Metachronous extragastrointestinal stromal tumor (EGIST) in utero: Report of an unusual case

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ABSTRACT

INTRODUCTION: The gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor in the digestive tract. Currently, GIST is the name given to CD117 positive mesenchymal tumors, primary of the digestive tract, mesentery, and retroperitoneum. Nevertheless, they have been reported in the mesentery, omentum, gallbladder, bladder wall, ovary, rectovaginal septum, and uterus, named extragastrointestinal stromal tumors (EGIST).

PRESENTATION OF CASE: Seventy-six-year-old woman with a history of the third recurrence of pelvic tumor located in the uterus initially diagnosed as uterine leiomyosarcoma. CT and MRI showed a tumor in the uterine corpus of approximately 10 cm. It was decided to perform the surgical rescue. The immunohistochemistry and anatomic pathology report revealed a tumor compatible with a uterine EGIST. It was decided to perform adjuvant treatment with imatinib. Currently, the patient continues to be disease-free 20 months after the surgery.

DISCUSSION: For years, GIST has often been confused with leiomyosarcoma, given that they are histologically almost indistinguishable. The IHC analysis for KIT (CD117) has become essential in the GIST diagnosis. On the other hand, stromal tumors arising outside the gastrointestinal tract are rare (5%), which have a histological and biological behavior similar to that of GISTs.

CONCLUSION: EGISTs are extremely rare and often incidentally detected. Currently, evidence about this location is scarce. According to the literature, this is the first case of uterine EGIST with a metachronous presentation.

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1. Introduction

Gastrointestinal Stromal Tumors (GISTs) represent 2% of gastrointestinal tumors and 80% of sarcomas in this location. Historically, GISTs were misclassified as leiomyomas or leiomyosarcomas [1]. Currently, GIST is the name given to CD117 positive mesenchymal tumors, primary of the digestive tract, mesentery, and retroperitoneum [2].

In terms of origin, it is postulated that they are derived from interstitial cells of Cajal or a more immature and pluripotent predecessor. The most common locations are the stomach (50–60%), small intestine (20–30%), colon (10%), and the remaining 15% in the rectus, esophagus, mesentery, and retroperitoneum [2]. Nevertheless, they have been described in the mesentery, omentum, gallbladder, bladder wall, ovary, rectovaginal septum, and uterus, named extragastrointestinal stromal tumors (EGISTs) [3,4].

The objective of this article is to report the case of a patient with a uterine extragastrointestinal tumor with a metachronous presentation. This manuscript is reported in line with the SCARE criteria [5].

2. Presentation of case

A 76-year-old woman with a pathological history of class I obesity (BMI 30 kg / m2), type 2 diabetes mellitus, osteoporosis and allergy to penicillin, no history of drug use, tobacco, alcohol abuse, or genetic alterations. She was referred from another institution, by the third recurrence of a uterine tumor. The early diagnosis corresponded to muscle-type spindle cell mesenchymal neoplasia (leiomyosarcoma), with immunohistochemistry (IHC) positive for smooth muscle actin (SMA), negative CD117, and Ki67 1%. She received adjuvant treatment only once, with scheme Docetaxel and Gemcitabine for six cycles, after the first surgery. She presented local recurrences; requiring two additional surgical procedures,
which were reported as exploratory laparotomies with partial hysterectomy.

On admission, her vital signs were: body temperature 37°C, pulse rate 80/min, respiration rate 14/min, blood pressure 110/70 mmHg, and SpO2 98%. She expressed perineal pain with difficulty in defecation and the physical examination revealed a bulky lesion protruding from the vaginal introitus. Her laboratory tests showed no significant abnormalities.

The computed tomography (CT) of the abdomen and pelvis showed an enlarged, globular, hypodense uterus displacing the bladder, and the rectus did not present detectable alterations (Fig. 1). An MRI was performed, finding a heterogeneous voluminous mass in the uterine corpus; it was solid, 10 cm in size in the craniocaudal view for 9.8 cm in the anteroposterior view for 9.6 cm in the transverse view. The remaining part presented no alterations (Fig. 2).

A videocolonoscopy was requested, but the patient refused to take it.

The case was analyzed by a multidisciplinary committee and it was decided to perform surgical rescue for suspected local recurrence of uterine leiomyosarcoma, in charge of the oncological and colorectal surgeons of our institution.

Laparotomy examination revealed a voluminous tumor, of approximately 10 cm in all its dimensions, which extended to the vagina. It was completely separated from the bladder. On a combined basis, the tumor was approached through the vagina until the abdominal cavity was identified and the two working planes were joined together. It was not possible to separate it from the upper rectus and sigmoid, where the tumor was firmly united by multiple adhesions of previous laparotomies; thus performing a block resection. It was decided to perform a pull-through technique with coloanal anastomosis (Fig. 3). The operative time lasted eight hours, with an estimated blood loss of 500 cc and a transfusion of three red blood cell units.

Immediate follow-up after surgery was in the intensive care unit showing positive clinical evolution. On the tenth day of admission, due to positive evolution, hospital discharge, with indications, and scheduled medical check-ups are indicated.

The anatomicopathological report and the IHC revealed spindle-cell neoplasia positive for CD34, CD117, and c-KIT; compatible with GIST and a mitotic count <5/50 HPF (Fig. 4).

Given the finding of an intermediate-risk uterine EGIST, adjuvant treatment with imatinib was started.

Twenty months after surgery, the patient continues under scheduled clinical and imaging controls, with good tolerance to treatment without showing oncological relapse, and with standardized adjuvant treatment (Fig. 5).

