GIST MIMETIZANDO TUMOR DE OVÁRIO – RELATO DE CASO

GIST MIMICKING OVARIAN TUMOR: A CASE REPORT

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DOI: 10.35984/fjh.v2i1.146

RESUMO

Objetivos: O relato de caso objetiva alertar quanto a apresentações atípicas de GISTs, especialmente como massa pélvica. **Métodos:** Relato de Caso. **Resultados:** Relatamos o caso de uma mulher de 67 anos, apresentando uma massa pélvica. Os achados imagenológicos indicaram tumor de ovário e a paciente foi submetida à ressecção cirúrgica completa. O anatomopatológico e a imunohistoquímica, todavia, confirmaram GIST, alterando o tratamento adjuvante da paciente. **Conclusão:** Nos casos os quais a clínica e os marcadores bioquímicos não condizem com o sítio tumoral apontado por exames de imagem, faz-se prudente a cogitação de diagnósticos diferenciais. No presente caso, o diagnóstico histológico só foi possível após a investigação imunohistoquímica (CD117+). Enaltece-se, portanto, a importância do estudo imunohistoquímico, pois a definição de GIST determinou a conduta terapêutica adequada, definindo assim, o prognóstico da paciente.

Palavras-chave: Tumor estromal gastrointestinal; GIST; Tumor de ovário; Massa Pélvica.

ABSTRACT

Aim: This case report aims to alert about GIST's atypical presentations, especially as pelvic masses. **Methods:** Case report. **Results:** The represent report is of a 67 years old woman presenting a pelvic mass. Imaging methods indicated ovarian tumor and the patient was submitted to a complete surgical resection. Anatomopathological study and immunohistochemistry, however, confirmed GIST, altering the adjuvant treatment. **Conclusion:** When clinical findings and biochemical markers are incompatible with the tumor site on imaging, differential diagnoses should be considered. In the reported case, diagnosis was only possible after immunohistochemistry investigation. This case stresses the importance of immunohistochemistry, once it was indispensable for the diagnosis, altered the pharmacological therapy and, thereby, improved prognosis.

Keywords: Gastrointestinal stromal tumor; GIST; Ovarian tumor; Pelvic mass

1. INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most frequently observed mesenchymal neoplasms of the gastrointestinal tract (ANTONESCUS, 2011). GISTs most likely arise from interstitial cells of Cajal which are responsible for regulating gastrointestinal peristalsis (RUBIN et al., 2016). Studies published in the late twentieth

century described the central role of proto-oncogene c-Kit (CD117) (HIROTA et al., 1998) mutations in the development of most GISTs (>80%) (RUBIN et al., 2016) and the involvement of the PDGFRA gene in a smaller number of cases (7.5%) (ANTONESCU, 2011). Eventually, the discovery that most GISTs are CD117-positive led to the inclusion of staining for CD117 in routine immunohistochemistry (IHC). As a result, the incidence of GIST rose from 1.1 to 2.1 per 100,000 pop (PATIL et al., 2011). Most GISTs (40-60%) develop in the stomach, but occurrence in the small bowel is almost as common (30-40%) (JOENSUU, 2006). Atypical sites include the colon (7%), rectum (5%) and esophagus (1%) (TRAN et al., 2000). Several authors (LEE, 2013; ZIGHELBOIM et al., 2003; ANGIOLI et al., 2008; ERKANLI et al., 2006) have described atypical GISTs resembling abdominal-pelvic masses or even mimicking ovarian masses or tumors (CARLOMAGNO; BENEDUCE, 2015). In order to make benefit of the extensive scientific knowledge accumulated about GISTs in the last 20 years, we must get to know its atypical presentations with the purpose of not missing diagnostic opportunity.

2. CASE REPORT

A 67-year old female patient was referred to our oncogynecology service due to a palpable pelvic mass on the right side with 2 months of progressive growth associated with local abdominal pain and constipation. A total abdominal ultrasound (US) examination revealed a fine-walled anechoic cyst in the rectouterine pouch measuring 11.4 x 6.8 x 10.2 cm, probably of benign origin, and a large, richly vascularized and lobulated solid nodule in the right iliac fossa, measuring 11.5 x 9.2 x 9.1 cm.

