

Successful surgical resection of solitary plasmacytoma of the liver mimicking hepatocellular carcinoma.



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A case report

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Successful surgical resection of solitary plasmacytoma of the liver mimicking hepatocellular carcinoma. A case report.

Solitary extramedullary plasmacytomas (SEMP) of the liver are very rare. We report the case of an elderly woman with a huge symptomatic SEMP of the liver mimicking hepatocellular carcinoma (HCC). The patient was a 89-year-old woman who presented with severe abdominal pain and a huge solid mass in the right hypochondrium. The laboratory data on admission revealed normal liver function tests. A multiphase computed tomography (CT) showed a huge solid mass of the left hemiliver, hypoattenuating on noncontrast images, dishomogeneously hyperenhancing in the late arterial phase, with washout in the portal venous and equilibrium phases. A 18F-FDG positron emission tomography (18F-FDG PET)-CT scan documented a marked FDG uptake within the lesion, without evidence of extrahepatic metastases. We considered the clinical and radiologic findings consistent with the diagnosis of high-grade HCC with areas of intratumoral necrosis precluding to possible tumour rupture.

Surgical resection was ultimately considered feasible with a reasonable risk and the patient underwent left hepatectomy with diaphragmatic resection. Pathological examination exhibited an extramedullary plasmacytoma. At immunohistochemical analysis neoplastic cells were positive for CD45, CD38, IRF4, HTPD52, kappa-chain, but negative for lambda-chain; Mib-1 proliferation index was 50%. Subsequent clinical evaluation excluded any sign of multiple myeloma, so that a diagnosis of truly localized SEMP of the liver was finally established.

To our knowledge, this is the first case of a solitary extramedullary plasmacytoma of the liver undergoing successful radical liver resection. The patient is alive and well 5 years after surgery without evidence of local recurrence and of systemic disease.

KEY WORDS: Extramedullary plasmacytoma, Hepatocellular carcinoma, Liver, Liver resection, Multiple myeloma

Introduction

Plasma cell neoplasms are characterized by a neoplastic proliferation of a single clone of plasma cells, and have heterogeneous clinical presentation. They typically present

as disseminated, bone marrow-based lesions (multiple myeloma), usually associated with multiple clinical, laboratory, and radiologic abnormalities. Localized plasma cell neoplasms represent 5% to 10% of all plasma cell neoplasms and are known as solitary plasmacytoma (SP)^{1,2}; they occur most frequently in bone, but can also be found outside bone in soft tissues (solitary extramedullary plasmacytoma, SEMP)². SP differentiate from myeloma for the absence of CRAB features (hypercalcemia, renal dysfunction, anemia, and multiple lytic bone lesions)². SEMP are solitary non-osseous neoplasms that arise outside of the bone marrow without evidence of multiple myeloma. They account for 3 to 4% of plasma cell

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malignancies and are usually located in the head and neck, most frequently in the upper aerodigestive (UAD) tract, but may also develop in the gastrointestinal tract, urinary tract, skin, lungs, etc.²⁻⁴. In most cases patients develop symptoms related to the location of the neoplasm, usually involving the UAD tract. Less than 20% of SEMP are located in the gastrointestinal tract, liver, pancreas, or in other sites. Regional lymph nodes may be metastatic^{2,3}.

SEMP of the liver are very rare. In a detailed review of the medical literature published until 1997, Alexiou et al reported only two cases of SEMP located in the liver out of 721 cases⁴. Three additional SEMP of the liver have been recently described⁵⁻⁷. Extramedullary plasmacytoma of the liver may sometimes mimic hepatocellular carcinoma (HCC) at presentation^{8,9}.

We report here the case of an elderly woman with a huge symptomatic SEMP of the liver mimicking HCC at preoperative evaluation, who underwent successful left hepatectomy with diaphragmatic resection.

Case Report

A 89-year-old white woman presented in February 2011 with severe abdominal pain of relatively rapid onset. She referred the appearance of an asymptomatic solid mass in the right hypochondrium since two months, without other relevant clinical symptoms. Her medical history revealed hypertension and nontoxic multinodular goiter.

Ultrasonographic examination of the abdomen had revealed an enlarged liver with a huge dishomogeneously hypoechoic lesion of the left hemiliver, without evidence of ascites. The laboratory data on admission revealed normal liver function tests, a negative viral hepatitis panel and serum α -fetoprotein levels within the normal range.

