Quiz

Correct answer to the quiz Pol J Pathol 2018; 69 (4). Check your diagnosis

Case report

Benign-looking primary fibrosarcoma of the uterus

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Fibrosarcomas are placed among the most infrequent malignant tumors of the uterus. We present a case of a 38 years-old woman, whose benign looking uterine mass was primary diagnosed as a sclerosing leiomyoma. However, the tumor relapsed in two years with multisite metastases in the abdomen. The complex differential diagnosis excluded the most common mesenchymal tumors of the gynecological tract. Finally, we diagnosed the tumor as an epithelioid sclerosing fibrosarcoma arising from the uterine.

Key words: progressive familial intrahepatic cholestasis, partial external biliary diversion, follow-up, children, liver, histopathology.

Introduction

Uterine sarcomas account for 3% of malignant tumors of the uterus. Leiomyosarcomas and endometrial stromal sarcomas comprise 90% of uterine sarcomas [1, 2, 3]. Among the remaining 10% of rare uterine sarcomas, the most common diagnoses encompass embryonal or pleomorphic rhabdomyosarcoma (ERMS/PRMS), malignant peripheral nerve sheath tumor (MPNST) and angiosarcoma (33%, 17% and 14% of rare uterine tumors, respectively) [2]. Other diagnoses, including uterine liposarcoma and fibrosarcoma are found exceptionally [2].

Sclerosing epithelioid fibrosarcoma (SEF) accounts for less than 1% of soft tissue malignancies and arises most commonly in lower extremities of middle-aged adults. SEFs are characterized by low histopathological malignancy, however the clinical course of this neoplasm is aggressive [4, 5].

We present an unusual case of primary uterine sclerosing epithelioid fibrosarcoma.

Material and methods

The patient was a 38 years-old woman suffering from myomatous uterus. In 2013, she underwent a subtotal hysterectomy with a diagnosis of a dissecting leiomyoma. The patient was discharged home and remained in a good condition for the next two years. In 2015, the patient started suffering from weight loss and chronic pelvic and abdominal pain. A computed tomography scan of the abdomen revealed multisite abdominal masses localized mainly in adnexes and a clinical suspicion of a metastatic ovarian tumor was made. In December 2015, the patient underwent a debulking surgery with excision of adnexes, the remaining part of cervix, greater omentum, appendix and visible tumor masses. Because of the unusual appearance of the disease progression, the specimen from the second surgery (2015) was sent for consultation at our Department. A routine histopathological examination followed by a complex panel of immunohistochemical and histochemical stainings were applied (Table I). Immunohistochemical analysis used monoclonal antibodies {FLEX Monoclonal Mouse Anti-Human, Ready-to-Use (Link), Dako, Denmark} and EnVisionTMFLEX+ (Dako, Denmark) for the visualization. The tests were carried out using Autostainer Link 48 (Dako, Denmark).

Table I. The immunohistochemical and histochemical analysis of the tumors. All stainings are routinely executed in our Department with utilization of EnVisionTM FLEX+ system (Agilent Technologies, Santa Clara, CA 95051, United States)

Stain	Result
Ki67	Proliferation rate of 5% in hot-spot
vimentin	positive
CD10	negative
ER	negative
PR	negative
CD34	negative
desmin	negative
CD117	negative
SMA	negative
inhibin	negative
calretinin	negative
CD56	negative
HMB-45	negative
S100p	negative
broad spectrum cytokeratin	negative
Masson-trichrome	positive
MUC4	positive

Results

In the macroscopic examination from the first surgery (2013), the uterine corpus was deformed and partially dissected by a single whitish and solid tumor of 13 cm in diameter. In the macroscopic evaluation from the debulking surgery (2015), multiple well-limited, solid and whitish tumors were present in all surgical specimens with the diameters ranging from 0.4 cm to 6.0 cm. Intraoperatively, the masses were described as mesenchymal tumors without unequivocal features of malignancy.

