Case Reports

Solitary splenic metastasis of endometrial carcinoma ten years after hysterectomy. Case report and review of the literature

C. Hadjileontis[1, 2], *M.D.*; **I. Amplianitis**[1], *M.D.*; **C. Valsamides**[3], *M.D.*; **G. Harisis**[3], *M.D.*; **H. Nepka**[1], *M.D., Ph.D.*; **A. Kafanas**[1], *M.D.*

[1]*Pathology Department, Serres General Hospital;* [2]*Pathology Department, Medical School, Aristotle University of Thessaloniki*
[3]*Surgical Department A., General Hospital Serres (Greece)*

Summary

Solitary carcinomatous metastases to the spleen are rare. The reports of such cases in the literature usually concern late stages of the disease, with generalized carcinomatosis and metastatic foci in several other organs.

Primary tumors that most often metastasize to the spleen are carcinomata of the breast, lung and ovaries, as well as malignant melanomata. Less often, carcinomata of the stomach, large bowel and kidneys are reported to implicate the organ with metastatic disease. The presence of solitary splenic metastasis of endometrial origin however, is extremely rare.

We present a case of a 53-year-old female patient who ten years after hysterectomy due to the presence of endometrial carcinoma developed a metastatic focus to the spleen. This focus was diagnosed on the grounds of histology and immunohistochemistry, after splenic excision, to be of endometrial origin.

Together with this case presentation, several aspects of the disease and its differential diagnosis are discussed, in correlation with the current literature.

Key words: Endometrial carcinoma; Solitary splenic metastasis; Immunohistochemistry.

Introduction

Endometrioid carcinoma is the most common infiltrative carcinoma of the female genital tract. The risk of its development is estimated to be 3% in all women during their lifetime, most of the cases however concern postmenopausal age [1].

Carcinoma metastasizes by order of frequency to the regional lymph nodes, the ovaries, the liver, lungs and pleural cavity, bones, brain, intestinal tract and adrenals [1, 2]. The potential of splenic metastasis is – based on a study of 111 autopsies of women with a history – reported to be 3.6% and usually concerns advanced stages of the disease with generalized carcinomatous spread [2].

The presence of such metastatic foci in the spleen is indicative of carcinomas with high metastatic potential, which express endothelial adhesion molecules and usually colonize the organ through the blood circulation [8]. About 60% of all gynecological cancers are reported to be of such a potential. On the other hand, malignancies that affect the spleen with solitary metastatic foci are of adenocarcinomata type originating predominantly from the ovaries. Diffuse metastases to the spleen however usually originate from the breast and lungs [12].

Splenectomy remains the treatment of choice in cases of splenic metastatic disease, nevertheless complementary chemotherapy and Roentgen radiation therapy seem to restrict the chances of recurrence [5, 6, 12].

Revised manuscript accepted for publication May 14, 2003

The most accurate way to reach a diagnosis, especially in cases of solitary splenic metastasis, is the histological examination of core biopsy aspirates, usually are performed under ultrasound or CT guidance [7, 12].

Case Report

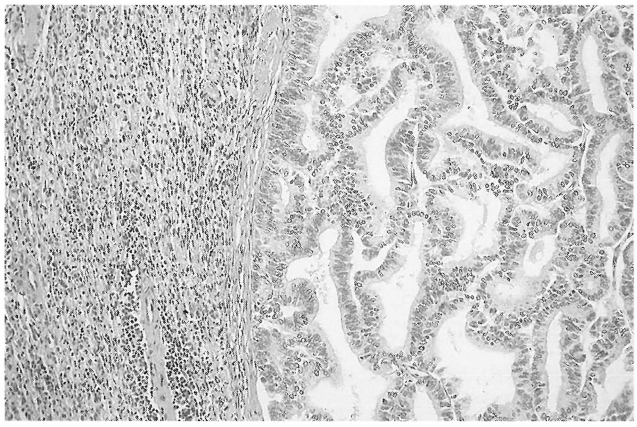
We present a case of a 53-year-old female patient, who ten years after hysterectomy and complementary hormonal chemotherapy performed due to the development of endometrial carcinoma, presented with symptoms of anemia. Clinical examination revealed splenomegaly and the CT-scan showed a solitary mass at the spleen measuring 5 cm in diameter with central fusion. Such foci were not spotted in other organs, and no lymphadenopathy was noted. The histological examination of the bone marrow biopsy that followed showed neither hematologic malignancy nor metastatic disease. The red cell line was found to be shifted to the left.