Figure 1 – 3: obtained by CT showing the findings described during the case report.

The patient was submitted to chest, abdominal and pelvic computerized tomography (CT) and CA-125 testing. The latter yielded 25.8 U/mL, which is considerably less than the values observed for most ovarian tumors (>35 U/mL) (DE ALMEIDA et al., 2007). Abdominal and pelvic CT (Images 1-3) revealed a heterogeneously enhanced, expansive solid lesion in the right adnexal region measuring ~11 x 8.3 cm, extending towards the right hemi-abdomen and touching/displacing the adjacent bowel loops. The image was suggestive of primary ovarian tumor. In addition, an expansive thin-walled unilocular cystic lesion measuring ~12 x 8.3 x 14 cm was observed in the left adnexal region (contralateral to the malignant lesion) with no vegetations or solid components inside.

Imaging was followed by laparotomy for tumor evaluation, hysterectomy with resection of contiguous organs, and bilateral inguinal-iliac and retroperitoneal lymphadenectomy. The anatomopathological (AP) study of the right ovary revealed a malignant undifferentiated spindle cell neoplasm (i.e., undifferentiated sarcoma) adhering to the wall of a small enteric segment. The study of the left ovary revealed a 14-mm mucinous cystadenoma. The peritoneal lavage was negative for malignant cells.

Figure 4: Images obtained through hematoxylin and eosin method, 200X. Figure 4 is composed by Image 1: Fusiform malignant neoplasm with large cell capacity and nuclear atypia; cells are arranged in interlacing bundles. Image 2: Malignant fusiform neoplasm with great cellularity and nuclear atypia. Cells are arranged in interlacing bundles.

The IHC study of the specimen retrieved from the right adnexal region showed a 14-cm high-grade, CD117-positive GIST (clinical stage IIIB) adhering to the right ovary, with over 50 mitoses per 50 high-power fields (HPF). Imatinib was adopted as adjuvant oncological therapy.

3. DISCUSSION

GISTs are most common in adults between the fourth and sixth decade of life (our patient was 67 at the time of diagnosis), with rare cases diagnosed in patients under 40 (WINGEN et al., 2005). Any part of the digestive tract may be affected, including the omentum, the mesentery and the peritoneum, but GISTs generally develop in the stomach or the small bowel (MATTEO et al., 2008). Exceptionally, they

occur in sites outside the digestive tract: in our patient, the tumor invaded the ovary, with image findings suggestive of malignant adnexal mass on the right side. GISTs manifesting as pelvic mass are easily mistaken for ovarian tumors (CARLOMAGNO; BENEDUCE, 2015). Symptoms are mostly unspecific (nausea, vomiting, abdominal distress, bloating, weight loss). The most common signs and symptoms include abdominal mass, bleeding, hematemesis, melena and anemia (MOTEGI et al., 2005). Some patients display more acute symptoms such as intestinal obstruction and peritonitis secondary to perforation. In general, pain depends on tumor size (WINGEN et al., 2005). About one tenth of cases remain asymptomatic due to small tumor size (<2 cm) (DORFMAN et al., 2006). In our patient, a large, palpable abdominal mass was observed on the right side associated with localized abdominal pain and constipation. The literature provides a classification system to determine the risk of aggressiveness based on tumor size and mitotic rate (Table 1) (RUBIN et al., 2016). The reported case was classified as high risk: tumor size 14 cm (largest diameter), and 62 mitoses per 50 HPF.

Table 1: Stratification of risk of GIST aggressiveness based on tumor size and mitotic rate:

Stratification of risk	Tumor size and mitotic rate
Very low risk	<2 cm and <5/50 HPF
Low risk	2-5 cm and <5/50 HPF
Moderate risk	5-10 cm and >5/50 HPF
High risk	>5 cm and >5/50 HPF or >10 cm and any mitotic rate or Any size and >10/50 HPF

GISTs are almost impossible to diagnose preoperatively because of their rarity, variable presentations and, most importantly, because diagnosis is based on cell morphology and immunophenotyping. CD117 positivity is a defining trait of GIST (DORFMAN et al., 2006), being positive in up to 95% of cases (Table 2). Radiographic findings are unspecific to a point that a pre-surgical diagnosis based on imaging is practically impossible (DA RONCH et al., 2006). CT, the imaging modality of choice for patients with pelvic mass, provides information on both preoperative stage and the presence of metastases, but no GIST-specific findings. PET scans and endoscopy are helpful in the monitoring of disease progression. In the reported case imaging methods not only weren't capable of diagnosing GIST, but also strongly suggested ovarian tumor (PATIL et al., 2011).

