HA inactivated for HNF-1 α , accounting for 30 to 40% of HA,
- 2.) Inflammatory adenomas, accounting for 40-55%,
- 3.) β -catenin activated adenomas accounting for 10 to 20%, and
- 4.) Unclassified adenomas, accounting for 5%. This classification is associated with the risk of malignant transformation into adenoma. Among these groups, β -catenin activated adenomas is associated with the highest risk for malignancy, this group being more frequent in men, which could at least in part explain the high risk of malignant transformation reported in male patients [2].

HA appearance on T1-weighted magnetic resonance images varies from slightly hypointense to mildly hyperintense and predominantly hyperintense relative to liver on T2-weighted images [15].

The risk of bleeding complication is related to the size of the adenoma, with the accepted clinically relevant size being 5 cm, superficial location and growing more than 20%. If clinical evidence of hemorrhage occurs, embolization can be performed to control active bleeding. Treatment decisions are based on gender, size and tumor progression. In men the resection is indicated irrespective of size and in women surgery is recommended for nodules equal or greater than 5 cm and those continuing to grow [2,16].

Liver adenomatosis is out-date term, formerly meaning the presence of more than 10 adenomas, but now replaced by the term multiple hepatic adenomatosis. The clinical presentation and the risk of complications (malignant transformation or bleeding) do not differ from those in patients with a single adenoma, being driven by the size of the largest nodules, rather than the number of them [16].

A conservative approach is recommended in asymptomatic patients with small adenoma, in women contemplating pregnancy the tumor resection is indicated, in pregnant women the tumor resection is recommended in the second trimester and in symptomatic patients with large adenomas presurgical embolization is indicated [2,7].

Procedure Details

Intra-arterial embolization should be as selective as possible, in branches feeding the lesions. Arteriogram is performed and related to individual anatomy (anatomic variations must be considered) and the catheter is advanced to avoid non-target vessels. The development of micro catheters has provided useful tools for selective embolization. The embolic material to be used can be chosen according to the operator's experience and preference. In our experience the materials for embolization are: spherical embolic polyvinyl particles and steel coils. The material most used by our work team was spherical embolic particles of Polivinil Alcohol (500 μ m-700 μ m), which produced mechanical occlusion of the vessel in addition to activation of thrombine and inducing fibroblasts ingrown which leads to a relative permanent occlusion, and then, the feeding artery was plugged with coils if there were an arterial pedicle to ensure the total vascular exclusion of the tumor. The surgical intervention took place 4 to 7 days after embolization [7,17].

It has to be emphasized that in our experience severe pain may result from big tumors being embolized. In post procedure management, analgesic therapy with morphine pump is required plus antiemetic therapy (ondansetron and dexamethasone).

Although further studies with larger samples and long-term follow up are required, in conclusion provided there is a consensus among the multidisciplinary team, we consider presurgical embolization of benign liver lesion to be a useful option in the perioperative management of giant and/or symptomatic tumors. This offers a bleeding control in emergencies and reduces the intraoperative hemorrhage risk and could be considered to be a possible alternative treatment method in unresectable lesions.

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