Dear Editor,

We present a case of a primary abdominal extra-gastrointestinal stromal tumor (E-GIST) in a 75-years-old female patient. E-GISTs are rare, non-epithelial, mesenchymal tumors arising from the soft tissues of the abdomen—mesentery and retroperitoneum. These tumors are histologically and cytologically similar to the stromal tumors of gastrointestinal tract, composed of round or fusiform cells or a mixture of both in a myxoid background. The recognition of these tumors is important because of their aggressive biological behavior, the metastatic potential and the high rate of recurrence.

Case report

A 75-year-old female presented at the University Hospital of Crete with lower abdominal pain and ascites. Her past medical history was uneventful. Physical examination was unremarkable. Ultrasound examination of the lower abdomen showed a hypoechoic mass of 3x2 cm. Contrast enhanced scan showed a large heterogeneous moderately enhancing mass at the rectovaginal septum. It was inseparable from both the vagina and the rectum replacing the rectovaginal connective tissue (Fig. 1A). She had no lymphadenopathy and hematological work-up was within normal limits.

A diagnostic paracentesis of ascitic fluid was performed and sent for cytological evaluation. Cytologic slides were prepared from the fluid after cytocentrifugation for 4 min at 400 rpm (rounds per minute). Four slides were fixed in 95% ethanol and stained with Papanicolaou stain, and six were air-dried fixed for Giemsa stain and immunocytochemistry. Three biopsy specimens were obtained under CT guidance.

The cytological smears revealed many neoplastic cells isolated or in small aggregates, with large and hyperchromatic oval-to-fusiform shaped nuclei, without visible nucleoli or mitoses. The cytoplasm of the neoplastic cells was abundant (Fig. 1B). The immunocytochemical study showed that these neoplastic cells were negative for BerEP4 and WT1 indices, but strongly positive for c-kit (Fig. 1C) and vimentin. The cytological diagnosis was of an extra-gastrointestinal stromal tumor (E-GIST). Histology and molecular analysis confirmed the diagnosis. In biopsy specimens many spindle fusiform or oval neoplastic cells with large nucleus without visible nucleolus with abundant eosinophilic cytoplasm, rare mitoses and moderate polymorphism were identified (Fig. 1D). Immunohistochemically, the tumor cells were positive for c-kit, SMA, vimentin, but negative for CD34, S100, desmin, myogenin, inhibin, ER, PR, Cam5.2 and WT1 indices. A molecular DNA analysis was performed using the automatic analyzer sequencer 3000-Avant ABI, which revealed neoplastic cells with the mutation C.23876>Ap.R796K on the exon 17 of c-kit. No mutations were detected in other regions of exons 9, 11, 13 of c-kit oncogene. The tumor was unresectable during the initial surgical exploration but it was removed after treatment with imatinib (Gleevec®). There has been no recurrence 18 months after surgery. The patient is undergoing surveillance.

Discussion

Extra-gastrointestinal stromal tumors (E-GISTs) are very rare tumors accounting only the 5-7% of all GISTs (1). Pathogenesis, incidence, clinicopathological features and prognosis of E-GISTs have not been completely defined yet (2-4). Approximately 80%
of E-GISTs are located in the omentum or mesentery, and the remaining develops in the retroperitoneum. E-GISTs arising in the retroperitoneum are extremely rare: To date there have been only 58 cases described in the literature (5,6).

The risk of malignant behavior of E-GISTs ranges from very low to high based on mitotic rate and size and also on location. Tumors larger than 5 cm with more than 5 mitoses per 50 HPFs are considered to be high-risk and E-GISTs of retroperitoneum are more aggressive.

Surgical removal is the gold standard treatment for non-metastatic E-GISTs and it is important to achieve a complete removal of the mass when possible “en block” with the contiguous tissues (7). The role of imatinib mesylate, which is the inhibitor of the tyrosine kinase activity of KIT in the treatment of E-GISTs, is unclear (8,9).

E-GISTs are cytologically and histologically similar to gastrointestinal stromal tumors (GISTs) which are cellular spindle cell or epithelioid tumors which express the CD34 and CD117 (c-kit) antigens (10). E-GISTs display various lines of differentiation which reflect the elements of the gut wall, showing differentiation towards smooth muscle and neural elements, duel differentiation and those that lack differentiation towards either cell type. E-GISTs occur commonly in adults presenting with abdominal pain or are discovered incidentally during a work up for an unrelated condition (11). Grossly, these tumors tend to be lobulated, nodular, well circumscribed and unencapsulated appearance. Areas of necrosis and hemorrhage are common in the malignant tumors.

Morphologically, E-GISTs are sub-classified to both of the spindle or epithelioid types. The cytology of these tumors have been described by Mills and Contos (12-14) in aspirate smears that are moderately cellular, composed of both aggregates and single cells with spindle shaped or oval nuclei, smooth nuclear membrane, inconspicuous nuclei and cyanophilic cytoplasm. In our case in ascitic fluid, the neoplastic cells had the same features but the smears were highly cellular because of the malignancy and the metastasis of E-GIST in the peritoneum. E-GISTs are an aggressive group of stromal tumors with a malignant potential.

Fig. 1. A. Contrast-enhanced CT scan shows a large, heterogeneous, moderately enhancing mass (arrows) at the rectovaginal septum. It is inseparable from both the vagina and the rectum. B. Ascitic fluid preparation. Neoplastic cells in small aggregate, with large and hyperchromatic oval-to-fusiform shaped nuclei, without visible nucleoli and the absence of mitoses. The cytoplasm is abundant. Papanicolaou stain x400. C. Ascitic fluid preparation. Neoplastic cells in small aggregate. c-kit positive. C-kit immunostain x400. D. Tumor section. Spindle fusiform or oval neoplastic cells with large nucleus without visible nucleolus with abundant eosinophilic cytoplasm, rare mitoses and moderate polymorphism. Hematoxylin-eosin stain x200.
and a high rate of recurrence. Our case had a malignant cytology. The malignant E-GISTs metastasize to the lung, liver and other organs (15). E-GISTs are treated by surgical resection and the administration of tyrosine kinase inhibitors, as in our case, with frequent follow ups to detect the recurrence.

In conclusion, E-GISTs are very rare aggressive tumors with high metastatic potential and a high recurrence rate. Cytology can be used as a confident diagnostic tool to detect these tumors. Histology and molecular analysis are mandatory for the assessment of the malignancy. We report the forth case of primary abdominal E-GIST diagnosed cytologically in ascites of the patient and confirmed by histology and molecular biology.

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References