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Isolated splenic metastasis of endometrial adenocarcinoma – a case report

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Rezumat

Metastaza splenică izolată de adenocarcinom endometrial – prezentare de caz

Splina este rareori sediul unor tumori solide, non-hematologice, determinările secundare splenice izolate de adenocarcinom fiind descoperiri extrem de rare, indiferent de proveniența și tipul histologic al tumorii primitive. Prezentăm cazul unei paciente cu metastază splenică unică descoperită tomografic la doar 20 de luni după intervenția chirurgicală curativă pentru adenocarcinom endometrial, la care diagnosticul de certitudine a fost stabilit prin examen histologic și imunohistochimic al piesei de splenectomie. Metastazarea pe cale hematogenă a cancerului endometrial se produce cel mai frecvent în plămâni, ficat sau oase, splina fiind foarte rar afectată. În literatura de specialitate sunt citate până în prezent doar 12 cazuri de metastaze splenice solitare având ca punct de plecare adenocarcinoame endometriale. Particularitatea cazului prezentat de noi este metastazarea splenică izolată precoce, la mai puțin de doi ani de la intervenția chirurgicală curativă (față de media de 4-5 ani citată în literatură) a unui cancer endometrial încadrat din punct de vedere histologic în grupul cu risc scăzut de recidivă (adenocarcinom endometrioid bine diferențiat). În concluzie, deși determinările secundare splenice solitare sunt foarte rare, incidența cazurilor raportate în literatura de specialitate este în creștere, iar apariția lor tardivă (la câțiva ani de la rezecția tumorii primare) și lipsa simptomatologiei până când tumora ajunge la dimensiuni apreciabile sau se necrozează, justifică explorarea imagistică abdominală periodică, pe termen lung, în cadrul supravegherii după intervenția chirurgicală curativă inițială. Tratamentul lor de elecție este splenectomia pe cale clasică, care trebuie urmată de chimioterapie, pentru a preveni dezvoltarea altor posibile micrometastaze.

Cuvinte cheie: metastază splenică izolată, adenocarcinom endometrial, splenectomie

Abstract

The spleen in rarely the place for solid, non-haematological tumors, isolated splenic metastases from adenocarcinomas being extremely rare findings, regardless of the origin and the histological type of the primary tumor. We present the case of a female patient with isolated splenic metastasis diagnosed by abdominal computer tomography at only 20 months after curative surgery for endometrial adenocarcinoma, in which the final diagnosis has been established by histological and immunohistochemical examination of the splenectomy piece. The haematogenous dissemination of the endometrial cancer occurs most commonly in the lungs, liver or bones, the spleen

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being rarely affected. In the medical literature there are cited up to date only 12 cases of solitary splenic metastasis from endometrial adenocarcinoma. The particularity of the case presented by us is the early appearance of an isolated splenic metastasis, at less than two years after curative surgery (compared to an average of 4-5 years cited in the literature), from an endometrial cancer which was classified histologicaly in the group with low-risk for relapse (well differentiated endometrioid adenocarcinoma). In conclusion, although solitary splenic secondary determinations are very rare, the incidence of the reported cases in the medical literature is increasing, their late appearance (a few years after the primary tumor's resection) and the lack of symptoms until the tumor reaches appreciable size or it complicates with necrosis, justifies the periodic abdominal imaging examination, on long-term, for postoperative monitorisation after the initial curative surgery. Their treatment of choice is open, classical splenectomy that must be followed by chemotherapy in order to prevent the development of other possible micrometastases.

Key words: isolated splenic metastasis, endometrial adenocarcinoma, splenectomy

Introduction

The spleen is rarely the place for solid, non-haematological tumors. Isolated splenic metastases from adenocarcinomas are extremely rare findings, regardless of the origin and the histological type of the primary tumor.(1) The appearance of the splenic metastases is usually late in the clinical onset, at 4-5 years after the surgical intervention for the primary tumor (2), and sometimes it may be the first manifestation of recurrence in gynecologic malignancies. (3) The discovery of the splenic metastasis at less than 2 years from the radical surgery for endometrial cancer, the rarity of this location, it's uniqueness and size are the reasons for which we present this case.

