Can hemangiomas enlarge over time?

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Learning objectives

To describe the imaging features and the clinical history of patients with hemangiomas which showed significant increase in diameter over time. To discuss the etiopathogenesis and the mechanism of the enlargement of hemangiomas. To highlight the imaging findings useful for differentiating hemangiomas enlarging over time from other focal liver lesions, especially in oncologic patients during the follow up.
Background

Hemangioma is the most common benign lesion. Prevalence in the general population ranges from 1-2% to 20%; the female-to male ratio varies from 2:1 to 5:1.

Hystologically hemangiomas consist of different multilocular vascular channels divided by fibromuscular septa and delimited by endothelial cells.

In some cases, thrombosis occur in the vascular channels and hemangiomas show multiple spotty calcifications.

Liver hemangiomas are usually asymptomatic and diagnosis is occasional although patients with giant or cavernous hemangiomas (diameter >4-6 cm) may have abdominal symptoms (pain or dyspepsia) correlated to a mass effect or to the onset of complications as spontaneous hemorrhage.

Hemangioma is usually detected at routine examination by means of US, CT, MRI.

US findings are extremely variable in relationship to the dimension of lesion and to the liver echostructure, even though the hemangioma most commonly appears as homogeneous hyperechoic lesion with defined borders. Contrast-enhanced ultrasound (CEUS) is able to characterize hemangiomas showing the typical enhancement pattern of peripheral globular enhancement during the arterial phase and the progressive centripetal fill-in of the lesion during the portal and delayed phases.

The same enhancement pattern allows to characterize hemangiomas by using contrast-enhanced CT and MRI imaging. Moreover, the hyperintense aspect of hemangiomas at T2-weighted images helps in diagnosing them by means of MRI. Giant hemangiomas are lesions with inhomogenous aspect, hypodense at CT examination with typical pattern of peripheral and globular enhancement during the arterial phase but with incomplete central enhancement in the portal and delayed phases due to the presence of necrosis, thrombosis, hemorrhage, fibrous and cystic degeneration.

A rapid and homogeneous fill-in of the lesion is infrequent (16% of hemangiomas) and it usually occurs in hemangiomas less than 1 cm in diameter.

Such lesions tend to show size stability over time, nevertheless some isolated cases in literature have showed a significant size increase in follow-up examinatons. Even though the mechanism involved in the size increase of hemangiomas is still unknown, the high frequency of enlarging hemangioma found in females who undergo hormonal therapy or who are pregnant, suggests a pathogenesis role of the estroprogestinic hormone.

The angiomatosis lesions don't show surface receptors for the estrogenic hormones, therefore any direct effect on the progressive size of the lesions is excluded. A more probable hypothesis is that estrogens determine an ectasia of vascular channels that
compose the hemangiomas. Winkler and Poulsen reported that oral contraceptives, which are estrogen analogs, might induce periportal congestion increasing the plasmatic volume. The hemodynamic status in pregnant women is different from that of non-pregnant woman; in pregnant women the increase of the plasmatic volume is determined by activated rennin-angiotensyne system, because the estrogens stimulate the synthesis of angiotensinogen and secretion of renin.

Some authors suggested the involvement of some cythochines with angiogenetic action, such as the FGF produced by fetus-placenta complex in pregnancy women, in the progression of the angiomatosis lesions.

The possibility that an hemangioma grows over-time, even though rare, creates problems in the differential diagnosis with metastases in oncological patients, especially in case of hemangiomas with atypical pattern.

We present some cases of enlargement of liver hemangiomas occurred in both oncologic and non oncologic patients.
The imaging findings (US, CEUS, MR, CT) of enlarged hemangiomas over time will be illustrated and correlated to the clinical history of the patients. Possible causes of increase in size of hemangiomas will be discussed on the basis of literature and personal data. Imaging features useful for differentiating hemangiomas from other focal liver lesions, such as metastases, will be highlighted.

Case 1

In December 2008, a 33 year-old woman with pain in the right upper quadrant and a history of estrogen therapy, underwent ultrasound examination showing the presence of an inhomogeneous hyperechoic lesion in the right liver lobe, with well-defined and regular borders, 7.6 x 6 cm in diameter (Fig. 1 on page 8). By using contrast-enhanced ultrasound (CEUS) the lesion showed the typical enhancement pattern of hemangiomas consisting on peripheral globular enhancement during the arterial phase (Fig. 2 on page 8) and progressive centripetal enhancement with almost complete replenishment during the delayed phase (Fig. 3 on page 9).

In August 2011 the patient underwent an ultrasound examination which demonstrated an increase in size of the hemangioma which was 11x10 cm in diameter (Fig. 4 on page 10, Fig. 5 on page 11). Therefore the patient underwent an abdominal MRI that confirmed the diagnosis of cavernous hemangioma enlarging over time: in fact the lesion appeared hyperintense in T2-weighted images (Fig. 6 on page 12), with nodular peripheral enhancement and progressive centripetal fill-in on delayed images (arterial phase Fig. 7 on page 13 portal phase Fig. 8 on page 14 and late phase Fig. 9 on page 15).

Case 2

A 40 year-old male patient: during an US examination, performed for dyspepsia, an hyperechoic oval lesion 2 cm in diameter, with regular borders, was incidentally detected in VI liver segment. The US findings were consistent with the diagnosis of liver hemangioma. (Fig. 10 on page 16).

