

Giant Cavernous Hepatic Hemangioma Diagnosed Incidentally in a Perimenopausal Obese Female with Endometrial Adenocarcinoma: A Case Report

TIVADAR BARA JR.¹, SIMONA GURZU², IOAN JUNG², MIRCEA MURESAN²,
JANOS SZEDERJESI³ and TIVADAR BARA¹

*Departments of ¹Surgery, ²Pathology, and ³Intensive Care,
University of Medicine and Pharmacy of Tirgu-Mures, Tirgu-Mures, Romania*

Abstract. Hemangiomas are the most common benign tumors of the liver, considered giant when they exceed 50-100 mm in diameter. In the present report, we present a case of a 5.2-kg hemangioma of the right hepatic lobe, with hemangiomatous foci in the left lobe, which was incidentally diagnosed in a 53-year-old obese female hospitalized for uterine bleeding. The computed tomographic scan and physical examination revealed a giant abdominal tumor and hepatic hemangioma of the right hepatic lobe was suspected. Right hepatectomy and total hysterectomy with bilateral ovariectomy was performed. The histological examination of the surgical specimens confirmed the extremely giant cavernous hepatic hemangioma, and a synchronous pT1a endometrioid endometrial adenocarcinoma was also diagnosed. The patient remains alive without postoperative disorders, 6 months after surgery. To our knowledge, this is the first reported case of such huge hemangioma incidentally diagnosed in an obese female, with a synchronous endometrial adenocarcinoma of the uterus. Because obesity may cause hyperestrogenism, it might both increase the growth rate of hemangioma and the genesis of endometrial cancer in perimenopausal females.

The hemangioma is the most common benign tumor of the liver and is considered to be a vascular hamartoma. The incidence of liver hemangiomas (LHs) in the general population ranges from 0.6% to 20% (1-4).

Correspondence to: Senior Lecturer Janos Szederjesi, MD, Ph.D., Department of Intensive Care, University of Medicine and Pharmacy, 38 Ghe Marinescu Street, 540139, Tirgu-Mures, Romania. Tel: +40 745316221, e-mail: simonagurzu@yahoo.com

Key Words: Endometrioid adenocarcinoma, extremely large hemangioma, massive hemangioma, liver, uterus, synchronous tumor.

Macroscopically, LHs are hypervascular poorly circumscribed lesions. Microscopically, they consist of large cavities filled with venous blood coming from the hepatic artery, lined by endothelial cells and separated by fibrous septa (1). Due to unreported malignant transformation of LHs, their slow growth and low risk for bleeding, simple observation of asymptomatic lesions is usually recommended (1).

LHs can be single or multiple and their size can vary from a few millimeters to over 20 cm (5). The term 'giant hemangioma' is commonly used for lesions larger than 4 cm in diameter (1-5). LHs over 10 cm are considered extremely large or massive, and only occasional cases over 30 cm or weighing more than 2 to 3 kg have been reported (3, 4).

In this report, we present a representative case of an extremely large LH (>30 mm) incidentally diagnosed in a female hospitalized for a uterine tumor. The principles of diagnosis, therapy and differential diagnosis of giant LHs, and possible relation between obesity, occurrence of endometrial carcinoma and the rate of growth of the hemangioma are also briefly discussed, based on a literature review.

Case Report

A 53-year-old previously healthy obese female (body mass index 36.8 kg/m²) was hospitalized due to a one-month history of abdominal pain, nausea, vomiting, fullness, increase in abdominal volume and metrorrhagia. She was firstly consulted by a gynecologist who performed an endometrial biopsy. Because the physical examination also revealed an asymmetrical abdomen, above the xiphoid-pubic plane, with a visible tumor formation occupying the epigastrium, mesogastrium, the right flank and iliac fossa, she was transferred to our Department of Surgery. At palpation, it was observed that the above mentioned mass was cranial-caudal mobile with respiratory movements, and was firmly consistent to the touch.

