A rare case of coexistence of ovarian cancer and gastrointestinal stromal tumor

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SUMMARY: A rare case of coexistence of ovarian cancer and gastrointestinal stromal tumor.

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Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors arising from the wall of the gastrointestinal tract with immunohistochemical reactivity for CD117 antibody, and usually prevalent in the fifth to seventh decade of life. The specific practical diagnostic criteria for GIST are c-kit expression (CD117), mitotic score, and the tumor size.

The stomach is the most common site of localization. Surgery is the mainstay of the treatment and complete resection is achieved in most cases.

Coexistence of malignant GIST and other malignancies from other germ layers have been reported in some unique cases. To the best of our knowledge the uncommon coexistence of GIST and ovarian cancer has not been reported in literature.

We report the first case of a 63-year old female patient with two independent synchronous tumors, a GIST and an ovarian cancer.

KEY WORDS: CD117 antibody - Mesenchimal neoplasm - Menopause.

Case report

A 63-year-old woman in menopause for 10-years, HCV-carrier, experiencing pelvic pain, with palpable pelvic mass extended to epigastric region and elevated CA-125 (803U/ml) and carbohydrate antigen 19-9 (GICA 149U/ml), was referred to our hospital.

The patient's medical record showed a history of antiviral treatment of chronic hepatitis C with interferon alfa for two years. Apart from this there was no personal or family history of major medical problems.

Transvaginal ultrasound showed a little median anteverted uterus with disomogeneous echostructure in senile-atrophy; behind the uterus there was a voluminous rounded ipoechogenic formation (136x94x67mm) and an amount of ascitic fluid.

MR-imaging confirmed the voluminous formation with compression of the uterus with an incom-
plete cleavage plane: the lesion showed low intensity signal in T1 sequences and iso-iperintensity of signal in T2 for the presence of a solid mass with a necrotic central area and some peripheral cystic formations.

The laparotomy revealed a rounded whitish formation of 1.6 cm of the intestinal wall and a resection was performed. Intra-operatively, the right ovarian appeared as a whitish formation with yellowish features with hemorrhagic streaks and necrotic aspect, 13 cm in diameter. No tumor deposits were present all over the pelvic peritoneum. Hysterectomy with bilateral salpingo-oophorectomy, infracolic omentectomy and appendectomy was performed.

Histologically the diagnosis was ovarian serous cancer, G3, with solid and necrotic aspects, interesting the ovarian surface (pT1c; Nx; Mx). The atrophic uterus had no evidence of tumor on gross or histologic examination. Omentum was congested without malignancy as well as the appendix.

The uncapsulated formation of the ileal loop was characterized by a fascicular proliferation of epithelioid and spindle cells with eosinophilic cytoplasm, elongated and hyperchromic nucleus, absence of necrosis. The mitotic score was very low <1 mitosis / 50 HPF (<1 pathological mitoses per 50 high-power field). Immunohistochemical examination showed positive staining for CD 117, while it was negative for CD34. The diagnosis was conclusive for low malignant GIST.

Resection margins were histologically negative. No other malignant pathologies in the abdomen were found.

The patient was referred to oncologist for treatment of ovarian cancer. Total body computed tomography was negative for disease. Haematological and biochemical values were in the normal range, except GOT (93 U.I./L) and GPT (51 U.I./L). The normalization of CA-125 levels and the persistence of CA-19.9 elevated values was observed (37 U/ml).

Therefore, in consideration of the stage of ovarian cancer, the patient began the treatment planning with carboplatin AUC 5 and paclitaxel 175 mg/m² for 6 cycles. No adjuvant treatment of GIST was made. Due to the lack of clear risk factors for recurrence and complete surgical resection of GIST, the patient began follow-up at the end of chemotherapy for ovarian cancer.

Discussion

GISTs are considered a group of mesenchymal neoplasm subject of debate and controversy regarding their nomenclature, histogenesis, criteria for diagnosis, prognostic manifestations, and classification (4).

The term of GISTs has been adopted and defined as tumors arising from the stroma with no definite cell line of origin and various patterns of differentiation (5).

GISTs may be present anywhere in the gastrointestinal tract, omentum, or mesentery. The most common sites are the stomach (60%), small intestine (15%), colon and rectum (5%), other abdominal organs including mesentery and omentum (5%).

GISTs give rise to metastases predominantly in the liver (more than 60% of metastases) or in peritoneum and may also be present as a pelvic mass or metastasize to the uterus and to the ovary.

Coexistence of an ovarian tumor and gastrointestinal stromal tumor is unreported in literature: Carlon-magno et al. (6) reported an epigastric mass associated with an ovarian cyst, and elevated CA-125 revealed a myxoid variant of GIST. Irving et al. (7) report five case of gastrointestinal tumors metastatic to the ovaries where microscopically tumors had a pure spindle cell morphology, and both spindle and epithelioid cell components. The diagnosis in all 5 cases was confirmed with positive c-kit (CD117) immunostaining. In this last report tumors were initially diagnosed as tumors of other types, leading to a misdiagnosis with significant therapeutic and prognostic implications.

