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CONTINUING EDUCATION

IMAGING OF BENIGN LIVER LESIONS

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Normal liver is made of various epithelial and mesenchymal cells, and benign lesions may develop from each of these cells. Benign proliferation of the hepatocytes leads to hepatocellular adenoma (HA) and to focal nodular hyperplasia (FNH), in which there is also biliary structure proliferation. These hepatocellular lesions are much rarer than hepatic hemangioma, which develops from endothelial cells, and cysts of congenital and developmental origin, which constitute the most common benign liver lesions. Benign liver tumors and tumorlike conditions are now being more frequently detected due to the widespread use of imaging modalities particularly ultrasonography (US). Characterization of these lesions by imaging is important for exclusion of malignant neoplasms and for avoidance of unnecessary invasive procedures. Spiral computed tomography (CT) and/or magnetic resonance (MR) imaging play a major role for these evaluations, using state of the art techniques including optimization of parameters and use of dedicated contrast agents. Then, the role of guided biopsies is actually limited for this purpose.

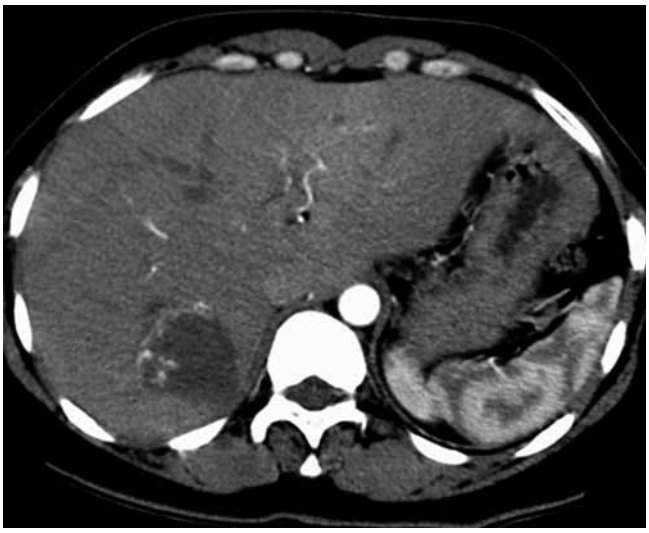

Fig. 1. — Liver hemangioma. Peripheral and discontinous globular enhancement at the arterial phase, on spiral CT.

Hemangioma

Hemangioma is a benign focal hepatic lesion that consists of blood-filled spaces lined by single layer of flat endothelial cells (1). Blood flows slowly within these spaces. Areas of thrombosis, fibrosis, haemorrhage and calcifications are sometimes encountered within large hemangiomas (2,3). The lesions are clinically silent (4). Hemangiomas remain constant in size over time particularly when they are less than 4 cm in diameter.

On US, the typical hemangioma appears as a well defined, homogeneous, and hyperechoic lesion with posterior acoustical enhancement. The lesions are usually located close to the liver surface or to hepatic veins. Atypical features on US include hypoechogenicity (especially in hemangioma located in a fatty liver), mixed echogenicity, and peripheral halo (7). The majority of hemangiomas show no signal on color-coded Doppler US (8). On CT, hemangioma appears hypodense to the liver before injection of iodinated contrast medium and its attenuation value is similar to that of blood in adjacent blood vessels. On spiral CT, hemangioma shows enhancement starting at the periphery as a discontinuous nodular enhancement, particularly observed at the arterial phase, and progressing with or without complete fill-in and persistent enhancement on delayed imaging (9) (Fig. 1). Difficulties on CT diagnosis of hemangioma arise when the lesions are too small to show the classical enhancement patterns or when hemangiomas appears hypervasular and homogeneous at the arterial phase, mimicking a benign hepatocellular tumors; these latter presentations are more and more frequently observed, using thin collimations on spiral CT, as well as some more rare unenhanced hypovascular hemangiomas. At the arterial phase, transient hepatic attenuation differences can be oserved just close to these hypervascular hemangiomas related to small arterioportal shunts (Fig. 2, 3). MR imaging is now considered the best imaging method for characterization of hemangioma which appears as a homogeneous well defined lesion, hypointense on T1-weighted images, and extremely hyperintense on heavily T2-weighted images. Two types of internal areas may be observed: thrombosis is marked by hypointense band and myxoid transformation or presence of a loose connective tissue, usually observed in large hemangiomas, by hyperintense areas within the hemangioma (Fig. 4). On dynamic gadolinium-enhanced MR, hemangioma shows peripheral nodular enhancement progressing centripetally to uniform homogeneous enhancement. Differentiation of metastases from hemangioma is of utmost importance particularly when a focal hepatic lesion is incidentally discovered in a patient with a known primary malignancy.