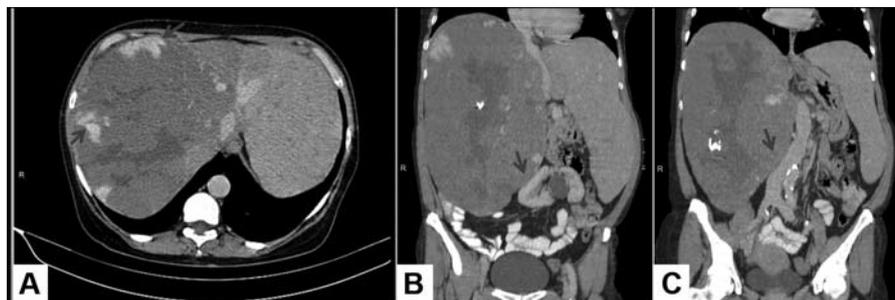


Figure 1. Computed tomography of the abdomen in axial view revealed a giant hemangioma in the right hepatic lobe, with specific progressive centripetal iodophilia (arrows) during venous/delayed phase (A). Compression of the kidney (arrow) (B) and cava vein (arrow) (C) was also apparent in the coronal view.

Ultrasonography and contrast-enhanced computed tomographic (CT) abdominal-pelvic examination revealed multiple hypoattenuating masses throughout the right hepatic lobe, with three small foci in the left lobe. The largest mass of the posterior segments of the right lobe were 180×160 mm in maximum axial diameter, and 310 mm in the cranial-caudal axis (Figure 1). These foci showed a progressive iodophilia from the periphery to the center, from the arterial through the venous/delayed phase, and had the specific appearance of 'tongues of fire', well observed in the main lesion. Giant hemangioma of cavernous type was suspected. The remnant hepatic parenchyma showed compensatory hypertrophy and diffuse heterogeneous iodophilia.

The inferior vena cava was compressed in the intrahepatic segment, with displacement of the suprahepatic veins and visualization of the right suprahepatic vein only in the distal region. The intra- and retroperitoneal abdominal structures, including the stomach, jejunum, ileum, pancreas, spleen, retroperitoneal large vessels and right kidney, were also compressed (Figure 1). Normal urinary excretion without dilatation of the calices was noted.

The uterus was normal in size, with homogeneous iodophilia. The serum parameters, including alpha fetoprotein, urea, creatinine, platelets, hemoglobin, and hematocrit, were within normal limits.

Because the endometrial biopsy showed a primary malignant tumor and the patient's status was not significantly modified, surgical management was decided. Signed informed consent was preoperatively obtained for performing surgery and publishing the case details. Intraoperatively, the extremely giant lesion was seen to involve the entire right hepatic lobe, without a well-defined capsule, and small bluish areas were also seen in the left hepatic lobe (Figure 2). Right hepatectomy, cholecystectomy, and total hysterectomy with bilateral ovariectomy was performed.

The gross examination of the liver surgical specimen showed a 310×210×135 mm bluish tumor with multinodular aspect, weighing 5,200 g. Several calcified and white myxoid

areas were seen on cut section (Figure 2). Microscopical examination confirmed the diagnosis of giant cavernous liver hemangioma.

In the uterine body cavity, a 25×15 mm exophytic tumor without invasion of the cervix was seen. Microscopically, the diagnosis of endometrioid endometrial adenocarcinoma with squamous cell differentiation was established. Because the invasion was limited to the inner part of the myometrium (2 from 10 mm), the tumor was classified as pT1a stage. The tumor cells expressed estrogen and progesterone receptors.

The postoperative evolution was favorable, without any recurrences or complains at six months after surgery. The left liver remnant foci did not grow in this period, and the patient lost weight (body mass index 34.4 kg/m²).