3. Discussion

GIST incidence is 10–20 cases per million inhabitants and the median age of presentation is 50–70 years, with a slight predominance in men. On the contrary, the real incidence of EGIST is unknown [6].
Clinical manifestations rely upon its size and location, being the most frequent abdominal pain, digestive hemorrhage, and abdominal mass, although there are many asymptomatic individuals [7].

Approximately 95% of GISTs express the receptor tyrosine kinase c-KIT, also known as CD117, considered as the gold standard for GIST diagnosis, although a small group of them are negative [8]. There are other markers positive as the CD34 (60–70%), SMA (15–60%), S-100 (5–10%), and Desmin (1–2%). However, none of them are specific to diagnose GIST in absence of positivity for KIT [8].

Recently, DOG1 expression has been described in up to 95–98% of cases, even in those CD117 negative. It is expressed in tumors with KIT-gene mutations and those with PDGFRA mutation [9,10]. Most mutations in the c-KIT gene occur in exons 9, 11, 13, and 17, corresponding to the extra-membrane domain (exon 9), the juxtamembrane intracellular regulation domain (exon 11), and the two intra-cytoplasmic tyrosine kinase domains (exons 13 and 17) and a large proportion of mutations in the PDGFRA gene occur in exon 18 (7–12% of cases). Being this useful for diagnosis in doubtful cases [11].
Extragastrointestinal stromal tumors (EGIST) were first described in the year 2000, as neoplasias of abdominal soft tissues, with a histological and biological behavior similar to that of GISTs. There are no large studies dedicated specifically to EGIST and these are often included in stromal tumor studies, accounting for 5% of the total [3,12].

Publications to date are a series of few cases, with a slight prevalence in females and an average size of 12 cm [13]. The case we present describes a rare location in the uterus. At present, few cases have been reported in this location, with incidental diagnosis in the context of a surgical procedure [4].

In the differential diagnosis of GIST located in the pelvis, leiomyosarcomas must be included. For years, GIST has been mistaken for leiomyosarcoma [14]. It was thought that intestinal leiomyosarcomas were the most common and GISTs were pure rarities. However, more and more institutes look their files for old biopsies of leiomyosarcomas, which, if under new criteria, would turn out to be from GIST in almost all its entirety. In this way, GIST positions itself as the most frequent variety of abdominal sarcoma [15,16].

In this report, the patient initially presented with a lump in the pelvic cavity with histomorphological characteristics and IHC correspondent to a uterine leiomyosarcoma; with two recurrences over the course of eight years, that were treated only surgically. No further IHC techniques were performed. IHC staining for KIT (CD117) has become essential for GIST diagnosis, almost 90% of which show activating mutations in KIT the receptor [9]. It was proved that EGISTs show c-KIT expression, which implies the presence of peacemaker cells outside the gastrointestinal tract, and besides they present with a histological and immunophenotypic appearance similar to GIST [10].

c-KIT represents a sensitive and reliable method to identify the gastrointestinal and extragastrointestinal forms of the disease [10].

Leiomyosarcomas and GISTs are virtually indistinguishable for the most exhaustive microscopic examination [1,7]. For this reason, we conclude that local recurrences corresponded to a GIST, which probably went unnoticed, given that pelvic masses were not recategorized by IHC techniques since the first finding and for low suspicion, considering its location. There is also a crucial difference; GIST is very sensitive to treatment with imatinib, whereas
leiomyosarcomas are resistant to its action. Survival has improved with the use of adjuvant imatinib for three years in high-risk tumors [17]. This resembles the evolution of our patient, who is currently under adjuvant treatment with imatinib and is disease-free.

We should mention that the presentation of EGIST was within seven years after the uterine leiomyosarcoma diagnosis, it would be then a metachronous presentation. The coexistence of GIST with other neoplasias has been widely reported in the literature. Almost a third of GISTS are discovered incidentally during research or therapeutic procedures for non-related diseases [2,6]. In this context, GISTS may coexist with different types of cancer, either synchronously or metachronously. The frequency of this association and the spectrum of neoplasias involved have not been sufficiently analyzed [18].

We have little information about the prognosis of EGIST, although in general, they tend to evolve more unfavorably, sharing characteristics with GIST located in the distal gastrointestinal tract [14,19].

In our report, the tumor size is approximately 10 cm and mitotic count <5/50 HPF, categorized in intermediate-risk, which is consistent with the behavior reported in this type of tumors.

4. Conclusion

EGISTSs are extremely rare and are usually detected incidentally. Its incidence, prevalence, and clinical aggressiveness have been underestimated.

Currently, there is little evidence regarding this location, this being the first case of uterine EGIST with a metachronous presentation.

Conflicts of interest

There is no conflict to be declared.

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No source to be stated.

Ethical approval

This is a case report study and ethical approval not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

1. Dr. René Manuel, Palacios Huatuco (data collection, editing the paper and interpretation).
2. Dra. Diana Alejandra, Pantoja Pachajoa (literature review, editing the paper, and approved the final version).
3. Dr. Rafael, Palencia (data analysis and literature review).
4. Dr. Matias, Parodi (surgical treatment of the patient, literature review, and approved the final version).
5. Dr. Alejandro Marcelo, Doniquian (interpretation, editing the paper, and approved the final version).
6. Dr. Facundo Ignacio, Mandojana (surgical treatment of the patient, literature review, and approved the final version).

Registration of research studies

1. Name of the registry: N / A *
2. Unique identifying number or registration ID: N / A *
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): N / A *

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