Solitary spleen metastasis and amyloidosis in a patient with endometrial cancer

H. Gogas[1], Th. Ignatiadis[1], Ch. Markopoulos[1], S. Karageorgopoulou[1], D. Floros[2], G. Vaiopoulos[1]

[1]1st Department of Medicine, National and Kapodistrian University of Athens, Laikon General Hospital
[2]Department of Pathology, Hellenic Air Force and VA General Hospital, Athens (Greece)

Summary

Background: In contrast to autopsy findings, solitary splenic metastases from solid tumors are extremely rare. It may occasionally be the first manifestation of recurrent solid cancers, and in particular of gynecologic malignancies. Secondary amyloidosis is also found in malignancy.

Case: A 52-year-woman originally diagnosed with a Stage IB, grade 2 endometrial carcinoma presented two and a half years later with a paroxysmal non-productive cough, weakness, loss of appetite and daily afternoon fever. On clinical examination wheezing on forced exhalation and painful splenomegaly was found. After an extensive work-up the patient underwent an explorative laparotomy and a splenectomy was performed. Histologic examination showed solitary spleen metastasis with amyloidosis. All symptoms resolved. As the patient had received a full course of postoperative irradiation after a total abdominal hysterectomy, six cycles of combination chemotherapy were administered. The patient remains free of recurrence, 46 months later.

Conclusion: A case of solitary spleen metastasis with amyloidosis in a patient with endometrial cancer is presented.

Key words: Solitary spleen metastasis; Amyloidosis; Endometrium; Cancer; Case report.

Introduction

Metastasis to the spleen from various neoplasms is rare [1]. Most splenic metastases are found at autopsy in approximately 7% of autopsied patients and generally constitute a late manifestation of widespread disease. Retroperitoneal tumors and pancreatic cancer may reach the spleen by direct extension, but breast, lung, ovarian and stomach cancer, and melanoma are the most common sources that metastasize via the blood stream [2]. In contrast, splenomegaly – as the clinical manifestation of metastatic spread – is extremely rare.

Moreover, amyloidosis is associated with an inflammatory process and is also found in malignancy.

The case history of a patient with Stage IB endomethial carcinoma who developed a solitary spleen metastasis and amyloidosis is presented.

Case Report

A 52-year-old woman, originally diagnosed in January 1996 with Stage IB, grade 2, endometrial carcinoma, presented in August 1999 with a two-month history of a paroxysmal non-productive cough, loss of apetite without substantial weight loss, and weakness. Twenty days prior to admission she had a daily afternoon fever up to 38.8°C and she presented without rigor. A feeling of weakness was attenuated and the hematocrit gradually dropped.

On clinical examination wheezing on forced exhalation was found. A tender spleen was palpable initially 1 cm below the left costal margin. No hepatomegaly or lymphadenopathy was present. The spleen was enlarged and painful (4 cm below the costal margin).

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On admission, laboratory findings were: hct: 22.9%, hgb: 7.1 g/dl, MCV: 78.1 fl MCH: 24.2 pg/μg, MCHC: 30.9 g/dl. Leucocyte count: 8,400/μl (neutrophils: 74%, lymphocytes: 17% and monocytes: 8%) platelets 350,000/μl, ESR: 146 mm/1 h CRP: 18.5 mg/dl (NV 0-3). Urianalysis: normal. Six blood and urine cultures negative.

ASAT: 20 mIU/ml, ALAT: 45 mIU/ml, (10-40 NV) LDH: 113 mIU/ml, ALP: 480 mIU/ml (5-136 NV) CA 15-3: 169 U/ml (< 30) γGT: 193 mIU/ml (5-55).

b2: microglobulin 2.198.9 μg/l (< 2080) Fibrogen: 7.3 g/l (1.8-3.5) Protein electrophoresis (albumin 32.4% a1 globulin: 11.2%, a2 globulin 25.1% b globulin 14% and γ globulin 17.2%) is shown in Figure 1.

No paraprotein was found in the serum or the urine.

Bronchoscopy: negative. Cytologic examination of washing showed inflammatory cells, negative for neoplasia. Upper GI endoscopy was negative. Colonoscopy: negative. The biopsy of the bowel was negative.

Bone marrow aspirate: all lineages were present and reactive bone marrow had high cellularity. Cancer cells were not found but antinuclear antibodies were positive: 1.80.

CT scan of the abdomen: Hepatomegaly and splenomegaly with a hypoechoic space occupying the lesion in the spleen (Figure 2).

CT of the chest: slight thickening of the tracheobronchial structures of mild and lower lung zones bilaterally consistent with mild chronic bronchitis or chronic obstructive pulmonary disease (COPD).

She was transfused with two units of blood.