Discussion

Hepatic hemangioma is more common in females (72%), the female-male ratio ranges between 2:1 and 6:1, likely due to sex-specific hormones (2, 4). Moreover, increasing estrogen levels during pregnancy or in the postmenopausal period and also the use of oral contraceptives, hormonal replacement therapy, or steroids is believed to accelerate the expansion of this malformative lesion and even its rupture (1-4). Because obesity may cause hyperestrogenism, we suppose that it might also increase the growth rate of hemangioma and the genesis of endometrial cancer in perimenopausal females, as in the representative case of this report.

As hemangiomas are often detected incidentally, the differential diagnosis should not only taken into account tumors such as liver adenomas that could also be related hyperestrogenism, but also hepatocellular carcinomas, which can be associated with peliosis, and extremely large dilated sinusoids (6).

The ideal treatment of giant LHs, *i.e.* those larger than 10 cm, is still controversial (3). It is accepted that large symptomatic hemangiomas require therapy, but the precise therapy is not clearly defined. Some surgeons recommend resection of these

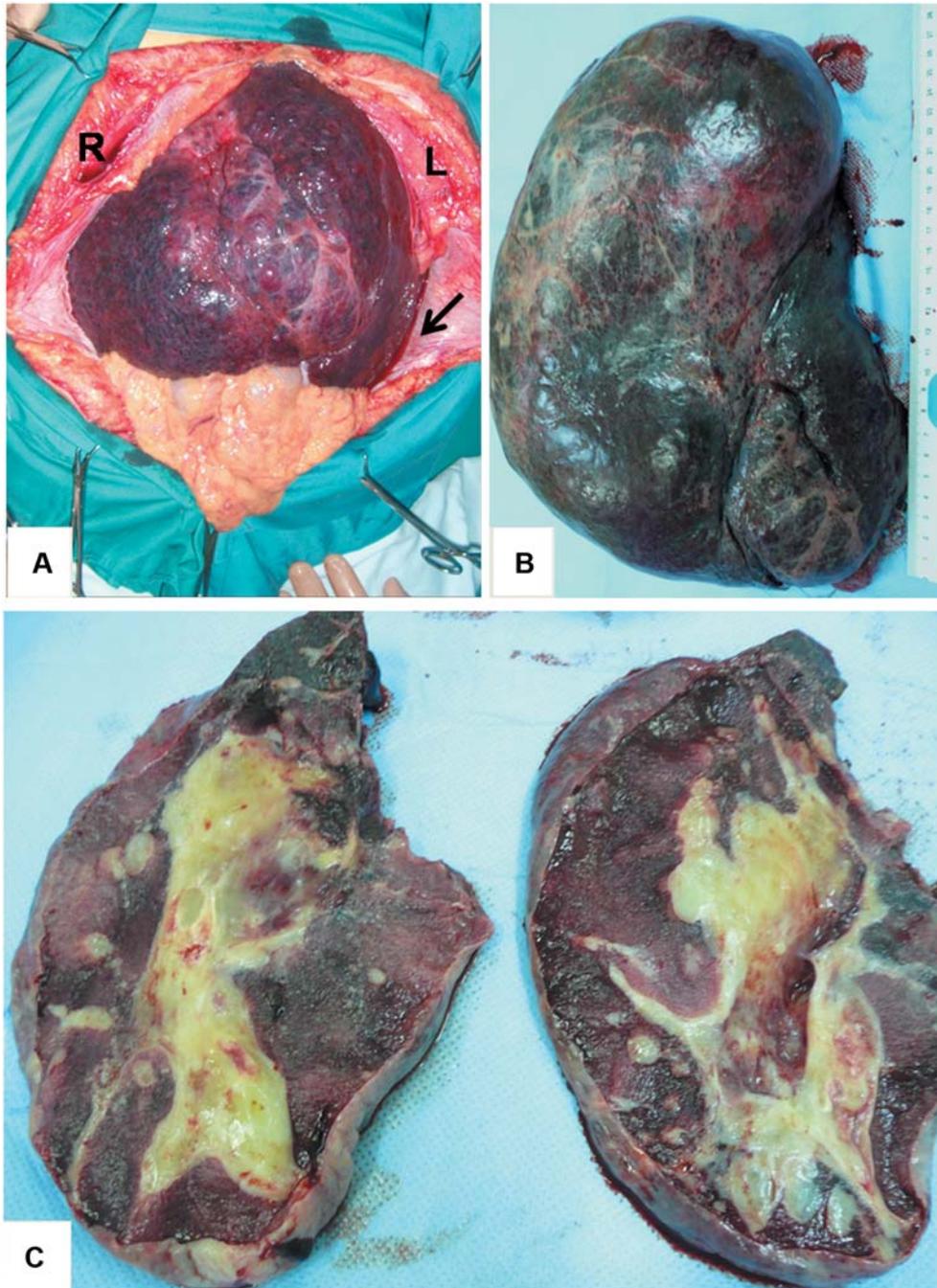


Figure 2. A: Intraoperative aspect of the giant hemangioma involving the entire right (R) lobe and a bluish hemangiomatous foci in the left (L) lobe (arrow). B: The surgical specimen of the right hepatectomy, weighing 5,200 g. C: Cut section of the resected tumor showing large yellowish degenerative myxoid areas.

lesions due to the potential risk of spontaneous rupture, yet spontaneous rupture is rarely described in the literature (7). In 1898, Hermann Pfannestil was the first to use hepatic resection to treat a hepatic hemangioma. Nowadays, palpable mass, association of gastrointestinal symptoms, thrombocytopenia,

traumatic or spontaneous rupture, Kasabach-Merrit syndrome, rapidly growing tumor and uncertain diagnosis are the main indications for surgery (3). Surgical resection refers to enucleation, hepatectomy, hepatic artery ligation, and orthotopic liver transplantation, depending on the location and size of the

