Managment of gastrointestinal stromal tumor in pregnancy: a case report

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Abstract

Background: The gastrointestinal stromal tumors are the most common mesenchymal cancer of the gastrointestinal tract. The diagnosis of gastrointestinal stromal tumors during pregnancy is very rare.

Case presentation: The reported patient was admitted at the University Hospital of Fez, Morocco, for gastrointestinal stromal tumor revealed during the fifth month of pregnancy. The patient was 42-years-old and was admitted for biliary colic pain with vomiting. The abdominal examination objectified a swollen abdomen with uterine height of 18 cm and epigastric mass of 10 cm. The ultrasound and magnetic resonance imaging demonstrated hepatic tissues and cystic mass expanding on the left liver. The endoscopy demonstrated aspects of extrinsic compression in the front of the stomach. A Cesarean section was scheduled by the 35th week of pregnancy for fetal extraction and rescue. The peritoneal cavity exploration during surgery revealed a highly vascularised hepatic mass expanding up to the umbilicus which was unresectable. The postoperative computed tomography scan revealed a large bilobed epigastric mass adhering to the stomach on the left of the liver. The histological and immunohistochemical study of hepatic process showed a gastrointestinal stromal tumor of high malignancy risk.

Conclusion: Very few cases of stromal tumors during pregnancy have been reported in the literature to date, and multidisciplinary patient care is required for better treatment and prognosis.

Keywords: Gastrointestinal stromal tumors, Pregnancy, Imatinib
Introduction
Gastrointestinal stromal tumors (GISTs) are mesenchymal cancers mostly evolving in the stomach and small intestine, and exceptionally in the rectum, colon, esophagus or mesentery tracts. GIST originates from Cajal or precursor cells with typical “CD117/KIT+ (95%)”, “CD34+ (70%)” phenotypes. These cells are often associated with mutations activating genes encoding tyrosine kinase receptor or PDGFRA (platelet-derived growth factor receptor, alpha polypeptide). The diagnosis of GIST during pregnancy is very rare. There are less than 20 reported GIST cases in the literature diagnosed during pregnancy [1]. We report a gastric GIST case diagnosed during pregnancy with favorable outcome, and we discuss the diagnostic and prognosis aspects involved in this pathological entity.

Case presentation
A 42-year-old mother of 7 children was admitted by the 20\textsuperscript{th} gestational week for moderate hepatic pain evolving seven months earlier associating an atypical epigastric pain. The clinical examination revealed a patient of good general state with a distended abdomen and uterine height of 18 cm; the patient showed a smooth epigastric and painful mass of 10 cm. The blood assessment showed a hypochromic microcytic anemia with a biological inflammatory syndrome. The morphological assessment including abdominal ultrasound revealed a hepatic cyst and tissue mass with thickened and irregular contours. The pelvic ultrasound demonstrated an evolving single-fetus pregnancy of 22 weeks. Given the gastric compressive aspect of the tumor, the upper gastrointestinal endoscopy was performed. This assessment highlighted an aspect of extrinsic compression in the front of the stomach without mucosa lesions. The hepatic magnetic resonance imaging (MRI) found a large heterogeneous lesion process in the epigastric region with two components. A liquefied center with high content of mucin and blood, then a very irregular peripheral component with irregular and asymmetric internal contours were seen. This mass was localized in the
epigastric region and directed to the left liver and in contact with the stomach wall in the same side of the small curvature (Figure 1 and 2).

The case was discussed within the framework of a multidisciplinary team; the gastric GIST diagnosis was suggested and the decision was to continue the pregnancy until fetal maturation with close and continuous follow-up, and evaluation. Corticosteroids therapy protocol was initiated and monitored every week until the 35th week of pregnancy. Then, a cesarean section was performed to extract a newborn weighing 2.5 kg without any apparent abnormality. The patient abdomen exploration during surgery objectified a highly vascularized mass expanding within the liver and reaching the umbilicus without possibility of resection.

The post operative abdominal computed tomography (CT) demonstrated a large limited and bilobed epigastric mass measuring 16x21x23 cm. Two components were identified; fleshy peripheral component enhanced after contrast agent injection and liquefied central component with significant vasculature. This tumoral mass has increased dimensions by 8 cm compared to earlier MRI results (Figure 3). The liver biopsy of the mass showed a gastrointestinal stromal tumor with high risk of malignancy. The immunohistochemistry revealed a positive CD 117, CD 34, PS100 and AML (Figure 4). An Imatinib dose of 400 mg/day was started to reduce the tumor size before surgical resection. Three months later, the size of the epigastric mass decreased but liver metastasis appeared.