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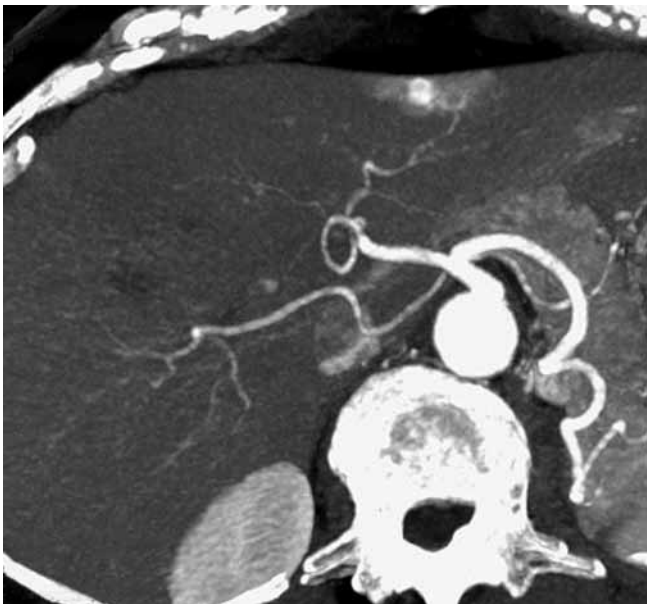
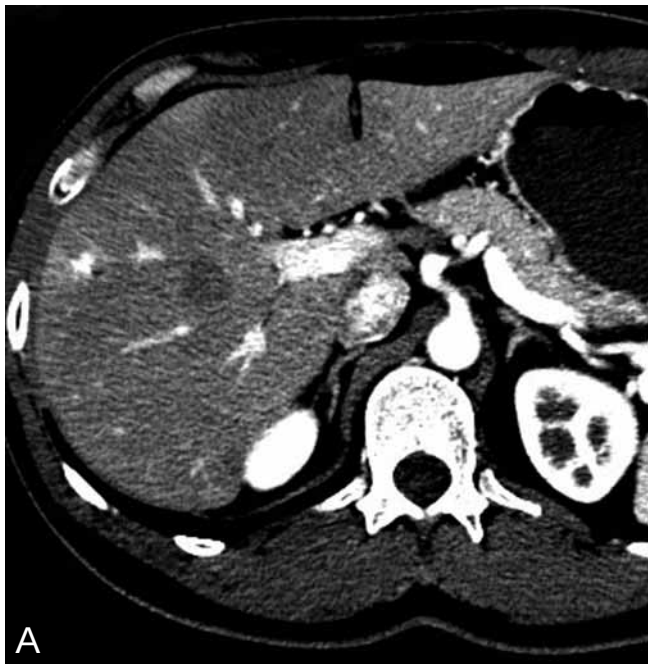


Fig. 2. — Hypervascular liver hemangioma.Transient hepatic attenuation differences (THADs) close to hypervascular and subcapsular hemangioma, located in segment III, related to arterioportal shunts.

Metastases are usually less hyperintense than hemangioma on T2-weighted images and this difference in signal intensity increases on increasing TEs. Besides, metastases do not show the characteristic enhancement patterns of hemangioma on dynamic gadolinium-enhanced MR imaging (11, 13). Hypervascular metastases were shown to have the following characteristics: - ring enhancement most intense and continuous at early phase,- washout of contrast material, resulting in heterogeneous intensity, with peripheral washout a common appearance,- uniform thickness of the enhanced ring, or jagged inner enhanced margins. The enhancement pattern of liver lesions on the immediate post-gadolinium images is the most useful feature to distinguish between hemangiomas and hypervascular metastases or hepatocellular carcinomas (HCCs) in cirrhotic patient. On MR imaging, atypical features of hemangioma are less frequently encountered than on CT or US (Fig. 5). A typical moderate signal intensity on T2-weighted images associated with atypical poor enhancement on the delayed post-contrast images may be observed in

Fig. 4. — Cavernous hemangiomas with myxoid transformation. The bright areas within the hemangiomas are related to the high water content of these areas, on long TR-long TE weighted MR images (TE = 150 msec).



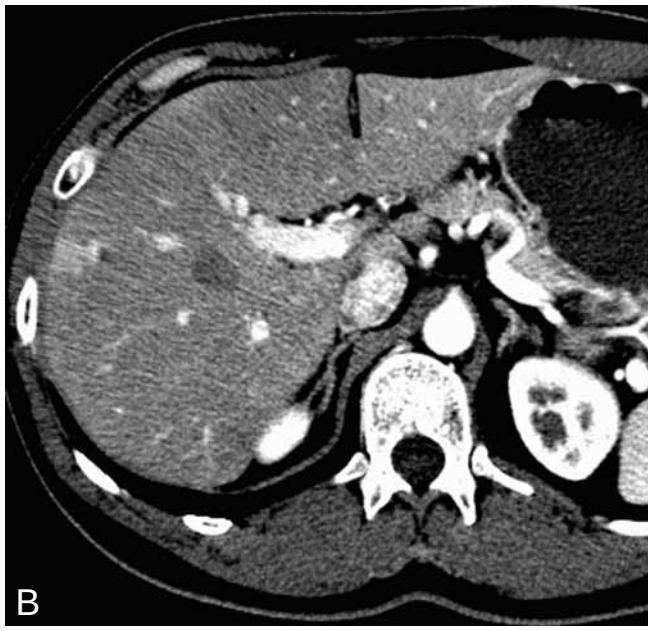
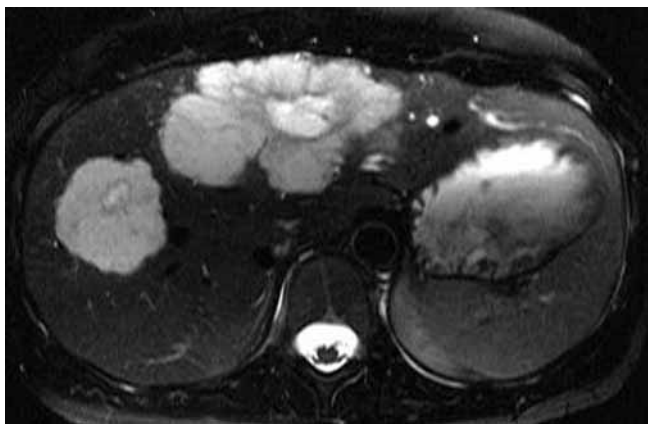


Fig. 3A and B. —Hypervascular hemangiomas in subcapsular location.THADs are more obvious than the lesion itself.