The patient underwent explorative laparotomy. A splenectomy and liver biopsy were performed. Careful examination of the abdomen failed to demonstrate lymph node or other metastases. A small lymph node of the hilum of the spleen was also excised.

The patient had an uneventful postsurgical recovery. The cough stopped and her temperature returned to normal.

Fig. 1

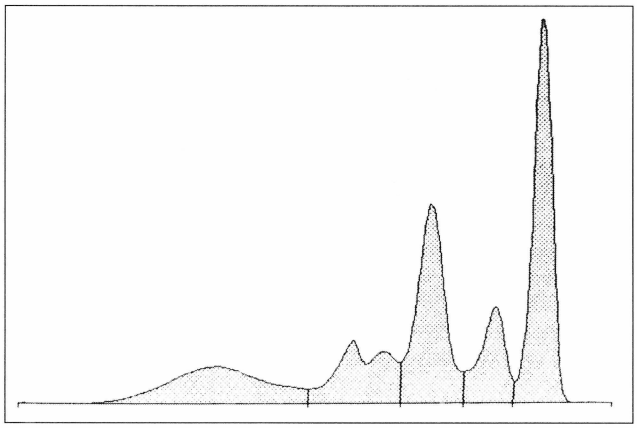


Fig.

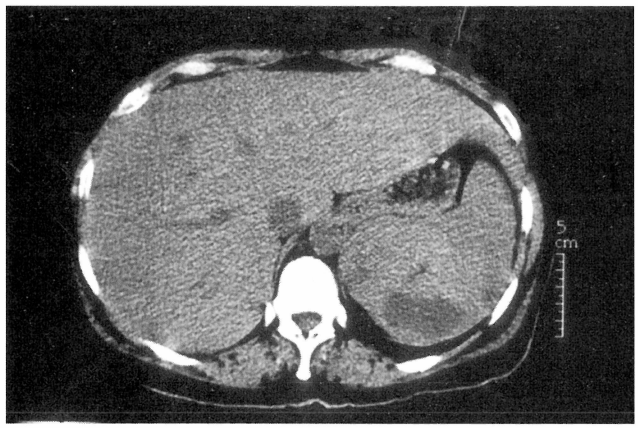
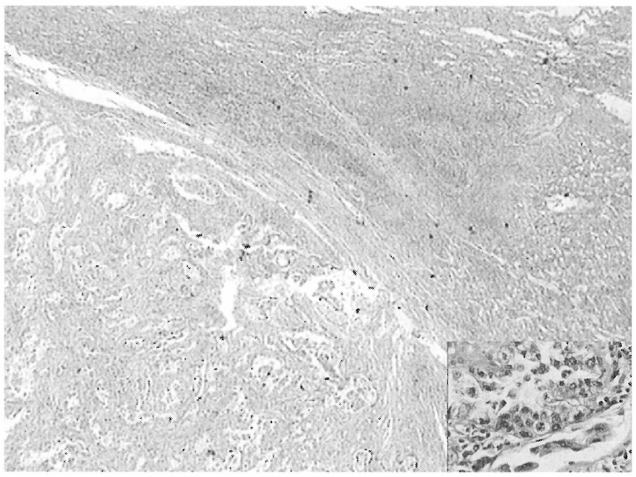


Fig. 3



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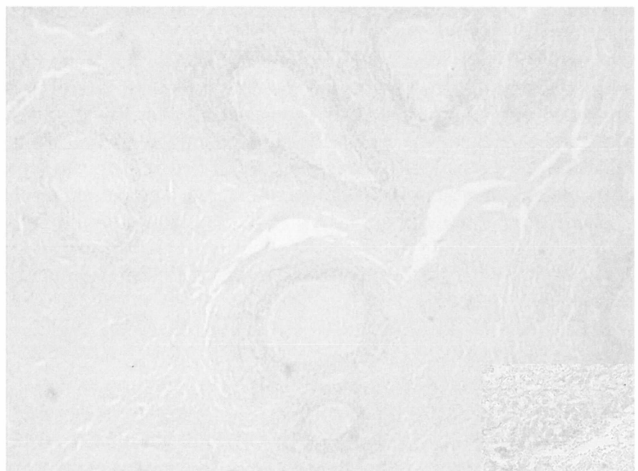

Figure 1.— Protein electrophoresis.
Figure 2. — CT scan of the abdomen.
Figure 3. — On the left, adenocarcinoma metastasis; on the right, white pulp surrounded by amyloids. Inset: Metastasis at higher magnification (H & E).
Figure 4. — Congo-red stains the amyloids. Inset: White pulp surrounded by amyloids at higher magnification.