A liver mass protocol computed tomography (CT) scan of the abdomen showed a 14x18 cm solid mass of segments S2-S3-S4, partially involving segment S8 and extensively in contact with the middle hepatic vein, which was hypoattenuating on noncontrast images, dishomogeneously hyperenhancing in the late arterial phase with areas of hypoattenuation (Fig. 1A), with washout in the portal venous and equilibrium phases (Fig. 1B); the right hemidiaphragm was dislocated by the tumour; the right hemiliver and the spleen were normal; the splenic and the portal veins enhanced normally; there was no evidence of ascites and of nodal or distant metastases. A chest CT scan excluded pulmonary metastases. A 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET)-CT scan documented a marked 18F-FDG uptake within the lesion (Fig. 2), without evidence of metastases in the regional lymph nodes or in extrahepatic sites.

We considered the clinical and radiologic findings consistent with the diagnosis of high-grade HCC with areas of intratumoral necrosis precluding to possible tumour rupture. The tumour biopsy was considered at risk of bleeding. An echocardiogram and a spirometric exami-

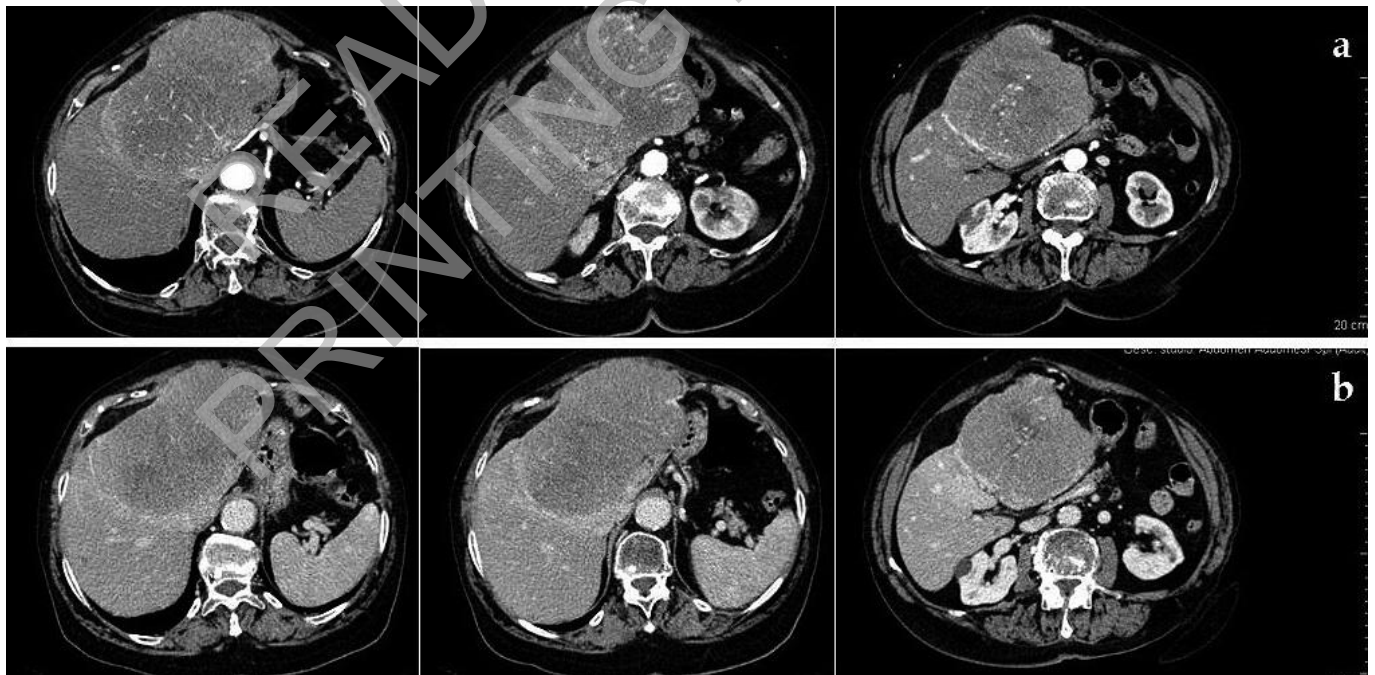


Fig. 1: The CT scan of the abdomen shows a 14x18 cm solid mass of liver segments S2-S3-S4, partially involving segment S8, hypoattenuating on noncontrast images, dishomogeneously hyperenhancing in the late arterial phase with areas of hypoattenuation (A), with washout in the portal venous and equilibrium phases (B).