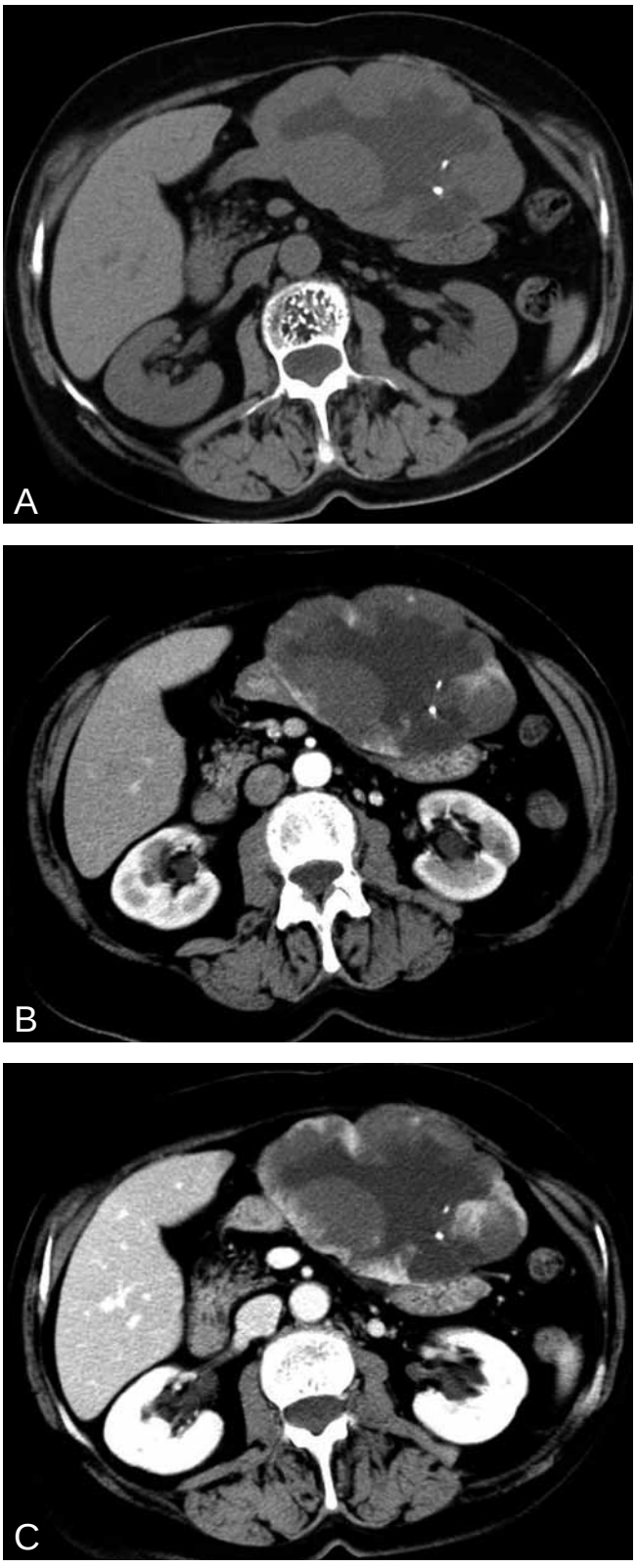


Fig. 5A-C. — Atypical cavernous hemangioma of the left lobe, atypiae marked by calcifications due to sclerosed areas.