The patient underwent splenectomy and the histological examination of the surgical specimen revealed the presence of adenocarcinoma (Figure 1). The tumor cells were distributed in a confluent glandular pattern with rare, cribriform and papillary formations in desmoplastic stroma, showing foci of squamous cell metaplasia (Figure 2). These morphological features were strongly indicative of endometrial carcinoma, which nevertheless should be differentially diagnosed in a spectrum of neoplasias.

The immunohistochemical investigation performed substantiated the endometriol origin of the solitary carcinomatous focus (Figures 3-6).

After surgery the patient was treated with hormonal chemotherapy and she is now in good clinical condition, showing no signs of relapse.

Fig. 1



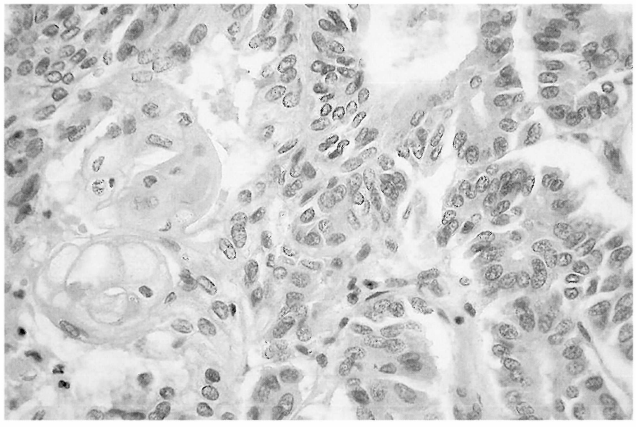
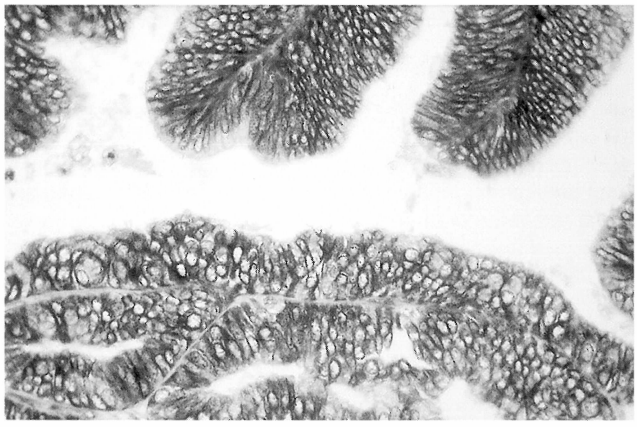


Fig. 3



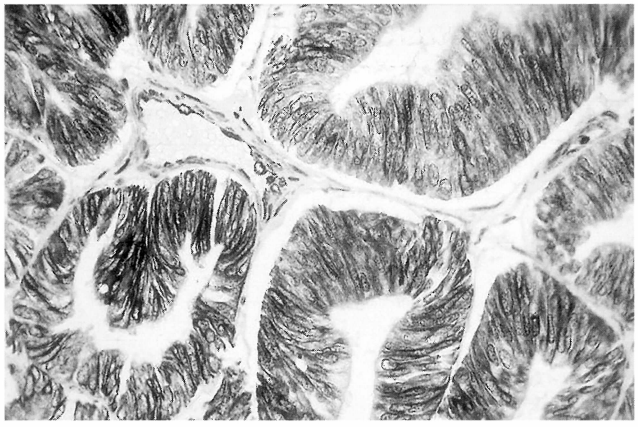
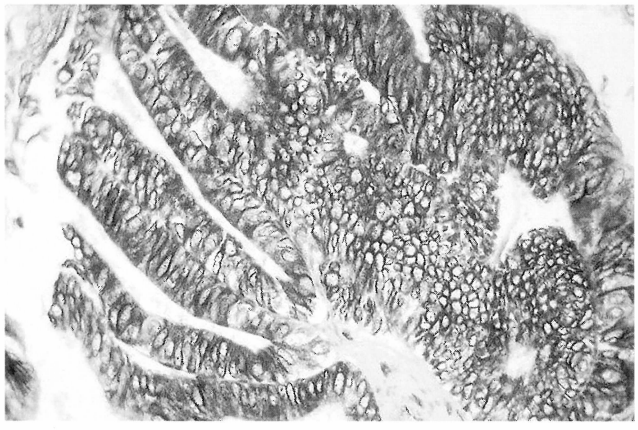