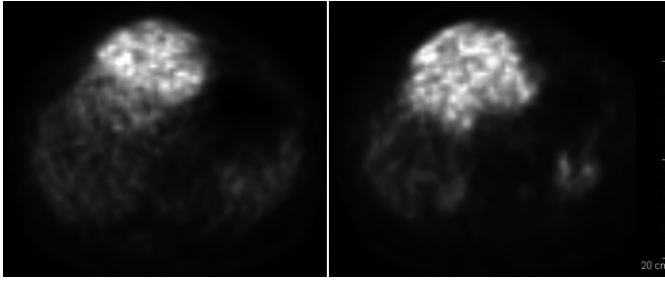


Fig. 2: The 18F-FDG PET-CT scan documents a marked FDG uptake within the lesion, without evidence of metastases in the regional lymph nodes.

nation, routinely performed in elderly candidates for major hepatic resection in our unit, showed substantially normal cardiovascular and respiratory functions. Surgical resection was ultimately considered feasible with a reasonable risk. Intraoperative exploration evidenced a huge tumour of the left hemiliver infiltrating the right emidiaphragm (Figs. 3A, 4A). Intraoperative ultrasonography (IOUS) showed a dishomogeneously hyperechoic

mass with hypoechoic areas, infiltrating the left portal vein and the left hepatic vein; the tumour was surrounded by a thin capsule and was extensively in contact with the middle hepatic vein, but without evidence of infiltration of the vessel walls; the right hemiliver was apparently free from disease. The infiltrated diaphragm was first resected to expose the confluence of the left and middle hepatic veins in the inferior vena cava; the confluence was then isolated and taped for safety (Fig. 3B). The left portal vein was isolated and ligated (Fig. 3C). IOUS-guided hepatic resection was then performed with the usual technique^{10,11}. The dissection plane was accurately monitored with ultrasonography. The middle hepatic vein was gently detached from the dorsal portion of the tumour along its thin capsule (Fig. 4B) and was ultimately spared. At the end of liver resection, the intraoperative echodoppler examination demonstrated a normal blood flow in the right portal vein and in the right and middle hepatic veins, with adequate perfusion of the remnant liver parenchyma. The hepatic stump was carefully inspected for bleeding and bile leak and was finally covered with a 95x48 mm TachoSil® Fibrin Sealant Patch (Fig. 3D), mainly to prevent bleeding from the wall of the middle hepatic vein denuded during the