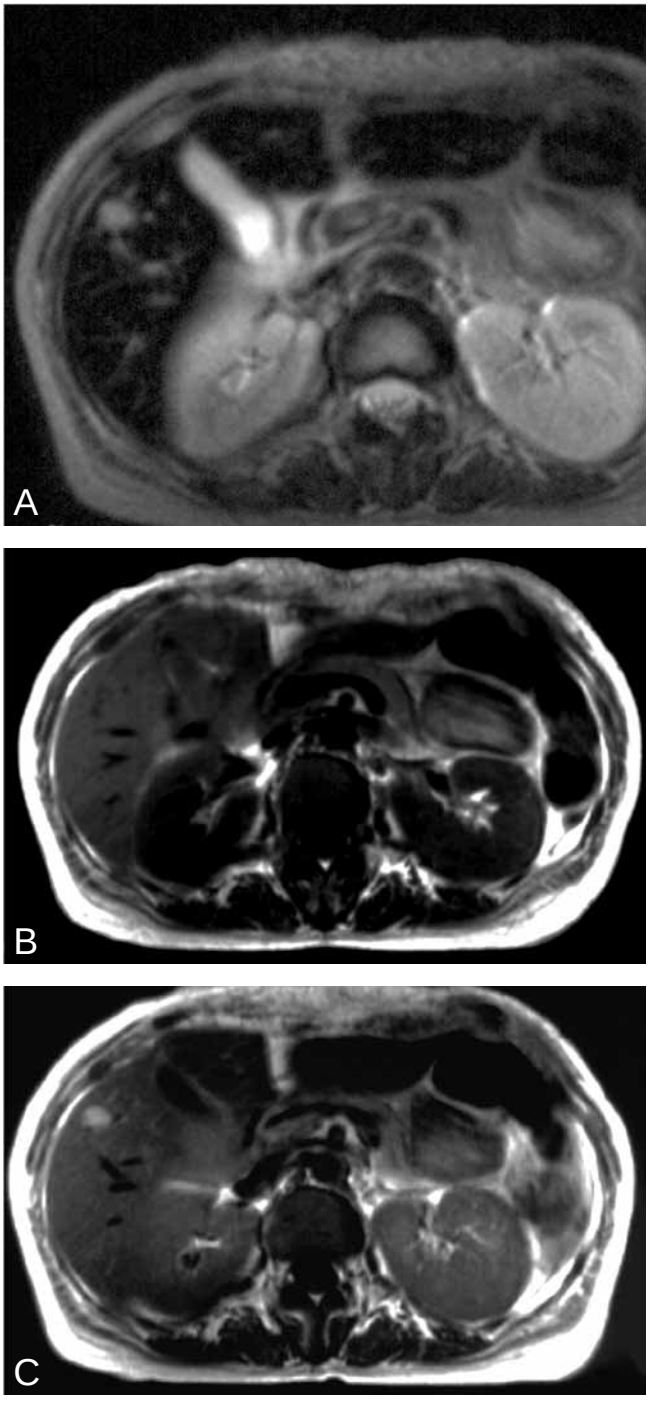


Fig. 6. — Liver hemangioma.On T2-weighted images, the lesion, located in segment V, is hyperintense (A). On T1-WI image, the lesion is isointense (B), and appears hyperintense related to the surrounding liver after SPIO particles injection, due to a vascular effect.

rare forms of sclerosed hemangiomas (14). It is only in such rare cases of atypical hemangioma on MR that imaging-guided fine needle biopsy is resorted to as a final problem-solving method. In spite of early warning reports, the technique is considered by some authors to be safe and accurate (15). The role of specific MR contrast agents is limited because these lesions have no hepatocyte nor Kupffer cells. However a T1-effect can be present using reticuloendothelial agents in hemangiomas particularly in small lesions due to a vascular effect (Fig. 6).

Focal nodular hyperplasia

Focal nodular hyperplasia (FNH) is a benign tumorlike condition which is thought to be a hyperplastic response to a local increase in blood flow rather than a true neoplasm (28). FNH is a well circumscribed noncapsulated lesion, It has usually a central stellate-shaped scar with incomplete peripherally radiating septa. The lesion is composed of normal hepatocytes arranged in nodules or thick layers and separated by thin fibrous septa. Arterial vessels are seen within the scar and they demonstrate intimal and medial fibromuscular hyperplasia. Kupffer cells within the lesion and biliary canaliculi within the fibrous septa are also seen. The lesion occurs predominantly in young females. Recently, our group has demonstrated that neither the type of oral contraceptives nor the duration can influence the size or the number of FNH lesions (29,30). During the follow-up, modifications of size were observed in only 4 % of studied patients with FNH, whatever continuation or discontinuation of low-dose oral contraceptives intake. The clinical course is usually silent, and the lesions are usually discovered incidentally. Complications of FNH are rare and then, this lesion may require only conservative management if the diagnosis is done.

On US, the echogenicity of FNH is variable (31). The scar may be demonstrated as a central small area of altered echogenecity. The lesion may be recognized only by its displacement or indentation of the adjacent veins, bulging of the hepatic contours, or subtle modification of the hepatic echopatterns. Color Doppler US may demonstrate the arterial vessels within the central scar (32). On spiral (CT), FNH appears isodense or slightly hypodense in the precontrast scan. After intravenous bolus injection of contrast medium, marked enhancement is observed in the arterial phase (Fig. 7) (31, 33). The lesion becomes isodense in the portal phase and on the delayed images. The scar appears hypodense to the lesion in the precontrast and the early postcontrast images. On delayed images, the scar appears iso or hyperdense. Usually, the supplying artery can be visualized within the scar in the arterial phase (31, 33). On MR imaging, FNH appears typically isointense or slightly hypointense on T1-weighted images and slightly hyperintense on T2-weighted images (Fig. 8). The scar appears hypointense to the lesion on T1-weighted images and hyperintense on T2-weighted images. Flow-sensitive MR sequences can be used to demonstrate intralesional arteries, particularly when these are unusually large. On dynamic MR imaging performed after intravenous bolus injection of extracellular contrast agents such as gadolinium-DTPA and gadolinium-DOTA, FNH becomes rapidly hyperintense in the arterial phase and then appears isointense or slightly hyperintense in the portal phase and on the delayed images, without capsule (Fig. 9). The central scar, appears unenhanced in the early images and hyperintense on the delayed images (34-36). On superparamagnetic iron oxide-enhanced T2-weighted MR imaging, FNH shows loss of signal due to the presence of Kupffer cells within the lesion. On MR images enhanced with hepatobiliary contrast agents such as manganese-DPDP, uptake of the contrast agents by FNH has been demonstrated due to their content of hepatocytes (Fig. 10). MR imaging is currently one of the best modalities for detection and characterization of FNH, with a sensitivity equal to 82% and a specificity reaching 100% in women, according to strict criteria including: (a)- homogeneity of the lesion, (b)- slightly hyperintense or hyperintense on T2-weighted MR images, (c)- hyperintense central scar on T2-