Case presentation

The 57 years old female patient, known with endometrial adenocarcinoma, operated in december 2009 in other medical institution (total histerectomy with bilateral anexectomy), with histopathological examination of the piece of surgical resection showing well/medium differentiated endometrioid adenocarcinoma (G1/G2) of the uterine corpus, postoperative stage pT1b pN1, is admitted in our clinic in July 2011 for the investigation of an abdominal pain located in the left superior quadrant, which appeared in the last month.

At the admission the patient presented with influenced general status, afebrile, with grade III splenomegaly and normal intestinal transit.

Biochemistry studies were normal.

The abdominal ultrasound and CT scan described a tumoral splenic mass of aproximately 12/8 cm, with necrotic aspect, without other important changes. (Fig. 1A, B)

The patient was subjected to surgery on July 19 2011, the intraoperatory finding being isolated splenic tumor, for which splenectomy by celiotomy was performed. (Fig. 2 A, B) A liver biopsy was also realised because the histological diagnose was established later on the rezection piece, therefore at the moment of surgery a haematological disease was not rouled out, and for it's staging the liver biopsy would have been necessary.

The histopathological examination of the surgical resection piece revealed:

1. *Splenectomy piece (Weight = 800 grames): the spleen is increased in volum and weight, transformed by a tumor (12,5 cm in diameter) formed from a grey color*