An US examination performed 12 years later showed the presence, in VI and VII liver segment, of a large slightly hyperechoic focal lesion, surrounded by fatty liver parenchyma, 9.8 cm in diameter and with an hypoechoic halo (Fig. 11 on page 17).

The patient underwent abdominal MRI to better characterize the liver lesion.
The lesion appeared markedly hyperintense in T2-weighted images (Fig. 12 on page 18) and showed the typical enhancement pattern of hemangioma (Fig. 13 on page 19, Fig. 14 on page 20 and Fig. 15 on page 21). Due to the exophytic development and the size of the lesion (Fig. 16 on page 22), the patient underwent surgical resection of VI liver segment (Fig. 17 on page 23 Fig. 18 on page 24). The final diagnosis was liver cavernous hemangioma. This was the only case of hemangioma’s enlargement with no history of estrogen therapy.

Case 3

A 67 year-old female patient with breast carcinoma: during the first abdominal US examination, an hypoechoic focal lesion in fatty liver, 1,5 cm in diameter, was detected in subdiafragmatic VIII liver segment. In order to characterize this lesion the patient underwent abdominal contrast-enhanced CT examination. The lesion showed an homogeneous enhancement during the arterial phase (Fig. 19 on page 25), persisting during the portal (Fig. 20 on page 26) and the delayed phases (Fig. 21 on page 27): the diagnosis was liver hemangioma.

Three years later, an US examination showed an increase in size of the lesion which measure 2,5 cm in diameter and was hypoechoic with acoustic posterior enhancement (Fig. 22 on page 28).

In CEUS examination the lesion showed typical globular enhancement during the arterial phase (Fig. 23 on page 29) with centripetal pattern enhancement (Fig. 24 on page 30) as well as in abdominal contrast-enhanced CT (Fig. 25 on page 31, Fig. 26 on page 32 and Fig. 27 on page 33) and in contrast-enhanced MRI: (Fig. 28 on page 34, Fig. 29 on page 35 and Fig. 30 on page 36).

US (Fig. 31 on page 37) and CT (Fig. 32 on page 38, Fig. 33 on page 39 and Fig. 34 on page 40) follow-up examinations performed 3 years later, showed a further slight size increase of the lesion.

Case 4

A 58 year-old female patient with breast carcinoma: first abdominal US follow-up showed severe fatty liver with two hypoechoic lesions located in III and IV segment, fairly detectable, less than 1 cm in diameter (Fig. 35 on page 41, Fig. 36 on page 42).

The patient underwent contrast-enhanced CT showing globular enhancement of both lesions during the portal phase (Fig. 37 on page 43, Fig. 38 on page 44); these lesions appeared homogeneously hyperdense during the late phase (Fig. 39 on page 45, Fig. 40 on page 46): CT diagnosis was liver hemangiomas.
These lesions have been stable in size for many years during the follow-up until 8 years later when, during an US examination, a dimensional enlargement and an echo-structural change of both lesions were demonstrated: the lesion located in the III segment appeared homogeneously hyperechoic (Fig. 41 on page 47) while the lesion detected in the IV segment appeared inhomogeneously hyperechoic (Fig. 42 on page 48). The surrounding liver parenchyma was less steatosic then in the first US control.

Abdominal contrast-enhanced CT (first lesion portal phase Fig. 43 on page 49, first lesion late phase Fig. 44 on page 50 second lesion portal phase Fig. 45 on page 51, second lesion late phase Fig. 46 on page 52) was repeated and the lesions enhancement pattern confirmed the diagnosis of hemangiomas.

Case 5

A 52 year-old female patient with breast carcinoma. During the US follow-up a focal hyperechoic lesion (2,3 cm in diameter) consisting with hemangioma, was detected in the VII liver segment (Fig. 47 on page 53). Two years later the lesion showed a dimensional enlargement (3 cm in diameter) and unchanged structure (Fig. 48 on page 54).

Case 6

A 60 year-old female patient with breast carcinoma. First US examination showed fatty liver and a hypoechoic liver lesion, 1,5 cm in diameter (Fig. 49 on page 55), located in the VIII liver segment and very similar to the lesion of patient 3.

A contrast-enhanced CT examination was performed to characterize the lesion which showed centripetal enhancement pattern (Fig. 50 on page 56, Fig. 51 on page 57 and Fig. 52 on page 58). The main CT feature useful to differentiate hemangioma from metastasis in case of a centripetal enhancement pattern is that, during the arterial or portal phase, metastases have peripheral continuous enhancement whereas hemangiomas show globular peripheral enhancement. The centripetal enhancement in metastatic lesions, more frequent in breast and colo-rectal metastases, is due to a fibrotic component present in the central part of these lesions which determines a persistent enhancement of the lesion during the late phase, causing differential diagnosis problems with hemangiomas.
Fig. 1

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Conclusion

Dimensional enlargement of hemangiomas, especially in oncological patients, can create problems in the differential diagnosis with metastases, particularly when metastases show a CT behaviour simulating the centripetal enhancement of hemangiomas, which is the case of breast or colon metastases with marked central fibrous component.

Therefore, it is important to know that hemangiomas can increase in size especially in patients under hormonal therapy, as patients with breast carcinoma which were the most of our cases.

It has been shown both by literature and by our cases, that hemangiomas can enlarge over time: this event, although quite infrequent, must be taken into consideration during the follow-up of oncological patients and also when evaluating patients without neoplastic illness.
References