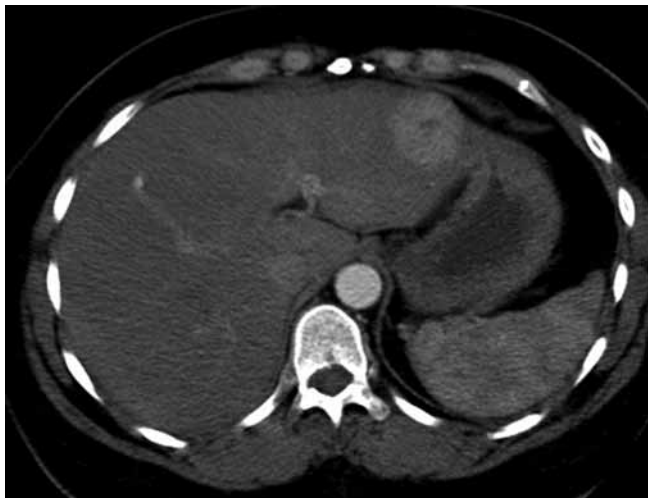


Fig. 7. — Typical signs of FNH of the left lobe, at the arterial phase, on spiral CT.

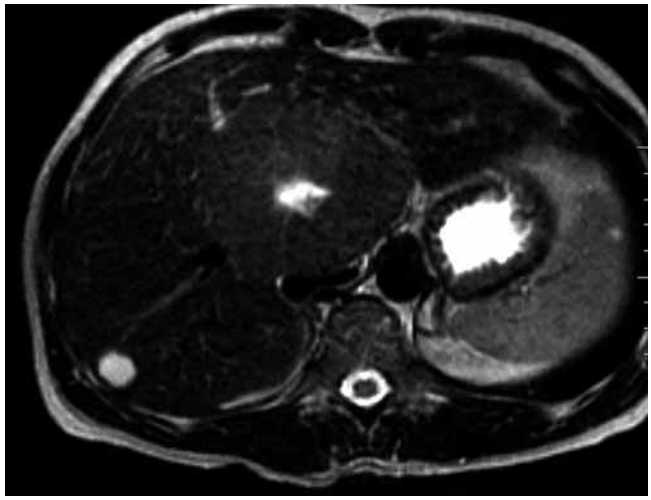


Fig. 8. — FNH of the caudate lobe, with typical signs on T2-weighted images, associated with a small hemangioma of the right lobe.