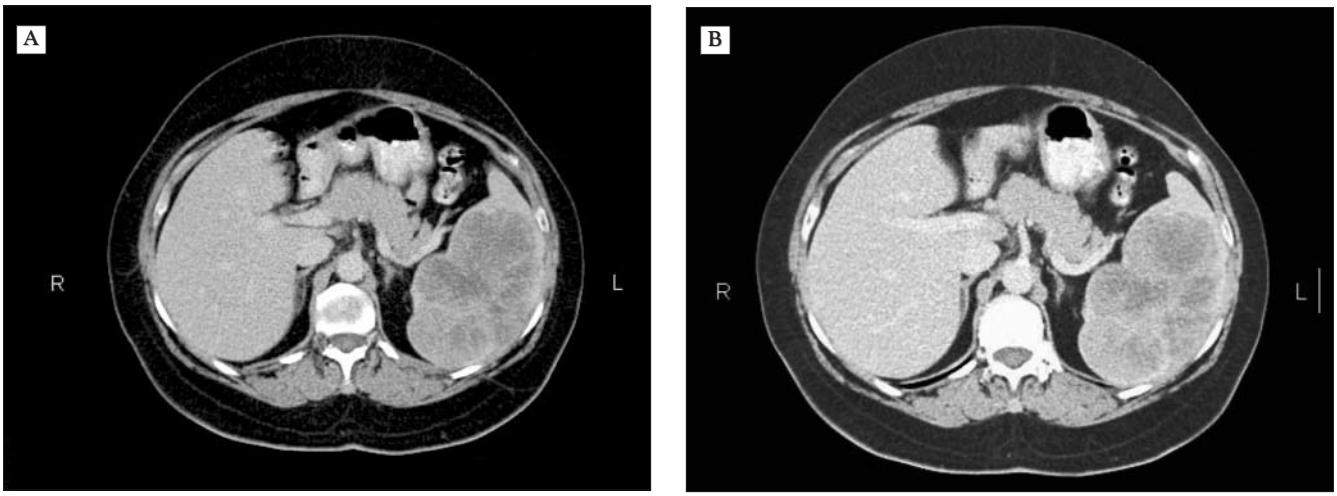

Figure 1 A, B. *Splenic tumor with necrotic aspect (CT scan).*

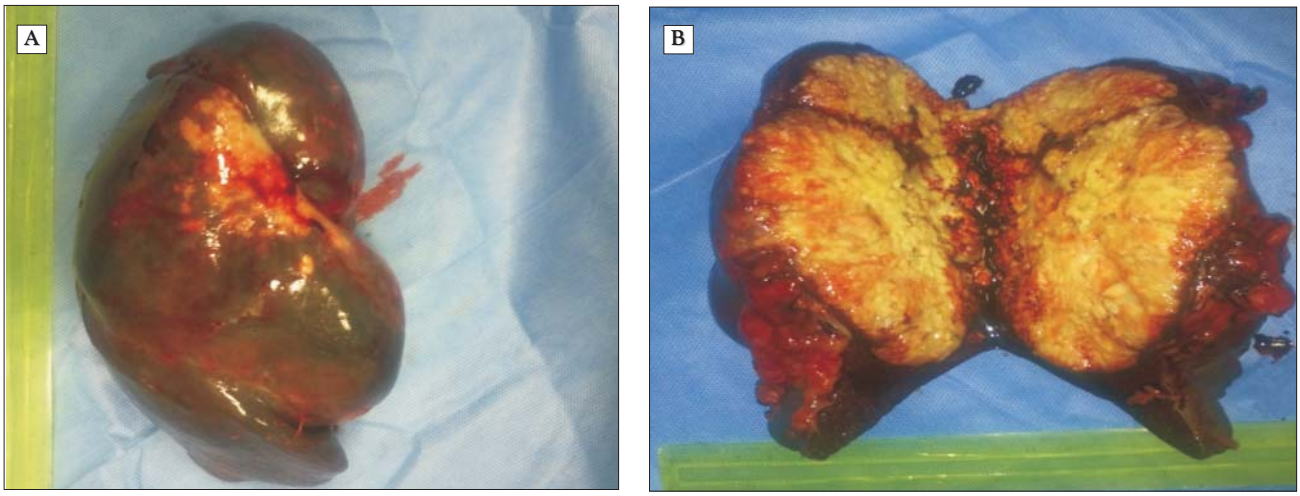

Figure 2 A, B. *Splenic tumor (splenectomy piece)*

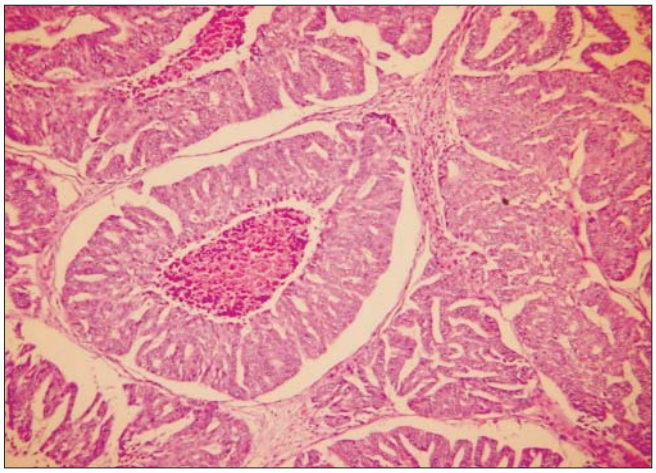

Figure 3. *Splenic metastasis of well differentiated tubulo-papilary adenocarcinoma (G1) (HE 10x)*

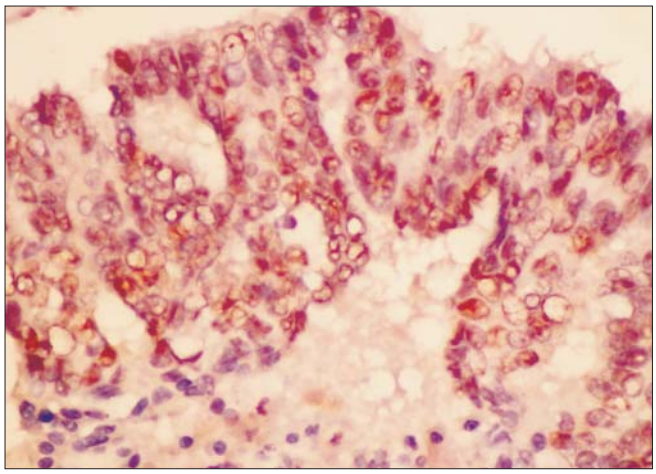

Figure 4. *Metastatic splenic adenocarcinoma positive for the estrogen receptors (imunohistochemical examination 40x)*

proliferation with the histopathological aspect of a well differentiated tubulo-papilary adenocarcinoma (G1). (Fig. 3)

2. *Liver tissue fragment (surgically obtained) presenting intralobulary lesions of grade I macrovesicular steatosis.*

The immunohistochemical examination was positive for the estrogen (Fig. 4) and progesterone receptors (Fig. 5), as well as for vimentin in the tumoral cells (Fig. 6) – similar to the immunohistochemical examination of the histerectomy piece from 2009.