Fig. 5



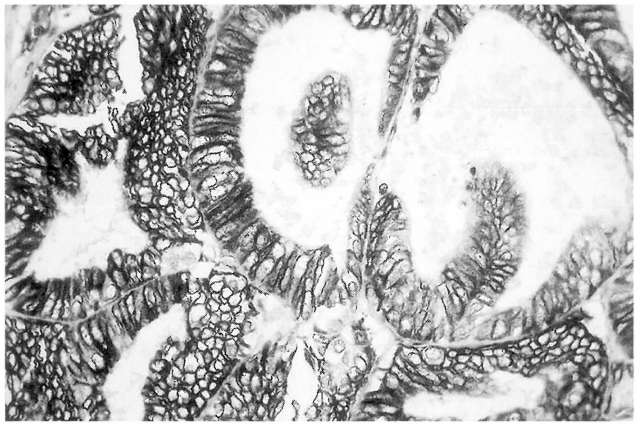


Figure 1. — Metastatic focus of adenocarcinoma in the spleen with histological features compatible with endometrioid carcinoma (H&E x 100).
Figure 2. — Malignant cells are distributed in a confluent glandular pattern with rare, cribriform and papillary formations, showing foci of squamous cell metaplasia (H&E x 400).
Figure 3. — Positivity of most of the neoplastic cells to the immunohistochemical stain of vimentine (x 400).
Figure 4. — Positive reaction of the neoplastic cells to the immunohistochemical stain of cytokeratin 7 (x 400).
Figure 5. — Cytoplasmic expression of the immunohistochemical stain CA 19-9 by most of the tumor cells (x 400).
Figure 6. — Positive immunohistochemical reaction of the tumor cells to CEA (x 400).

Material and Methods

The surgical specimen was fixed in 10% formalin buffer for 24 hours and histological sections were taken and embedded in paraffin wax. Sections, 3 μm thick, were then taken from the paraffin blocks and stained with hematoxylin and eosin (H&E), while for the immunohistochemical investigation the avidin-biotin-peroxidase technique [4] was performed. The antibodies used and their sources are listed in Table 1.

Results

The tumor cell immunoreactivity comprehensively listed in Table 2 was compatible with the morphological findings that indicated the endometrial origin of the tumor.

Vimentine (Figure 3) was uniformly expressed in all neoplastic cells, while most of these cells expressed cytoplasmic positivity for cytokeratin 7 (Figure 4) and CA

Table 1. — *Antibodies applied for immunohistochemical investigation and their sources.*

Antibody	Source	Antibody	Source
Vim	DAKO	Cytokeratin 18	DAKO
CEA	DAKO	Cytokeratin 19	DAKO
Cytokeratin 7	DAKO	Cytokeratin AE III	DAKO
Cytokeratin 8	DAKO	CA19-9	Novocastra

Table 2. — *Immunophenotype of tumor cells.*

Antibody	Immunoreactivity	Antibody	Immunoreactivity
Vim.	+	Cytokeratin 18	+
CEA	+	Cytokeratin 19	+
Cytokeratin 7	+	Cytokeratin AE III	–
Cytokeratin 8	+	CA19-9	+

19-9 antigen (Figure 5). Carcinoembryonic antigen (Figure 6) and cytokeratin 19 exhibited both cytoplasmic and membranic distribution.

Discussion

Endometrial carcinoma and their rare incidence of splenic solitary metastatic foci may easily be misdiagnosed since they appear with no significant signs or symptoms until the late stages of the disease and may not express any tumor markers in the peripheral blood [12].

Such metastatic foci in the spleen, especially in women with no previous history, are usually found incidentally during CT-scan investigations. This finding should however be differentially diagnosed in a large spectrum of diseases that expands to lymphomas, hemangiomas, hamartomas and furthermore splenic abscesses, infarcts and parasitic cysts [5, 8, 12].

Furthermore metastatic carcinoma in the spleen may originate from the breast, lung, stomach, large bowel, kidneys and ovaries, or may concern malignant melanomata. In these cases the only way to reach a diagnosis is by cytological/histological examination of bioptic material from the lesion under radiological guidance [1, 2, 5, 7].

The histologic examination on the other hand may present its own restrictions. These may concern insufficient sampling in cases of FNAB and core biopsy, or defective fixation in cases of surgical specimens. As far as the spleen is concerned, it is important to cut the specimen into 1.5 to 2 cm thick slides before fixing it in the formalin buffer and keep them there no longer than 24 hours. This enables a proper fixation of the whole matrix of the organ before autolysis occurs, while on the other hand its maintenance in 4% formalin buffer for 24 hours permits the sufficient expression of several cellular antigens for immunohistochemical evaluation [3].