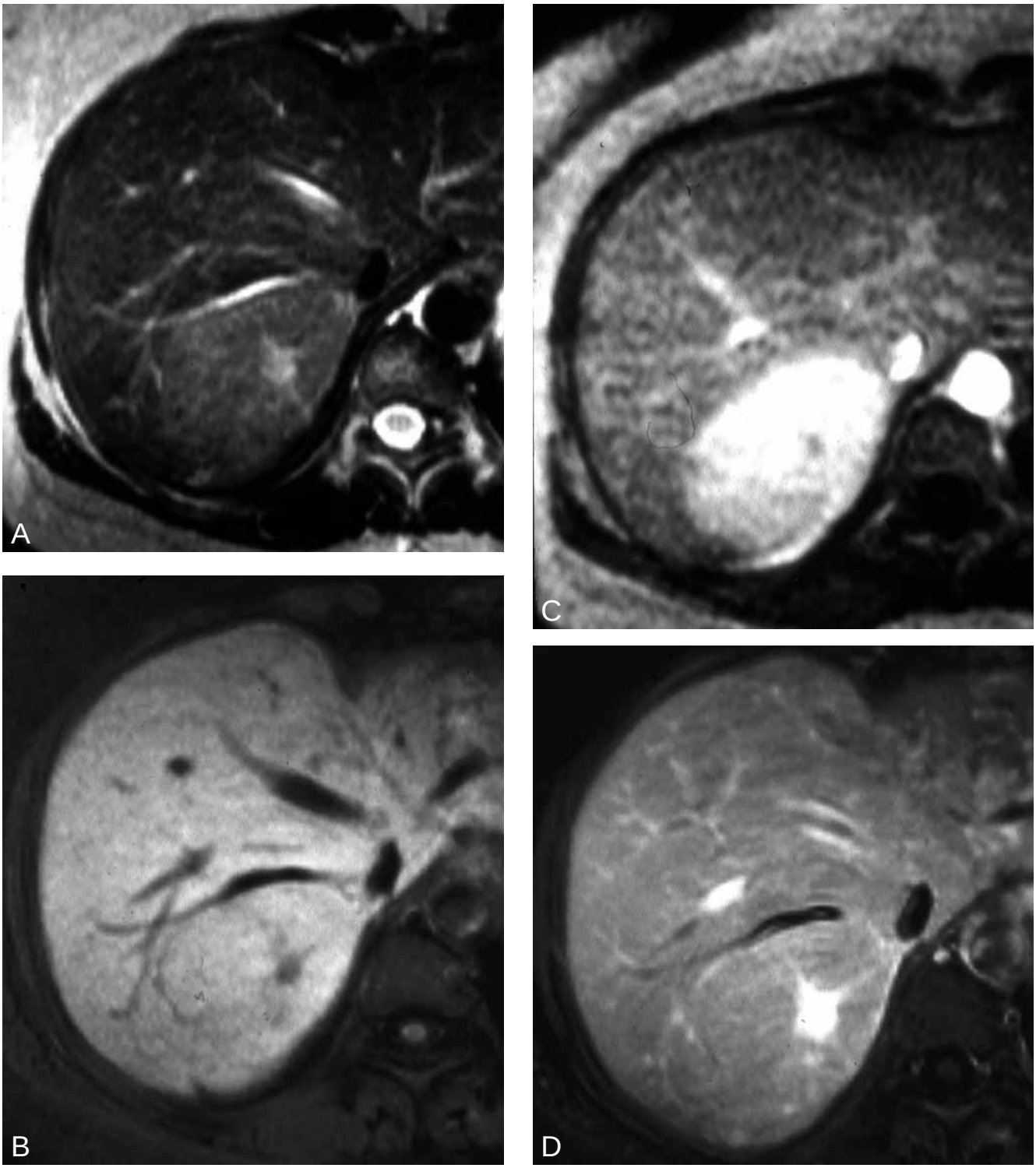


Fig. 9. —Typical findings of FNH located in segment VII, on T2-WI (A), on fat suppressed T1-WI (B), after bolus injection of gadolinium chelates (C), on delayed CE-fat suppressed T1-WI (D).

weighted MR images, (d)- tumoral arterial enhancement, (e)- delayed gadolinium enhancement of the central scar on T1-weighted MR images, (f) absence of capsule on the pre and post-contrast MR images (29, 30). In the rare cases in which atypical features of FNH are encountered on MR imaging, histological examination of the lesion is resorted to (37).

Hepatocellular adenoma

Hepatocellular adenoma (HA) is a benign hepatic neoplasm with a recent decrease of prevalence. It is associated with intake of oral contraceptive (OC) agents and glycogen storage disease. The widespread use of low dose OCs is probably the consequence of this low prevalence in comparaison with previous decades where hige dose OCs were

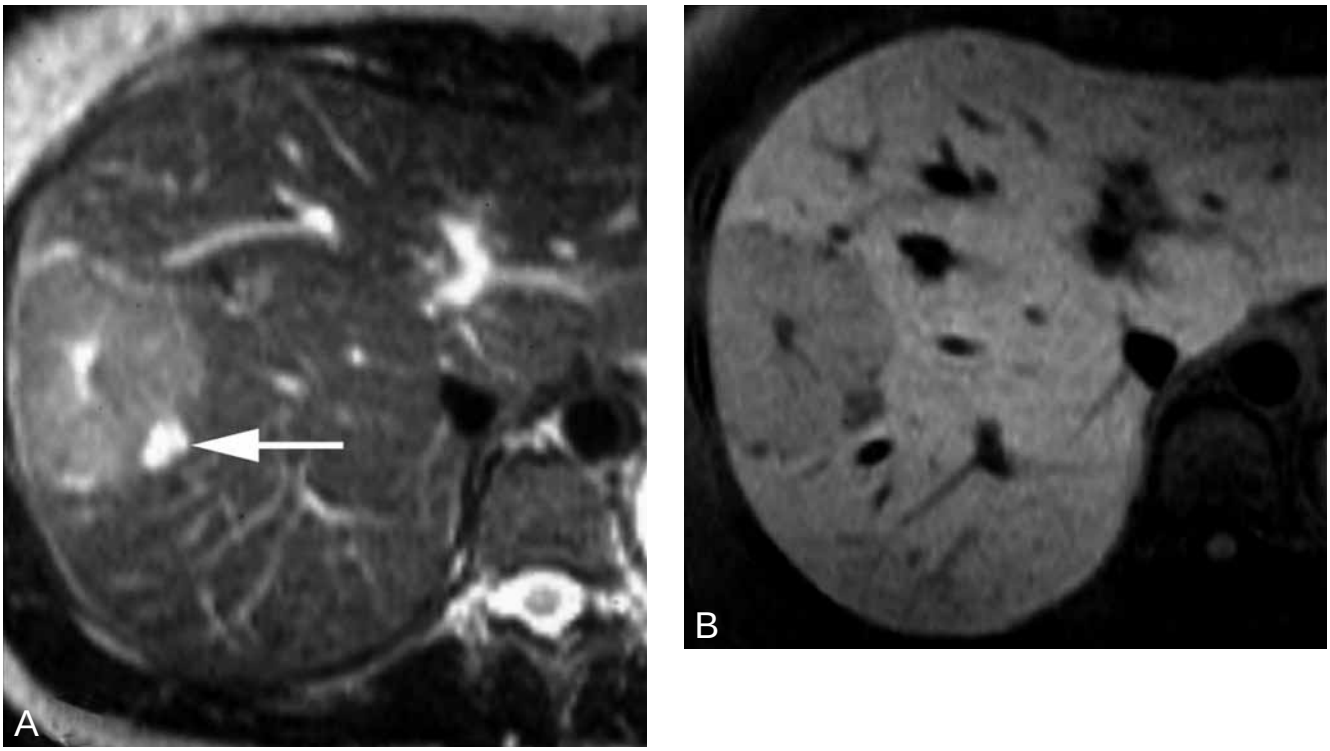


Fig. 10. — FNH associated to a small hemangioma (arrow) on T2-WI (A). On T1-WI, the both lesions are hypointense (B) and the FNH is enhanced after MnDPDP injection with no uptake by the hemangioma (C).