The postoperative evolution was favorable, with the resumption of the intestinal transit and of the digestive tolerance, without complications. After the recovery from surgery, the patient was reffered to the oncology department, where carboplatin chemotherapy was initiated.

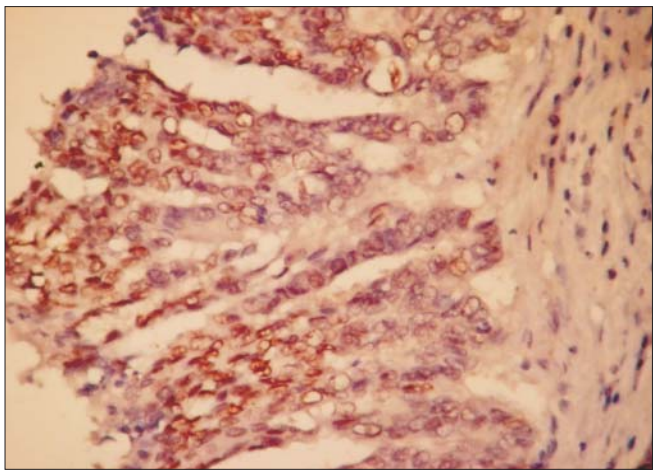

Figure 5. *Metastatic splenic adenocarcinoma positive for the progesterone receptors (imunohistochemical examination 40x)*

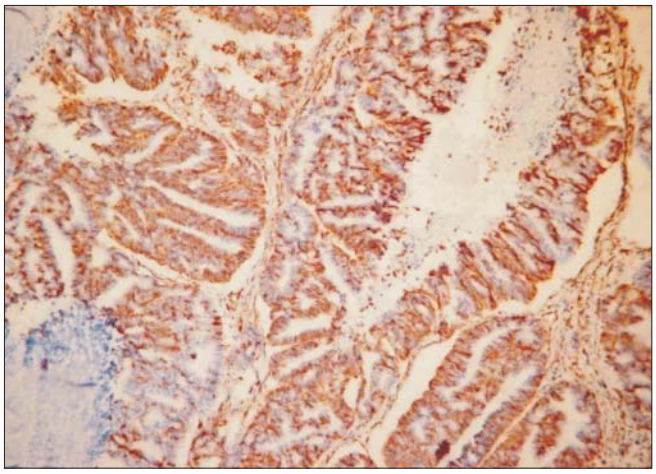

Figure 6. *Metastatic splenic adenocarcinoma positive for vimentin (imunohistochemical examination 20x)*

Discussions

The non-lymphatic splenic tumors are divided in:

1. Cystic tumors;
2. Benign solid tumors;
3. Primitive malignant solid tumors (others than systemic neoplasias of the lymphatic tissue and of the reticulo-endothelial system);
4. Secondary malignant solid tumors (splenic metastases);
5. Pseudoinflammatory tumors.

The spleen is rarely the place in which solid, non-haematological tumors appear. While cystic tumors have frequently parasitic ethiology, only some of them being non-parasitic cysts, (4) primitive solid splenic tumors are of vascular or connective tissue origin. Splenic metastasis of solid tumors are more common than primitive solid tumors, the incidence of reported cases being increasing, however, they remain rare findings (about 7% in necroptic studies)(2), and can be found in the case of intraperitoneal dissemination of the primitive tumor - sometimes along with other locations, being positioned in the splenic capsule or subcapsulary and usually multiple or, rarely, isolated intraparenchimatous metastases, often with bigger size, occurring through haematogenous dissemination. The most common primitive sources for multiple splenic metastasis are breast, lung, colon and rectum, ovary and melanoma, while solitary splenic metastases are coming especially from colorectal or ovarian cancers. (5) In the medical literature there are cited so far about 100 cases of solitary splenic metastasis, approximately half of them having as primary site the female genital tract, most frequently ovarian tumors, in only 12 cases the primary tumor being endometrial adenocarcinoma. (6)