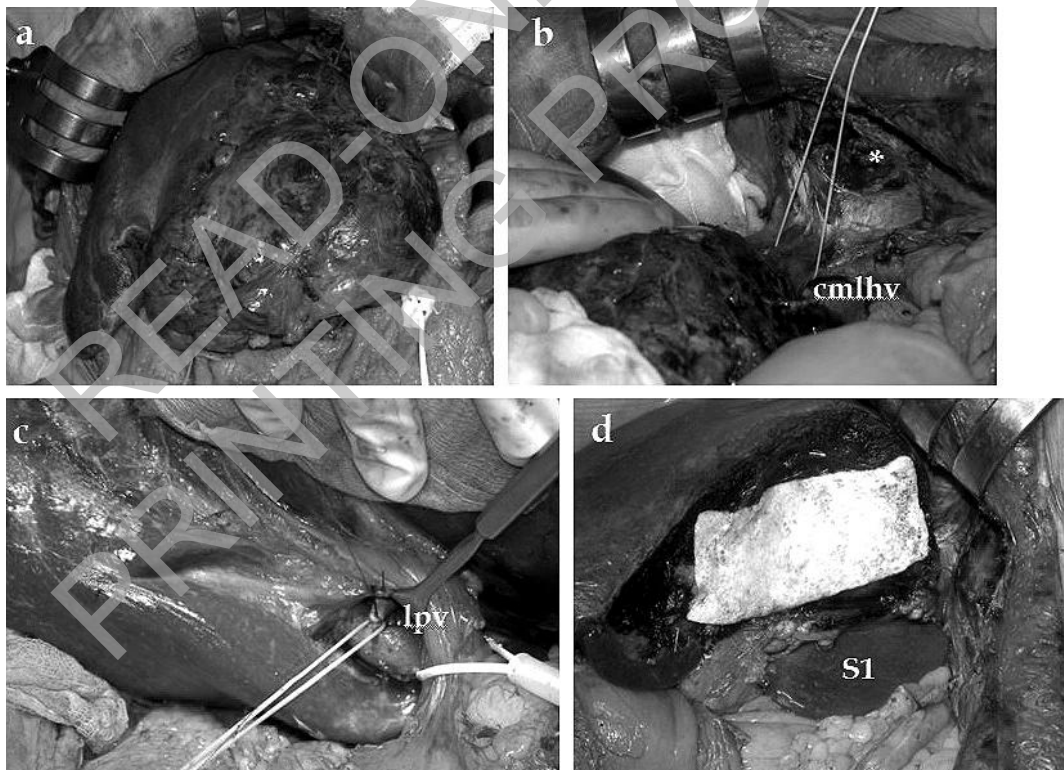


Fig. 3: At surgical exploration a huge tumour of the left hemiliver infiltrating the right emidiaphragm is evident (A). The infiltrated diaphragm has been resected to expose the confluence of the left and middle hepatic veins in the inferior vena cava; the confluence is isolated and taped for safety (B). The left portal vein has been isolated and ligated (C). After careful inspection for bleeding and bile leak, the hepatic stump has been finally covered with a 95x48 mm TachoSil® Fibrin Sealant Patch (D), to prevent bleeding from the wall of the middle hepatic vein denuded during the resection. clmhv: confluence of the left and middle hepatic veins; *: diaphragmatic resection; lpv: left portal vein; S1: caudate lobe.



Fig. 4: The specimen of the left hepatectomy (A). The margin of the dorsal portion of the tumour has been detached along its thin capsule (B) from the middle hepatic vein.