GIST metastases are most often found in the peritoneum, omentum, mesenteric region and liver. However, the peritoneal and retroperitoneal lymph nodes, the omentum, the uterus, the peritoneal lavage and other biopsies of our patient were negative for malignant cells. In addition, the pathological study of the right ovary identified an unruptured undifferentiated sarcoma adhering to the wall of a small enteric segment, with expansive neoplastic borders, moderate nuclear pleomorphism, necrosis. Only the muscle tissue of the small bowel was compromised, but no venous,

neural or lymphatic infiltration. The overall 5-year survival rate of GIST patients is 28-60%, depending on disease progression (LEE, 2013).

The gold standard treatment for GIST is complete surgical resection, with free surgical margins whenever possible. Biological therapy with imatinib helps control advanced and/or metastatic GIST. The risk of recurrence is high, and the 2-year survival rate after imatinib therapy is 50-70%. Interruption of imatinib therapy after one year is associated with high risk of recurrence, even in patients with complete remission. Although imatinib can elicit a partial response and stabilize the disease in most patients, response is seldom complete and around half the patients develop resistance to the drug. Sunitinib, a recently approved option, may be used in such cases (BLAY et al., 2007; ANTONESCU, 2011).

Our patient was submitted to complete surgical resection (hysterectomy with resection of contiguous organs and bilateral inguinal-iliac and retroperitoneal lymphadenectomy) and prescribed adjuvant treatment with imatinib (400 mg/day) for 3 years. Currently, the patient is clinically stable and followed quarterly.

In summary, we report the case of a 67-year old woman presenting with a pelvic mass, but with a CA-125 test of only 25.8 (Table 2). Imaging was suggestive of ovarian tumor, and the patient was submitted to complete surgical resection. A 14-cm GIST adhering to an enteric segment was confirmed on AP and IHC, with over 50 mitoses per 50 HPF (high histological grade). The patient has been on postoperative imatinib therapy for over one year, with no sign of recurrence.

Table 2: Tumor markers for GIST and ovarian sarcoma vs. findings of the reported case:

Tumor markers	Ovarian sarcoma	GIST	Reported case
CA125	>35 U/mL	<35 U/mL	25.8 U/mL
C-KIT (CD 117)	-	+	+
CD-34	-	+	-
DOG-1	-	+	+
Estrogen receptor	+	-	-

4. CONCLUSION

When clinical findings and biochemical markers are incompatible with the tumor site on imaging, differential diagnoses should be considered. In the reported case, an expansive lesion was identified on US and CT, but imaging failed to determine the primary tumor site and made a diagnosis of GIST seem unlikely. Nevertheless, the finding of CD117 positivity on IHC made it possible to establish a diagnosis of GIST. The reported case stresses the importance of IHC to ensure timely diagnosis and proper treatment of GISTs (especially when its presentation is atypical), thereby improving prognosis.

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Financing:

"No sponsorship was received for the study and publication of the article".

Authorship:

"All authors named in this work meet the criteria established by the International Committee of Medical Journal Editors (ICMJE), assuming full responsibility for the integrity of all work and final approval of the version to be published".

Disclosures:

Daiana Fistarol declares that it has no conflict of interest.

Leonardo Zilotti declares that it has no conflict of interest.

Ademar Dantas Junior declares that it has no conflict of interest.

Dante Morelli declares that it has no conflict of interest.

Compliance with ethical guidelines:

All steps of the study were in line with the ethical standards of the Committee responsible for human experimentation (institutional and national) and in accordance with the Helsinki Declaration of 1964, revised in 2013.