The histopathological view was consistent among tumors resected during the second surgery from each site involved by the disease (Fig. 1A-D). Microscopically, the neoplasm presented the proliferation of fibrotic tissue with multiple foci of sclerosis and collagen formation. The tumor cells had an epithelioid look with very low rate of atypia and scarce mitoses. The neoplastic areas invaded and dissected the adjacent tissue. A primary suspicion for an unusual presentation of a sex cord stromal tumor was made, but the tumors were consistently negative for CD56, calretinin and inhibin. In the further immunohistochemical analysis, the tumors were negative for SMA, desmin, h-caldesmon, CD117, ER, PR and CD10, which vouched strongly against the diagnosis of leiomyosarcoma or endometrial stromal sarcoma (Fig. 2A-D). The stainings for CD34, S100p, HMB-45 and broad-spectrum cytokeratin were also negative. The tumors were strongly positive for vimentin and MUC4 (Fig. 2E). The Masson-trichrom histochemical stain revealed the bundles of collagenous tissue invading and intersecting the adjacent tissue (Fig. 2F). The Ki67 proliferation index was low reaching 5% in hot-spot areas. For details on the results from the immunohistochemical analysis see Table I. Basing on the uncommon both histologic and immunophenotypic features of the tumor, as well as clinical presentation as a malignant neoplasm, we indicated on a diagnosis of a low-grade mesenchymal malignancy with fibroblastic differentiation. Because of the epithelial look of the cells, low mitotic rate and extensive areas of sclerosing collagen bundles, we suggested a diagnosis of sclerosing epithelioid fibrosarcoma.

To verify our diagnosis, we requested the specimens from the first surgery (2013). The histopathological view of the primary tumor, which dissected the uterine corpus, was indistinguishable from the tumors removed in the second surgery. This not only confirmed our prior diagnosis, but also led to the hypothesis that the uterine corpus was the primary site of the sarcoma.

The second consultation at the Institute of Oncology corroborated our diagnosis. The patient was