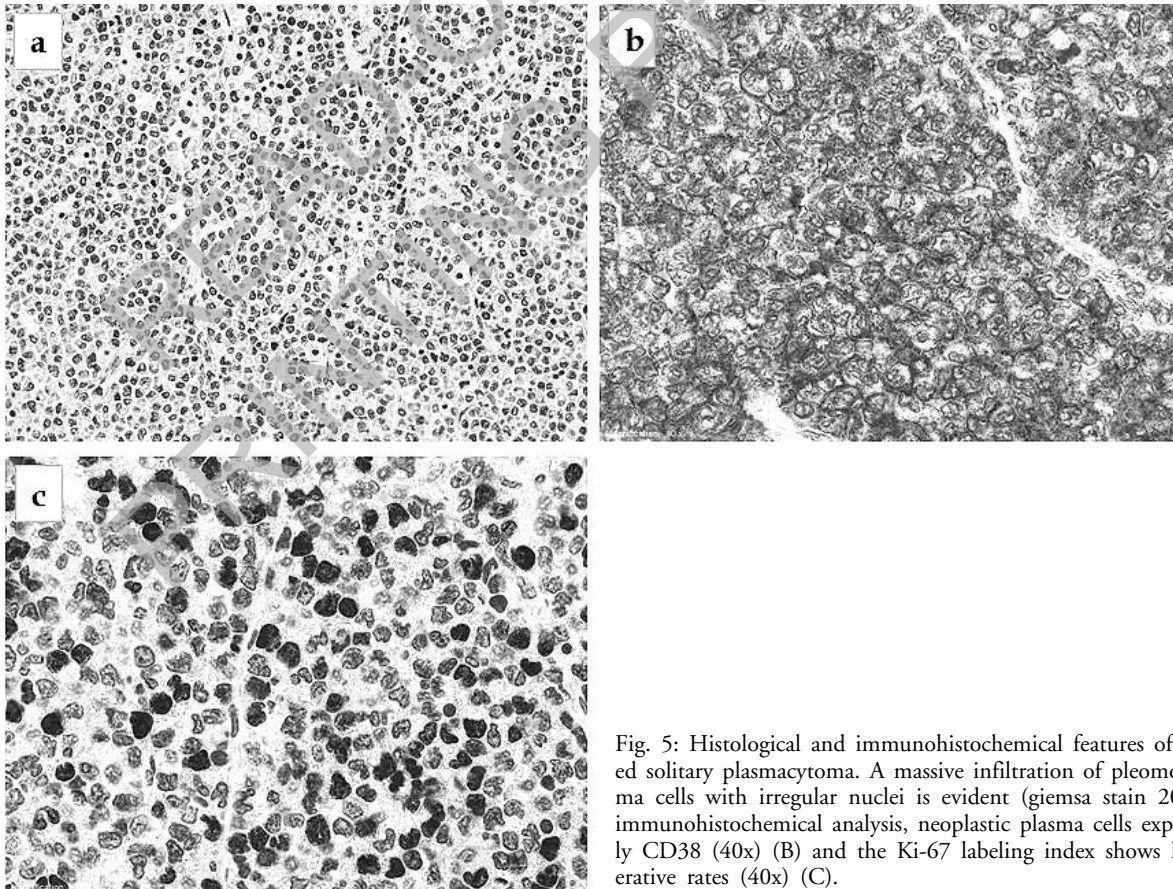


Fig. 5: Histological and immunohistochemical features of the resected solitary plasmacytoma. A massive infiltration of pleomorphic plasma cells with irregular nuclei is evident (giemsa stain 20x) (A). At immunohistochemical analysis, neoplastic plasma cells express strongly CD38 (40x) (B) and the Ki-67 labeling index shows high proliferative rates (40x) (C).

resection. The diaphragmatic hole was repaired with a Gore-Tex® patch. Intraoperative blood transfusions were not required.

Pathological examination showed that the hepatic parenchyma was massively substituted by neoplastic plasma cells with areas of necrosis, suggesting the diagnosis of extramedullary plasmacytoma of the liver (Fig. 5A); the tumour was partially surrounded by a thin capsule (Fig. 4B) without evidence of neoplastic infiltration and the resection margins were free of disease. Immunohistochemical analysis revealed that neoplastic cells were positive for CD45, CD38, IRF4, HTPD52 (Fig. 5B), positive for kappa-chain, but negative for lambda-chain; Mib-1 proliferation index was 50% (Fig. 5C).

The patient spent the first four days in the intensive care unit; the postoperative course was substantially uneventful and the patient was discharged 12 days after surgery. She was readmitted four weeks later in the Hematology Unit of our hospital to complete diagnostic evaluation. Bone marrow aspirate and biopsy were substantially normal without evidence of clonal plasma cells. A 18F-FDG PET-CT scan again excluded either bone disease or metastases in the regional lymph nodes and in extrahepatic sites. Levels of serum calcium, creatinine, albumin, lactate dehydrogenase, beta-2 microglobulin, C-reactive protein, immunoglobulins and free light chains were normal; serum protein electrophoresis and immunofixation were normal; urinary protein electrophoresis, immunofixation and Bence-Jones protein were normal. A diagnosis of truly localized SEMP of the liver was finally established.

Postoperative evaluation included ambulatory visit, routine blood and urine tests including serum calcium, creatinine, albumin, lactate dehydrogenase, beta-2 microglobulin, C-reactive protein, immunoglobulins and free light chains, serum protein electrophoresis and immunofixation, urinary protein electrophoresis and immunofixation, and contrast-enhanced thoraco-abdominal CT scan at six-month intervals, and 18F-FDG PET-CT scan at one-year intervals. The patient is in good conditions without recurrence or evidence of multiple myeloma 60 months after surgery.

Discussion

SEMP are solitary non-osseous neoplasms that arise outside of the bone marrow without evidence of multiple myeloma. They account for about 3% of plasma cell malignancies, occur at a median age of 55 to 60 years, and develop in males in approximately two-thirds of cases²⁻⁴. Patients usually develop symptoms related to the location of the neoplasm, involving the UAD tract in over 80% of cases. Less than 20% of SEMP are located in the gastrointestinal system, urinary tract, skin, lungs, etc.²⁻⁴.