The haematogenous dissemination of the endometrial cancer occurs most commonly in the lungs, liver or bones, the spleen being rarely affected. (7)

The rarity of the intrasplenic metastases from solid tumors can be explained by the peculiarities of vascularization (as known the venous circulation of the gastrointestinal tract is largely tributary to the portal vein that carries blood to the liver, the main place for secondary tumoral determinations, cells that escape this first filter often reaching the lung, the second organ in the frequency for occurrence of metastases; also the sharp angle of the splenic artery, which makes it difficult for tumor emboli to enter the spleen, the rhythmic contractile nature of the spleen and the absence of afferent lymphatics) (8) and the inhibitory effect of the splenic environment on metastatic tumor cells (many of which are destroyed by activation of the immune response, some suffering a temporary inhibition and developing after a latent period that may last several years). (5) In our case the diagnosis of the splenic metastasis was established 20 months after total hysterectomy with bilateral ovarectomy for the endometrial adenocarcinoma. It is worth mentioning that the postoperative staging after the initial surgery for endometrial cancer was pT1b pN1 (one of eight regional lymph nodes analyzed showed carcinomatous invasion), so although the invasion of the uterine wall did not exceed half of it's thickness, the patient had a postoperative TNM stage IIIc. Postoperative course of treatment for malignant tumors in stage III endometrial cancer for which curative surgery was possible is currently controversial, the last ESMO giudelines in 2008 stipulating that it is similar to the treatment of patients with stage I or II disease, but individualized according to specific clinical and pathological data.(9) In our case the tumor type was endometrioid adenocarcinoma with a high degree of differentiation (G1/G2), that classifies it in the group with low risk of relapse, so the patient did not undergo post-operative adjuvant treatment.

Returning to the present situation, to the splenic tumor diagnosed by imaging procedures, the main problem of differential diagnosis was lymphoma, the lack of systemic or lymph node involvement being an important argument against a lymphoid malignancy. The presence of a cystic tumor was ruled out by imaging studies, which revealed the solid density of the splenic tumor. Vascular tumors or pseudotumors were also into discussion, diagnostic certainty being established by the histological examination of the splenectomy piece, (10) which revealed metastatic adenocarcinoma. Confirmation of the endometrial primary site for this secondary determination was obtained by immuno-histochemical examination, (7) which showed positivity of vimentin and of progesterone and estrogen receptors in the tumoral cells. (11)

Regarding the treatment of splenic metastases from carcinoma, it varies depending on the type of dissemination of the tumor. For subcapsular metastases, often multiple, occurring in by peritoneal dissemination of ovarian or colorectal cancer, splenectomy is usually not curative, unless it is possible to also remove by complex surgical intervention the affected peritoneum. Splenectomy is, by the other hand, the treatment of choice in solitary secondary tumors that develop in the spleen parenchyma, (6) followed later by chemotherapy in order to try the destruction of other possible micrometastases. Intraoperative manipulation of the spleen, which usually has considerable dimensions (in our case only the

tumor had 12 cm), must be made with caution to avoid tumor rupture, (12) therefore the classical splenectomy is indicated, as it was performed also in the case we present, and not the minimum invasive laparoscopic approach, in which the spleen is fragmentated in the endo-bag to be extracted. (13)

Endometrial cancer chemotherapy schemes may include (alone or in combination): platinum salts, cyclophosphamide, 5 fluoro-uracil, isofosfamid, paclitaxel. (14) In tumors showing progesterone receptors, hormone therapy can also be effective, the most used drug from this category being medroxyprogesterone acetate. (15) Our patient was guided after the postoperative recovery in the oncology department for chemotherapy initiation, the scheme applied in this case being based on carboplatin.

Conclusions

Solitary splenic secondary determinations of endometrial adenocarcioma are very rare, but the incidence of the reported cases in the medical literature is increasing, their late appearance (a few years after the primary tumor's resection) and the lack of symptoms until the tumor reaches appreciable size or it complicates with necrosis, justifies the periodic abdominal imaging examination, on long-term, for postoperative monitorisation after the initial curative surgery. Their treatment of choice is open, classical splenectomy that must be followed by chemotherapy in order to prevent the development of other possible micrometastases.

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