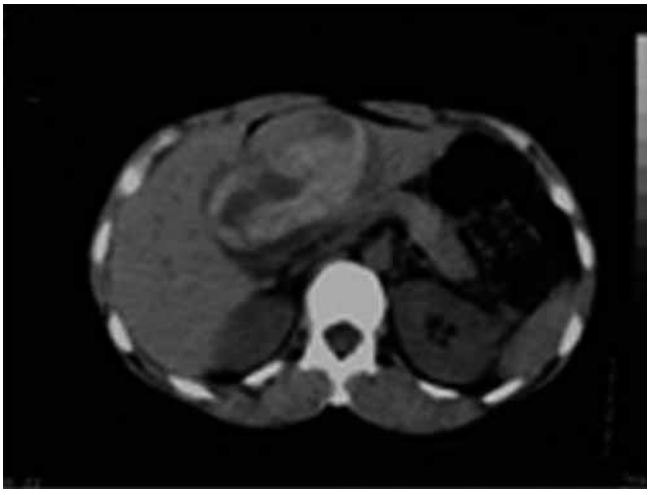


Fig. 11. — Hepatocellular adenoma (HA) with hyperdense area corresponding to hemorrhage.

commonly used. The clinical course of HA remains usually silent until complications occur. Surgical resection is the treatment of choice of HA due to the associated risk of life-threatening hemorrhage (38) and malignant transformation (39). Pathologically, HA is composed of hepatocytes. Hemorrhage, necrosis, fatty infiltration, sinusoidal dilatation, and scar formation may be observed within the lesion.

US is rather nonspecific for diagnosis of HA (32). Color Doppler US enables detection of intratumoral veins within HA (40). CT may demonstrate hemorrhage within HA as high attenuating areas and it may also, though less commonly, demonstrate fatty deposition within HA as low attenuating areas (Fig. 11) (41). Due to its higher sensitivity for fat and hemorrhage, MR imaging is superior to spiral CT in characterization of HA. On MR imaging, HA appears hyper- or iso-intense on T1- and hyperintense on T2-weighted images in the majority of cases (Fig. 12). Heterogeneity of signal intensity has been considered one of the most constant features of HA (42-44) due to the wide range of pathological changes which can occur within the lesion. HA shows also variable features as regards their vascularity on angiography and enhancement characteristics on dynamic contrast-enhanced MR imaging. However, the majority of cases appear hypervascular. On MR images enhanced with hepatobiliary contrast agents such as manganese-DPDP, uptake of the contrast agents by HA has been demonstrated due to their content of hepatocytes. Due to the frequent absence or low content of Kupffer cells in HA, the lesions do not enhance after superparamagnetic contrast agents on T2 weighted images (Fig. 13). For this diagnostic purpose, the role of all the imaging modalities is to exclude FNH and to propose surgical biopsy or HA and resection, because HA cannot be differentiated from HCC on imaging alone.

From this brief survey of the commonly encountered benign hepatic lesions, it is clear that MR imaging