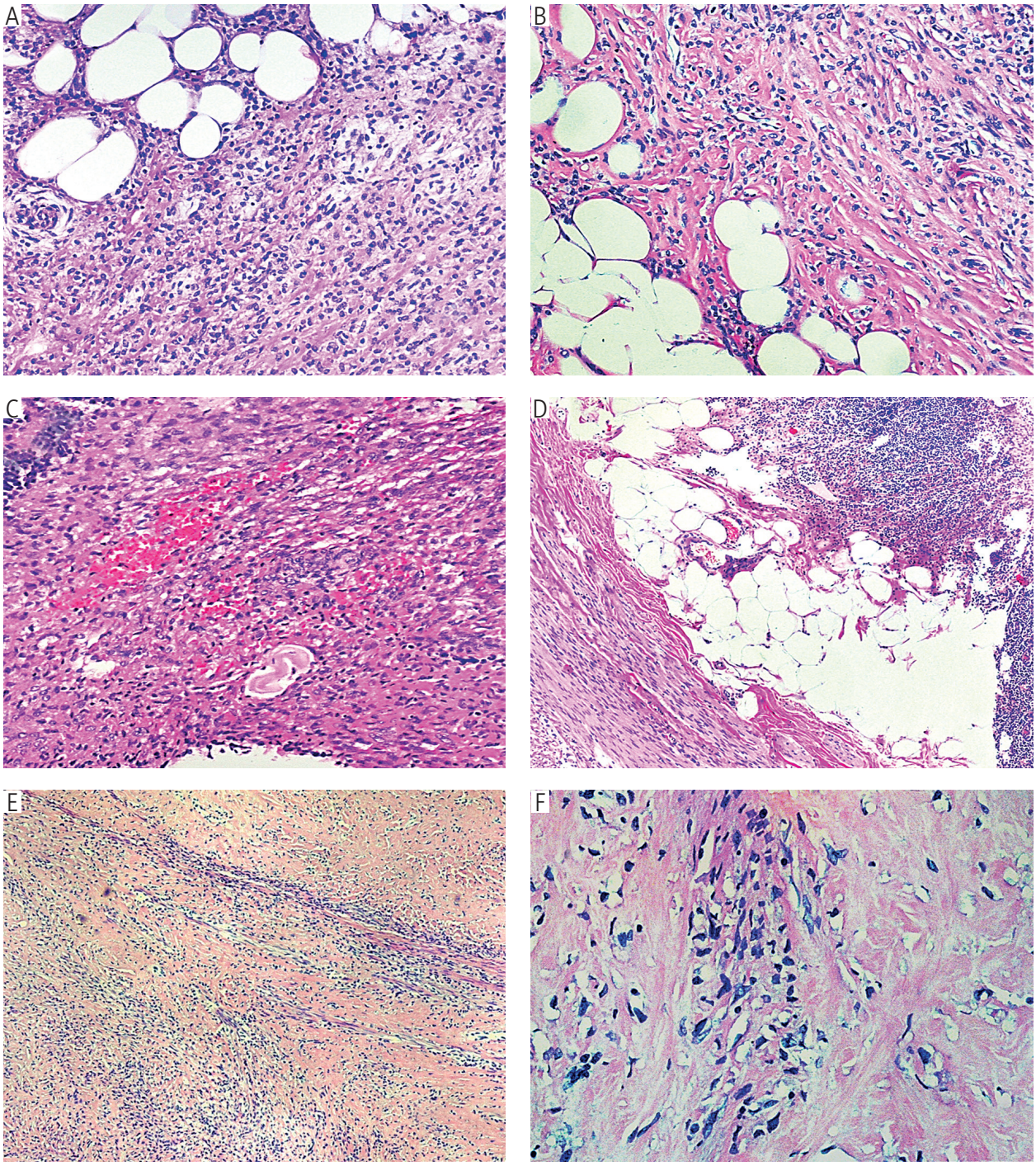

Fig. 1. Histopathological presentation of the tumors (HE). Nests of epithelioid cells with low atypia and low mitotic rate, dissected by thick bundles of sclerosing collagen, invade the structures of: greater omentum (A, B, at 100× magnification), ovary (C, at 100× magnification), appendix (D, at 4× magnification) and uterus as primary site of the disease (E, F, at 20× and 200× magnification, respectively)

referred to the reference Department of Soft Tissue/Bone Sarcoma and Melanoma. In March 2016, the radiologic imaging revealed the relapse of the disease with multisite tumors in the abdomen. The patient was disqualified from surgical treatment and was administered CyADIC chemotherapy regimen [6]. The patient remained in a good condition and the disease was stable according to RECIST until May 2017, when the progression was described in the radiologic evaluation. The patient undergone another debulking surgery in May 2017 and was administered postoperative chemotherapy with Gemcitabine and Docetaxel. As of November 2018, the disease is stable according to RECIST.