Histologic examination showed a 7.5 x 7 x 6.5 cm tumor in the spleen compatible with metastasis from a grade 2 adenocarcinoma of the endometrium. The size of the spleen was 21 x 12 x 8.5 cm and extensive hyaline deposits in the splenic parenchyma with histochemical and morphological features of amyloidosis (Congo Red+) (Figures 3 and 4) were found.

The lymphocytes and plasma cells of the splenic tissue were normal in appearance and with polyclonic immunophenotype. The liver parenchyma architecture showed no pathological findings.

Twenty days after surgery all the lab values returned to normal: hct: 44.5% hgb: 13.4 g/dl, MCV: 85 fl, MCH: 25 pg/μg, MCHC: 30 pg/dl, leucocyte count: 7,600/μl with a normal differential (neutrophils 61%, lymphocytes 33%, monocytes 4%, eosinophils 2%) platelets 530,000. ESR: 9 mm/1 h, ALP: 130, γGT: 40, CA 15-3 < 30 and normal protein electrophoresis. As the patient's symptoms resolved after splenectomy, no further investigations for systemic amyloidosis were performed (i.e., biopsy of the rectum). The patient had received a full course of postoperative irradiation after the total abdominal hysterectomy and bilateral salpingo-oophorectomy so six cycles of combination chemotherapy were administered with doxorubicin and cisplatin. The patient is currently being followed and remains free of recurrence 46 months later.

Discussion

It is usually stated that secondary tumors in the spleen are rare even though in autopsy studies, splenic metastases are found in approximately 7% of autopsied patients; breast cancer, lung cancer and melanoma are the most common sources [1-3]. These metastases are part of a widespread disease. In order to further argue this, in Berge's study microscopic splenic metastases were identified in 50% of all subjects who had metastases in five or more organs or organic systems [2]. In a large population-based study from Sweden, of 7,246 subjects examined postmortem, 7,165 primary malignant tumors were found [4]. Of the 7,165 carcinomas, 4,404 (61.5%) were found to have spread to one or more organs. Metastases were found in the spleen in 312 cases (7.1%). It was shown that the spleen was the tenth among the most frequent sites of secondary tumors. Again breast, lung, ovarian and stomach cancers, and melanoma were the most common, especially having metastasized to several organs via the blood stream.

Among these, eight cases with primary in the uterine

cervix and four cases in the uterine body were identified. In contrast to the findings at autopsies solitary spleen metastasis in solid tumors is extremely rare. In these few cases splenomegaly was the clinical manifestation of splenic metastases and it can be clinically significant [5-8]. In the current series, the time from diagnosis until the development of splenomegaly varied from seven to 42 months. Weight loss, fever and fatigue may also be presenting symptoms [6], as was the case in our patient. Hypersplenism with pancytopenia may also occur. Our patient had severe anemia, but white blood cells and platelets were within normal limits. Lymphocytes were markedly reduced.

In all cases reported, especially the gynecologic ones, nodal metastases were not found at surgery and multiple biopsies of nodes were histologically negative. This contrasts with the usual pattern of spread, in which lymph node metastases precede organ involvement. Thus splenic involvement in solitary metastases must be due to hematogenous dissemination. This was also the initial theory of Marymount and Gross who concluded that splenic metastasis arises from cells that have been conveyed to that organ by the arteries [3]. As a result, when solitary spleen metastasis is suspected in a clinical setting aggressive treatment is indicated, with splenectomy followed by combined modality treatment radiotherapy to the involved area to prevent local recurrence and chemotherapy or hormonotherapy to prevent dissemination of the disease.

Amyloidosis is classified as 1) primary with no evidence of preceding or co-existing disease except multiple myeloma, 2) secondary with co-existence of other conditions such as rheumatoid arthritis or chronic infection 3) localized, 4) familial, 5) senile, 6) endocrine and 7) dialysis arthropathy [10]. Secondary amyloidosis (AA amyloid type) is not only associated with an inflammatory process but is found in malignancy. Hodgkin's disease, lymphoma, renal cell carcinoma are among the commonest tumor types that account for secondary amyloidosis. Cases of thyroid, lung and basal cell carcinoma have been described in association with amyloid A [11-13]. Monoclonal protein is not found in the serum or urine.

Treatment of AA amyloidosis depends on the underlying disease. There has been a report of regression of amyloidosis after nephrectomy for renal cancer [14].

We believe this is the first reported case of solitary metastasis to the spleen from endometrial cancer associated with amyloidosis. Interestingly, all symptoms – fever, cough, weakness – resolved after splenectomy and all laboratory parameters gradually normalized. Chemotherapy was administered as the patient was at high risk for recurrence.

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Address reprint requests to:
H. GOGAS, M.D.
Lecturer in Medical Oncology
1st Department of Medicine
Laikon General Hospital
University of Athens
P.O. Box 14120
11510 Athens (Greece)