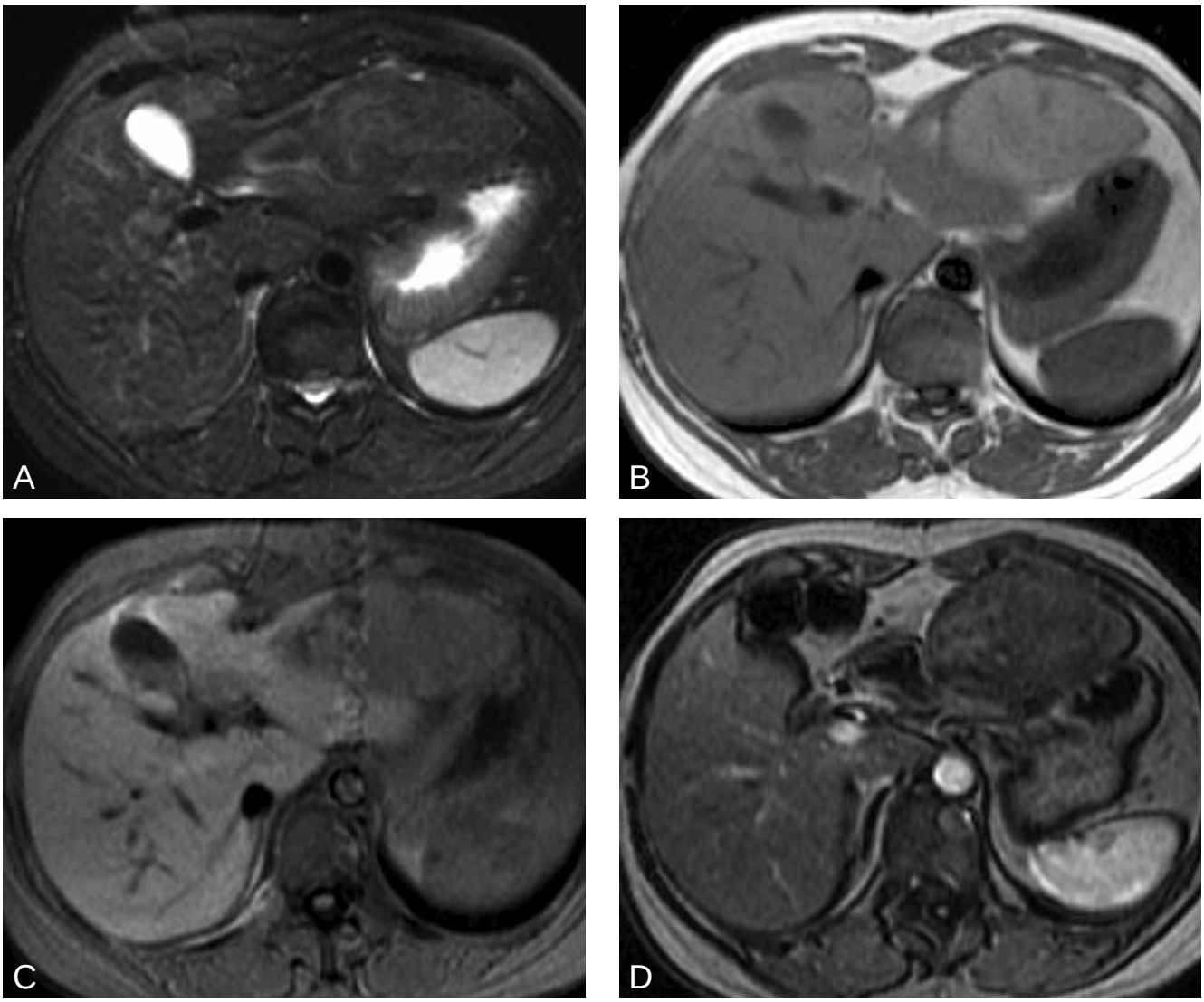


Fig. 12. — Hepatocellular adenoma of the left lobe. The lesion is isointense on T2-WI (A), hyperintense on T1-WI (B), and hypointense on fat-suppressed T1-WI (C), and is not enhanced after bolus injection of gadolinium chelates (D). Fatty HA.

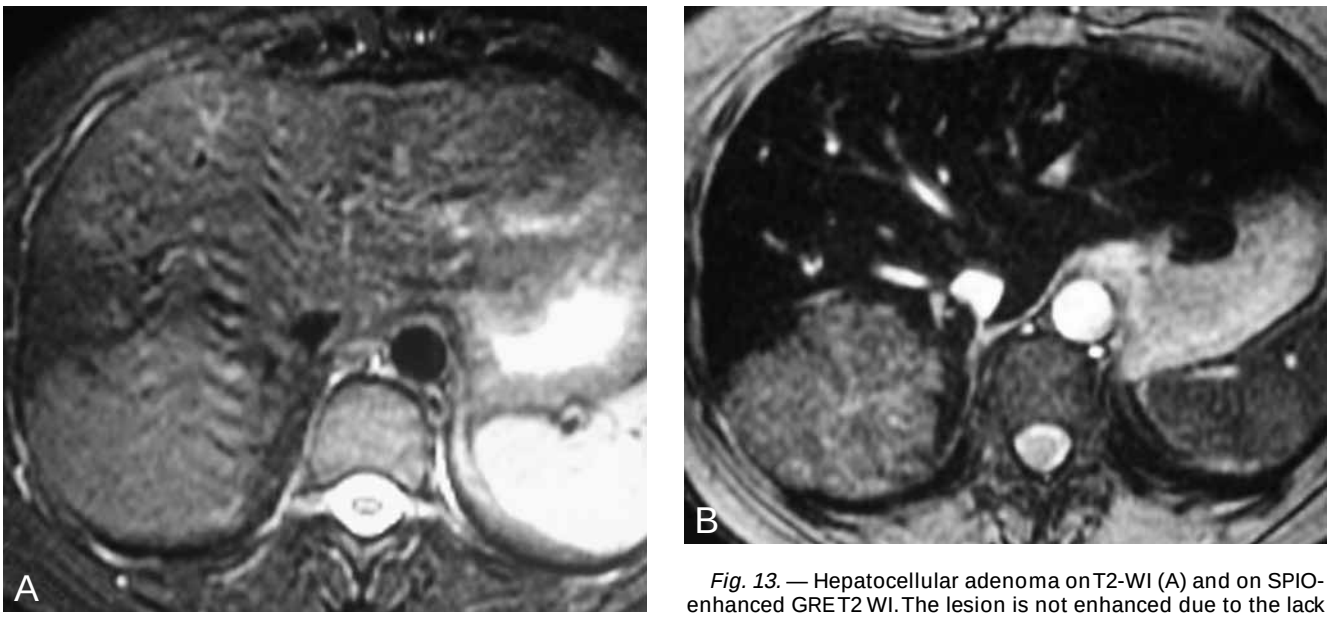


Fig. 13. — Hepatocellular adenoma on T2-WI (A) and on SPIO-enhanced GRE T2 WI. The lesion is not enhanced due to the lack of Kupffer cells.

gives the clue to the correct diagnosis in the majority of benign hepatic lesions by demonstration of typical features, particularly in case of hemangioma and focal nodular hyperplasia. In the rare occasions when benign lesions demonstrate atypical features, or when malignant neoplasms mimick the typical features of benign lesions, histological diagnosis through biopsy or surgical resection would be indicated.

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