The diagnosis of SEMP is based on the following fea-

tures: histologically proven tumour with evidence of clonal plasma cells in a single extramedullary site with or without lymph node involvement; absence of lytic lesions attributable to multiple myeloma at evaluation of the spine and pelvis with either PET-CT or magnetic resonance imaging; absence of clonal plasma cells at bone marrow aspirate and biopsy; no evidence of anemia, hypercalcemia, or renal insufficiency that could be related to clonal plasma cell proliferative disorders; low serum M-protein concentration²⁻⁴. The bone marrow of patients with SEMP should have no clonal plasma cells. Patients with clonal plasma cells up to 10 percent should be considered as having both SEMP and monoclonal gammopathy of undetermined significance and may have a higher risk of progression to symptomatic myeloma³. SEMP are highly radiosensitive and the treatment of choice is at present radiotherapy; for extramedullary tumours located in sites other than head and neck, curative surgical removal should be however considered a valid option if feasible, with or without combined radiotherapy; the role of chemotherapy, alone or in combination with other treatment modalities, is still controversial²⁻⁵.

SEMP has the best prognosis among all plasma cell tumours. Only a minority of patients with SEMP will develop local recurrence after successful radiotherapy, while about 10 to 15% of patients will ultimately develop multiple myeloma³. SEMP are considered to have better prognosis than solitary plasmacytomas of the bone, that progress to multiple myeloma in over 50% of cases; patient with SEMP that experience multiple myeloma during the follow-up are expected to have 100% 5-year survival rates, compared to 33% of patients with solitary plasmacytoma of the bone^{2,4}.

In a series of 721 patients collected from the literature between 1905 and 1997⁴, SEMP in non-UAD regions were located in the digestive system in 40% of cases, in the urogenital region in 25,2%, in the skin in 16,8%, in the lung in 9,7%; other sites were anecdotal; regional lymph nodes were involved in less than 3% of cases. Surgery alone or in combination with radiotherapy was performed in more than 75% of these patients. After treatment 64,7% of patients remained free of recurrence or multiple myeloma, while 21,2% developed a recurrence and 14,1% converted to multiple myeloma. The authors concluded that surgical excision alone is sufficient for resectable SEMP localized in the soft tissues, while postoperative radiotherapy should be considered for patients not eligible for radical removal.

In the same series, only two cases of SEMP were located in the liver, which accounted for 1,3% of SEMP situated outside the UAD tract areas⁴.

Petrucci et al reported a liver plasmacytoma without evident systemic disease treated with six courses of melphalan and prednisone with 5-year clinical remission; however the bone marrow biopsy showed 10% of plasma cells infiltration, which should be considered indica-

tive of both SEMP and monoclonal gammopathy of undetermined significance³. Three additional SEMP of the liver have been recently described⁵⁻⁷. In all the cases the liver was the only localization, the tumours were composed at histology by clonal plasma cells and the diagnosis was confirmed at immunohistochemical staining, bone marrow biopsy and bone imaging were normal, with no evidence of a monoclonal protein in the serum and urine. All the patients were successfully treated with local radiation without further evidence of disease at follow-up.

Plasmacytoma of the liver may sometimes mimic hepatocellular carcinoma (HCC) at presentation. Ghobrial et al described the case of an elderly man presenting with nonspecific abdominal pain and a 4,4-cm hepatic tumour; at multiphase CT, the neoplastic mass demonstrated an enhancement pattern identical to that expected for HCC; in the absence of the common risk factors for hepatic cirrhosis, a core biopsy of the mass, as well as additional clinical and radiologic assessment, finally documented a multiple myeloma⁸. Ueda et al reported the case of a 76-year-old woman with a past history of multiple myeloma with IgA type, admitted with sudden onset intense abdominal pain and severe anemia. Abdominal dynamic CT revealed two liver tumours at segment S1 and S6, respectively; the nodule in S1 was enhanced at the arterial-phase and washed out at the portal-phase, with hematoma and accumulation of ascites around the tumours; a spontaneous rupture of HCC was diagnosed and treated with transarterial chemoembolization (TACE); the subsequent clinical course was however atypical for HCC rupture, as shown by the development of a huge extrahepatic abscess extending from the liver tumours. Immunohistochemical analysis of the tumour biopsy specimen revealed massive infiltration of plasma cells expressing IgA and κ chain, and a diagnosis of spontaneous rupture of extramedullary liver plasmacytoma was finally accomplished⁹.

