Primary ovarian leiomyosarcoma. Proliferation rate and survival

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Summary

Objective: A case of Stage IIA primary ovarian leiomyosarcoma (LMS) with an unfavorable outcome 24 months after total abdominal hysterectomy with bilateral salpingo-oophorectomy, despite chemotherapy treatment, is described. Eighteen months from surgery the patient showed peritoneal spreading with ascites, liver and lung metastases. The present study was aimed to compare tumor growth fraction with cell density, lesion stage and clinical course.

Methods: The surgical specimens were evaluated by histological, histochemical, and immunocytochemical methods. Under microscopy, mitotic index (MI) was estimated, as a ratio of mitotic figures per 1,000 tumor cells. Immunohistology was also carried out to reveal some intermediate-type filamentous proteins, as histogenetic markers, and the MIB_1 monoclonal antibody was used to assess the percent of MIB_1-positive nuclei (MIB_1 labeling index).

Results: The histologic findings and immunohistology of the assayed intermediate filamentous proteins substantiated a diagnosis of LMS, with associated coagulation necrosis and not rare mitotic figures. A dual tumor component was observed, representing both the *pleomorphic* and *myxoid* LMS-variants. On the basis of the quantitative findings, a MI of 10.9 and a MIB1-LI of 23.1 were calculated, on average.

Conclusions: The proliferation indices in the described variant of ovarian LMS, denote a fast growing malignancy. They agree with the tumor stage at operation and the subsequent fatal outcome.

Key words: Primary ovarian leiomyosarcoma; Proliferation indices; MIB_1-labeling index.

Introduction

Primary ovarian leiomyosarcoma (LMS) is an infrequent spindle-cell malignancy whose origin has been ascribed to gonadal stromal components [1]. Previous follow-up studies perspected tumor stage, cell density and mitotic figures [MF_s] as conventional prognosticators [2], but the proliferation indices were considered to be more reliable predictors of survival for non-ovarian LMS_s [3]. Considering tumor stage and follow-up, a recent case of pleomorphic/myxoid ovarian LMS was investigated to assay both its Mitotic index [MI] and MIB_1-labeling index [MIB_1- LI] in relation to cell density, tumor stage and unfavorable clinical course.

Materials and Methods

A 66-year-old multiparous woman was admitted with abdominal pain and enlargement. A sonographic examination revealed a nonhomogeneous mass of the right ovary adhering to the posterior uterine wall and extending up to the rectouterine excavation. Hysterectomy with bilateral salpingo-oophorectomy was performed with subsequent chemotherapy. The patient was well for 18 months, when peritoneal tumor spreading occurred with ascites, liver and lung metastases. She died six months later. Grossly, the right ovary, measuring 14.0 x 10.8 x 9.6 cm and weighing 740 g, showed a firm subcapsular nodular tumor, whitish-grey in color, that extensively replaced the ovarian parenchyma. Its cut surface, solid in appearance, displayed hemorrhagic and necrotic areas. Tissue samples were fixed in 10% buffered formalin and paraffin-embedded: the sections were stained with hematoxylin-eosin and Alcian blue dye, for diagnostic and quantitative analyses. Immunohistology was also performed using cytokeratin [CK], vimentin [Vim], and desmin [Des] antibodies. In addition, a MIB_1-antibody was employed to reveal the Ki-67 nuclear antigen. The MF_s were counted to compute the MI, as a ratio per 1,000 cells, while the percent age of MIB_1-labeling nuclei was quantitated to calculate the MIB_1-LI.

Results

Light microscopy showed a solid neoplasm with a varied density of medium-size or large spindle cells, with an eosinophilic cytoplasm, distinct empty-spaces or vacuoles and a blunt-ended, nucleolated nucleus. A low cell-density tumor component displayed an Alcianophilic extra-cellular matrix, while frequent pleomorphic cells and atypical MFs also occurred (Figure 1). The malignant cells were CK-negative, but strong cytoplasmic immunostaining of the malignant cells was obtained by the Des-, Vim- and MIB_1-antibodies.The MIB_1-positive nuclei were quantitated so that a MI of 10.9 ± 6.5 and a MIB_1-LI of 23.1 ± 4.8 were calculated on average.

Discussion

Primary ovarian LMS is an aggressive neoplasm, unresponsive to radium-chemotherapic treatment [4]. Survival rate is up to 54 months and only three cases have been

Revised manuscript accepted for publication January 5, 2004

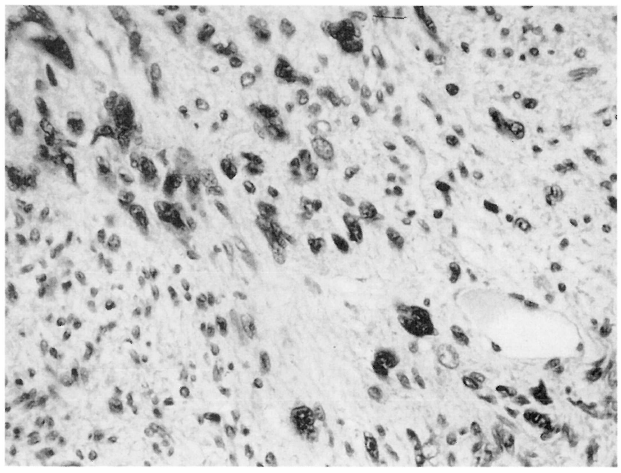

Figure 1. — Primary ovarian LMS with myxoid and pleomorphic components. Several pleomorphic tumor cells and a myxoid-type extracellular matrix can be seen (H&E, original magnification x225).

described to date with an exceptional survival over five years after surgery [1, 4]. The present neoplasm in a postmenopausal woman was Stage IIA at surgery, and gave rise to peritoneal spreading and metastases 18 months postoperation. The literature cases of ovarian LMS are mostly of the *classic* type,with a high cell density [2, 3, 5]. Both *pleomorphic* [4] and *myxoid* [6] LMS-variants have been reported in the ovaries as fast-growing malignancies, despite the low cell-density of the latter. Such growth patterns coexist in our case.The putative myogenic origin of the tumor cells is substantiated here by the Des-expressing elements, while the Vim-positive population may be considered as deriving from vascular smooth-muscle cells, as suggested for pleomorphic LMS[s] [4]. Concerning the assessed proliferation indices, MF[s] and MIB_1-positive nuclei are highly quantitated and agree with the otherwise estimated growth fraction in poorly behaving ovarian LMS in the literature [2, 3, 5, 6], irrespective of tumor cell-density.

Conclusions

The neoplasm reported herein consisted of a dual myxoid and pleomorphic component, whose high proliferation indices denoted a fast growing malignancy, substantiating Stage IIA at operation, tumor spread and fatal outcome within two years.

The MI and MIB_1-LI averages are consistent with the classical features of malignancy, such as cell pleomorphism and necrosis, thus rendering the estimated proliferation indices as reliable quantitative prognosticators of tumors with a low cell-density component, as the present case.

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