The immunohistochemical profile of endometrial carcinoma is rather diverse, concerning the expression of both epithelial markers such as keratins of low molecular weight and CEA, as well as mesenchymal markers such as vimentine. In most cases estrogen and progesterone are also detected, while some tumor cells also contain GFAP. Several other markers are also reported to be expressed by the malignant cells, none of them however is indicative of their origin. CA 125 and CA 19-9, on the other hand, are two relatively novel antibodies, regarded to express specialty in the detection of endometrial carcinomas [11]. CA 19-9 was expressed by most of the tumor cells in the present case, affirming the endometrioid origin of the metastatic foci.

Despite the fact that metastatic carcinomatous foci to the spleen usually occur as a result of generalized colonization of the neoplasm, in the present case the metastatic disease was confined to the spleen, without any other clinical or laboratory evidence of relapse. This fact related to the history of the patient could be interpreted as a gradual development of a carcinomatous clone that colonized to the spleen during the active phase of the disease before hysterectomy and resisted the postoperative chemotherapy [9, 10]. Its gradual proliferation was furthermore a result of the patient's negligence to present for follow-up evaluation and manifested with symptoms of anemia ten years later.

Conclusively, all women with a history of endometrial adenocarcinoma should undergo frequent and full clinical-laboratory re-evaluations in order to avoid the high recurrence incidence in the course of the disease [9-10, 12]. Furthermore metastatic foci of endometrial carcinomata should always be included in the spectrum of differential diagnoses of solitary splenic nodules, whenever all the other common primary malignancies have been excluded.

References

[1] Arent P., Amuli M., Algada R., Blondiau J.V., Wauters G., Chamiec M. *et al.*: "Isolated splenic metastasis of endometrial adenocarcinoma. A case report and review of the literature". *J. Gynecol. Obstet. Biol. Reprod.*, 1992, *21*, 182.

[2] Berge T.: "Splenic metastasis". *Acta Pathol. Microbiol. Scand.*, 1974, *82*, 499.

[3] Cheson B.D., Bennett J.M., Grever M.: "National Cancer Institute Working Group guidelines for chronic lymphocytic leukemia: Revised guidelines for diagnosis and treatment". *Blood*, 1996, *87*, 4990.

[4] Falini B., Taylor C.R.: "New developments in immunoperoxidase techniques and their application". *Arch. Pathol. Lab. Med.*, 1983, *107*, 105.

[5] Gilks C.B., Acker B.D., Cleament P.B.: "Recurrent endometrial adenocarcinoma: Presentation as a splenic mass mimicking malignant lymphoma". *Gynecol. Oncol.*, 1989, *33*, 209.

[6] Giuliani A., Caporale A., Di Bari M., Demoro M., Mingazzini P.: "Isolated splenic metastasis from endometrial carcinoma". *J. Exp. Clin. Cancer Res.*, 1999, *18* (1), 93.

[7] Hamy A., Letessier E., Guitlard Y., Paineau J., Visset J.: "Splenectomy for isolated splenic metastasis from endometrial adenocarcinoma". *Acta Ostet. Gynecol. Scand.*, 1995, *74*, 745.

[8] Jorgensen L.N., Chrintz H.: "Solitary metastatic endometrial carcinoma of the spleen". *Acta Obstet. Gynecol. Scand.*, 1988, *67* (1), 91.

[9] Klein B., Stein M., Kuten A. *et. al.*: "Splenomegaly and solitary spleen metastasis in solid tumors". *Cancer*, 1987, *60*, 100.

[10] McClure J.N., Park Y.H.: "Solitary metastatic carcinoma of the spleen". *South Med. J.*, 1975, *68*, 101.

[11] Podczaski E., Kaminski P.F., Zaino R.: "CA 125 and CA 19-9 immunolocalization in normal, hyperplastic, and carcinomatous endometrium". *Cancer*, 1993, *71*, 2551.

[12] Siamak A.M., Roy Y.C.: "Solitary splenic metastasis. Case report and review of the literature". *Am. J. Clin. Oncol.*, 2001, *24* (3), 306.

Address reprint requests to:
A. KAFANAS, M.D.
Pathology Department
Serres General Hospital
Third kilometer of Serres-Drama Highway
62100 Serres (Greece)