To our knowledge, we report the first case of truly localized SEMP of the liver undergoing surgical resection. After extensive preoperative evaluation, we considered the clinical and radiologic findings consistent with the diagnosis of high-grade HCC with areas of intratumoral necrosis precluding to possible tumour rupture. The absence of liver cirrhosis and of increased levels of alpha-fetoprotein were not considered in contrast with the diagnosis of HCC, especially in presence of a negative viral hepatitis panel¹². Cardiovascular and respiratory functions were substantially normal despite advanced age, so that the surgical resection was ultimately considered feasible with a reasonable risk. IOUS-guidance during hepatic resection permitted to perform an accurate dissection of the parenchyma and to spare the middle hepatic vein, gently detached from the thin capsule surrounding the tumour; at the end of liver resection, the intraoperative echodoppler examination demonstrated an adequate perfusion of the remnant liver parenchyma; this

case confirms the paramount importance of IOUS-guidance during hepatic resection to spare liver parenchyma and to prevent dangerous damages of major intrahepatic vessels^{10,11}. The adequate treatment of the hepatic stump is also mandatory in these circumstances, to prevent either bile leakage or risky bleeding from the wall of denuded major intrahepatic vessels.

In conclusion, we report here the case of an elderly woman with a huge symptomatic SEMP of the liver mimicking HCC at preoperative evaluation; she underwent successful left hepatectomy with diaphragmatic resection and is alive and well 5 years after surgery without evidence of local recurrence and of systemic disease. Potentially curative surgical resection is an adequate option for the treatment of solitary extramedullary plasmacytoma of the digestive system.

Riassunto

Il plasmocitoma extramidollare solitario (SEMP) del fegato è una neoplasia estremamente rara. Viene riferito il caso di un'anziana donna affetta da un voluminoso SEMP con caratteristiche simili a quelle di un carcinoma epatocellulare (HCC). Si tratta di una donna di 89 anni giunta alla nostra osservazione con un dolore addominale piuttosto severo, di recente insorgenza, ed una voluminosa massa situata nell'ipocondrio destro. I dati di laboratorio all'ingresso non evidenziavano alterazioni della funzionalità epatica; i valori di alfa-fetoproteinemia erano nella norma; non erano presenti markers di un'infezione da virus dell'epatite B e C. Una tomografia assiale computerizzata (TC) multifasica documentava la presenza di una voluminosa neoplasia dell'emifegato sinistro, ipodensa alle immagini senza mezzo di contrasto, disomogeneamente iperdensa in fase arteriosa, e con "washout" nelle fasi portale e di equilibrio. Una tomografia ad emissione di positroni con 18F-FDG (18F-FDG PET)-TC evidenziava una marcata captazione del radiocomposto da parte della neoplasia, in assenza peraltro di metastasi a distanza. Le caratteristiche cliniche e radiologiche della lesione erano interpretate come compatibili con una diagnosi di HCC scarsamente differenziato con aree di necrosi intralesionale verosimilmente in evoluzione verso la rottura spontanea.

La valutazione clinica complessiva ci faceva reputare accettabile il rischio chirurgico e la paziente veniva sottoposta ad un'epatectomia sinistra con resezione parziale dell'emidiaframma destro. Il decorso postoperatorio era sostanzialmente regolare e la paziente veniva dimessa in 12° giornata postoperatoria. L'esame istologico definitivo deponeva per un plasmocitoma extramidollare. L'analisi immunoistochimica dimostrava che le cellule tumorali esprimevano CD45, CD38, IRF4, HTPD52, catene leggere kappa ma non catene leggere lambda; l'indice di proliferazione Mib-1 era del 50%. La successiva valutazione clinica permetteva di escludere qualsiasi manifesta-

zione di mieloma multiplo; si giungeva pertanto alla diagnosi di plasmocitoma extramidollare localizzato esclusivamente al fegato.

Stando ai dati della letteratura scientifica, si tratta del primo caso di SEMP del fegato sottoposto con successo ad una resezione epatica curativa. La paziente è vivente ed in buone condizioni cliniche a distanza di 5 anni dall'intervento chirurgico, in assenza di recidive loco-regionali e di manifestazioni di mieloma multiplo.

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