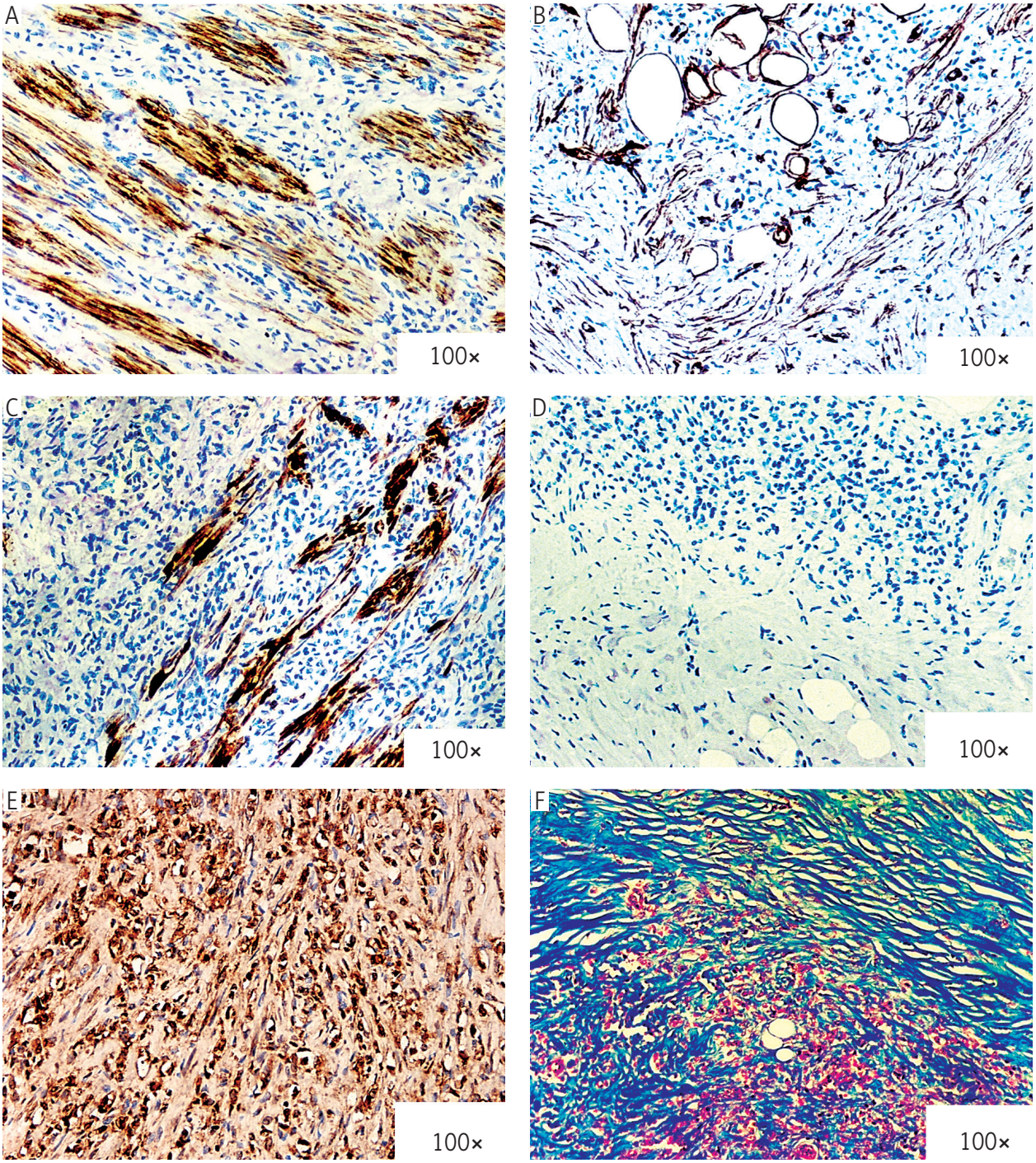

Fig. 2. Immunohistochemical stainings of the tumors. Neoplastic tissue is negative for desmin (A, uterus, at 100× magnification), SMA (B, greater omentum, at 100× magnification) and caldesmon (C, uterus, at 100× magnification), CD10 (D, greater omentum, at 100× magnification) invades and dissects the areas of residual smooth muscles (A, C). The tumor is positive for MUC-4 (E, uterus, at 100× magnification). Masson-trichrome stain revealed the thick bundles of collagen produced by neoplastic tissue (F, greater omentum, at 100× magnification)

Discussion

We present the second case of primary uterine low-grade fibrosarcoma described in the literature [2, 7]. We decided to report on the case, because of the tumor's unusual presentation and its similarity to a benign sclerosing leiomyoma, which together provided high diagnostic difficulty and delayed the proper therapeutic approach in the patient.

The patient presented firstly with a uterine mass, which was suspected clinically and radiologically as a benign fibroid tumor. Thus, the first surgery en-

compassed only uterine corpus (subtotal hysterectomy) and was performed at a regional health center. The approach to the pathological evaluation of the first tumor was standard for differentiating leiomyomas from malignant neoplasms [1, 2]. The tumor did not present with marked nuclear atypia, high mitotic rate or tumor necrosis and the only distinguishable features concerned bands of fibrous and sclerosing tissue, which dissected the more cellular, epithelioid component of the tumor. Therefore, the initial diagnosis was a benign leiomyoma and the patient was asymptomatic for the next two years. Only the fact that the patient presented with multisite metastases in the abdomen taken together with next careful histopathological and immunohistochemical examination of specimens from both surgeries lead us to the final diagnosis of a sclerosing epithelioid fibrosarcoma with uterus as the primary site of disease.

Sclerosing epithelioid fibrosarcoma is a rare soft tissue malignancy and has not been reported in the uterus, even as metastases [2, 4, 5]. In our case, the final diagnosis of primary uterine SEF was strictly the diagnosis of exclusion. The tumor did not express the markers characteristic for any mesenchymal tumors described as primary within gynecological tract. The only positive stains were with vimentin and Masson-trichrome, which provided the evidence for fibroblastic origin of the neoplasm. The well-differentiated histopathological look of epithelioid nests of cells with bundles of sclerosing collagen dissecting native tissue of involved structures brought us to the diagnosis of SEF [4, 5, 8]. The second consultation of the specimens corroborated our final diagnosis.

There are some limitations of our case report. The first one is that the tumor was not checked for molecular rearrangements using fluorescent in situ hybridization assays. These tests would help us corroborate the final diagnosis, however the lack of these results does not vouch against the diagnosis. What is more, the diagnosis was corroborated independently by three experts in soft tissue pathology. The second limitation concerns the scarce radiological imaging used at the initial diagnosis of the uterine mass. This covered standard abdominal and pelvic ultrasonographical scan without further diagnostics. Nevertheless, this USG scan revealed only the mass in the uterine corpus and indicated on a benign fibroid tumor. This not only explains why the patient was further approached with standard of care for uterine fibroid mass, but also vouches for the hypothesis that the uterine corpus was the primary site of the tumor.

The presented case is exceptionally rare, however it brings very important conclusions. Firstly, even little deviation from the morphologic image of a uterine fibroid tumor should be carefully examined. Secondly, the case emphasizes that an accurate diagnosis and therapy of soft tissue tumors requires a tight cooperation between medical professionals of various specialties. Lastly, the report shows that fibrosarcomas, including sclerosing epithelioid sarcoma, may arise in uterus as the primary site of the neoplasm.

The authors declare no conflict of interest.

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Quiz

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Anthracosis in an infant of the Spanish royal family from the XVth century.

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