LH but also on the associated complications (3-5, 7-10). However, in most studies, the hemangiomas were smaller than 10 cm, giant LHs mostly being presented as case reports (5). Moreover, the largest study that showed the principles of surgery for LHs larger than 10 cm (ranging from 10-35 cm) was performed in only 86 patients and was a retrospective observational study (3). Enucleation is indicated for well-delineated LHs, with a clearly defined fibrous capsule, and is rarely performed for giant LHs (3). Hepatectomy is the therapy of choice for giant hemangiomas or diffuse hemangiomatosis (3, 9, 10). Both enucleation and liver resection were proven to be safe for LHs larger than 10 cm (3). Orthotopic liver transplant is rarely performed in patients with large or diffuse lesions (4).

Other therapeutic modalities used in patients with symptomatic hepatic hemangiomas are laparoscopic or percutaneous radiofrequency ablation (11), and hepatic irradiation and chemotherapy (7, 8). Hepatic artery embolization may be the first option in patients with massive or diffuse lesions, or with comorbidities, where surgical resection is risky (4, 7). Polyvinyl alcohol, bleomycin, and lipiodol embolization are useful alternatives for patients whose hemangiomas are unsuitable for surgery (4, 7), the technique of transarterial embolization being similar to those used for hepatic metastases (12). Once the patient is stabilized, surgical resection can be performed. Transfusion might also be necessary in some cases.

In this report, due to an extremely large LH with multifocal aspect in both right and left lobes, and its compressive effect upon the surrounding organs, right hepatectomy was decided, with observational follow-up for the remnant liver. Due to the presence of two risk factors for hyperestrogenism (perimenopausal period and obesity), which might influence the growth rate of the remnant hemangiomatous foci, weight loss was recommended. This particular case highlights the necessity for complex examination of the patient to detect synchronous lesions. In obese patients, thorough imaging evaluation of the abdominal and retroperitoneal cavity is recommended, to detect slowly growing tumors.

Acknowledgements

The Authors acknowledge Dr. Claudia Constantin for technical assistance. The English language manuscript was polished by Lex Logos Editing Service.

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Received November 13, 2015

Revised December 12, 2015

Accepted December 18, 2015