About 70% of GISTs are composed of spindle cells, which look long and skinny, while about 20% are composed of epithelioid cells that look round or polygonal, and the other 10% show mixed cells of both spindle and epithelioid elements-pleomorphic type.

The best immunostaining method for identifying GIST is to test for expression of c-Kit, also called CD117, a cell membrane-spanning signaling molecule (receptor tyrosine kinase) which normally function in triggering cell growth when it is activated by its specific ligand stem cell factor.

c-Kit is normally expressed by the interstitial cells of Cajal (ICC), the “pacemaker cells of the gut” that send nerve signals to propel food along its course through the system via muscle contractions. With rare exceptions, c-Kit is not expressed by other abdominal tumors (8,9).

Another immunohistochemical marker often found to be positive in GISTs is CD34, a protein normally expressed by hematopoietic precursor cells and some interstitial cells of Cajal. Overall, about 60-70% of GISTs are positive for CD34, but this varies by tumor location. CD34 expression is highest in gastric GISTs (85%) but only about 50% of small intestinal GISTs express CD34 (4,10). Malignant GISTs show a slightly lower frequency of CD34 than benign ones.

About 30% of GISTs show focal reactivity for smooth muscle actin, 2% express positivity for desmin and under 5% stain for s-100. Finally neuron-specific enolase immunoreactivity is non specific.
The clinical presentation depends on the size and site of the tumor: small asymptomatic GISTs, usually 2 cm in diameter as reported in our case, are detected on serosal surfaces at laparotomy in specimens that have been resected for other conditions, while symptomatic tumor often present with vague abdominal discomfort. Larger tumors with ulceration occur with acute or chronic gastrointestinal haemorrhage (11).

Fletcher et al., (12) classified these tumors in to very low, low, intermediate and high risk categories according to tumor size and mitotic count. Tumors <2 cm and mitotic count <5/50 high power field (HPF) were categorized as very low risk; tumor size 2-5 cm and mitotic count <5/50 HPF as low risk; tumor size <5 cm and mitotic count 6-10/50 HPF or tumor size 5-10 cm and mitotic count <5/50 HPF as intermediate risk; tumor size >5 cm and mitotic rate >10/50 HPF as big risk and tumor size >10 cm and any mitotic rate or tumor any size and mitotic rate>10/50 HPF as high risk.

The tumor size at the diagnosis is an important predictive factor for recurrence. Lesions with diameter <2 cm and a low mitotic index are considered very low risk, lesions > 10 cm imply an elevated risk.

In our clinical-case, the GIST has been radically removed and, due to the low mitotic-index, there were no indications to the adjuvant treatment. However, the elevated GICA values (CA19-9), forced us to keep the patient with follow-up under close observation, monitoring carefully the GIST evolution in the course of chemotherapy.

Other prognostic histopathological criteria could include the proliferation index MIB-1, marker index Ki-67, high expression of bel-2, p16 INK4 (13,16).

A molecular target therapy, Imatinib Mesilato, inhibits c-Kit and therefore has a therapeutic effect. Immunohistochemical positivity for CD117 constitutes a prerequisite for this target therapy.

Gastrointestinal stromal tumors (GISTs) may be suspected from its appearance in imaging techniques such as CT scans, but the diagnosis can only be determined by a pathologist in biopsy, or from the entire tumor after it has been surgically resected. The main role of the pathologist is to determine the type of tumor.

Our case is unique and should draw physicians’ attention to the possibility of independent tumor coexistence when GIST occurs. This is especially important in making a decision of adjuvant therapy and only a careful histopathological examination gives us a correct diagnosis.

The current GISTs treatment guidelines of the European Society for Medical Oncology establish that the adjuvant therapy with Imatinib Mesilato can be applied in non-operable and metastatic tumors. Patients with resectable tumors without metastases should not receive adjuvant therapy.

The radiotherapy value as an adjuvant method for GIST is limited by potential toxicity to surrounding structures, especially to the bowel (17).

Due to the lack of clear risk factors for recurrence, and to complete surgical tumor resection, to our patient was advised only follow-up.

Conclusion

Considering that few patients with gastrointestinal stromal tumors have been reported in “gynaecological” literature, the awareness of such entity by a gynaecologist is necessary in order to facilitate a coordinated and multidisciplinary approach including gynaecologists and oncologists for improving the prognosis. A misdiagnosis can lead to significant therapeutic and prognostic implications. At surgery every effort should be made to identify the origin of the tumor and related anatomic structures. Therefore, in presence of a pelvic mass, especially if other unusual signs are present, the possibility of non gynecologic tumor must to be considered.

The identification of GISTs has become very important as the introduction of specific, target-therapy with kinase inhibitor offers a promising outcome for metastatic and non-operative GISTs.

References