One month later, the patient underwent surgery which revealed a cystic tumor of 30 cm in diameter; this dislocated the stomach back and left with an intimate contact with the lower side of the left liver lobe. A total gastrectomy was performed, with hepatic resection of the left lobe of the liver. This surgical approach allowed a full removal the tumor. Esophagus jejunum anastomosis and feeding jejunostomy were performed (Figure 5). The histological study showed a high grade gastric stromal tumor including more than 50% necrosis which was due to imatinib response. After lymphadenectomy, 26 non-metastatic lymph nodes were
found. A neoadjuvant treatment with imatinib 400 mg/day was started with good adherence and tolerability. Indeed the partial clinical and radiological response assessment was favorable. However, the patient presented a neutropenia with 800 elements/mm$^3$; this motivated reducing the daily dose of imatinib to half, with good tolerance and appropriate correction of neutropenia.

**Discussion**

The GIST is a rare tumor with an incidence rate of 10 to 20 cases/million/year [1]. Early diagnosis is important for favorable prognosis. The GIST are rarer during pregnancy, fewer cases were reported in the literature [2]. Indeed, GISTs are the most common mesenchymal tumors of the gastrointestinal tract. Microscopy and immunohistochemistry studies allowed classifying these tumors according to their phenotypes and possible prognosis. Two main tumoral markers were identified CD34, and KIT protein or CD117.

The GIST incidence in the United States is ranging between 3000 to 4000 cases per year, while the median age of occurrence was 60 years [3]. The most GISTs are localized in the stomach (60%) and small intestine (30%), especially when associated with pregnancy [1]; while 10% are localized in the esophagus and rectum [4]. Their detection is sporadic in most cases, while the genetical predisposition was reported including type I neurofibromatosis. Carney et al. has described an exceptional familial form related to a constitutional mutation of KIT or PDGFRA [5]. Although rare, the association of GIST to pregnancy are expressing early diagnosis challenge; hence recommending the efficient treatment without major impact on the fetal outcome. The diagnosis could be difficult because the age of GIST onset in a pregnant woman does not fit with the incidence profile reported in the literature. 20% of cases were diagnosed when performing an endoscopy for another indication. And 15 to 25% of GIST cases were revealed in the metastatic stage. The clinical presentation of GIST during pregnancy is not specific and might include gastrointestinal bleeding, unexplained
anemia or abdominal mass [6-7]. Reported GIST cases did not manifest any specific symptoms. However, only the histological study allows confirming the diagnosis.

There is not any recommendation for the management of GIST during pregnancy, the treatment decision has come-out from a multidisciplinary team including oncologist, gastroenterologist, pathologist, surgeon and obstetrician [8-9], such was done in our patient. The average diameter of symptomatic tumors was 6 cm against 1.5 cm for asymptomatic tumors [10]. Our patient had a tumor size exceeding 20 cm. The literature reported tumors diameter ranging from 4 to 17cm [11]. Useful tests for the GIST diagnosis depends on the size and localization of the tumor. Furthermore, tumors of less than 5 cm with gastric or colorectal localization might allow the endoscopy diagnosis and ultrasound confirmation. The diagnosis of small GIST in the small intestine is made by enteroclysis and/or enteroscopy. In case of very large GIST, the abdominal CT remains the gold standard [12]. The option of MRI in pregnancy is recommended, which was performed in our case.

All GISTs are potentially malignant. Indeed the recurrence risk after resection could be assessed according to the size and mitotic index. Other parameters such as gastric localization, presence of necrosis and the type of mutation have prognostic value [13]. GIST metastases are localized in the liver in 67% of cases and in the peritoneum in 25% of cases. Lymph node metastases are rare but do not justify their dissection whenever the diagnosis is suspected. Lung metastasis are also rare and their occurrence might justify reviewing the diagnosis [9]; their management is slightly different from the usual recommendations except for gestational cases where the prognosis is rarely impacted by the pregnancy [1].

The surgical resection is the only curative treatment of GIST tumors. Currently, metastatic GIST is fatal, since being totally resistant to the available chemotherapy and radiotherapy protocols [9]. However, the targeted therapies development especially with inhibitors of tyrosine kinase receptors, such as imatinib mesylate has significantly improved the survival of
metastatic GIST.3 over 4 metastatic GIST cases associating pregnancy reported in the literature, have survived at least 9 years after the diagnosis [9].

The management of GIST during pregnancy is varying according to the expertise involved and the resources available in each center. Some treatment protocols suggest achieving initial surgical treatment during pregnancy to avoid the tumor evolvement that might become harder to extract after delivery. Scherjon et al. described a favorable outcome of patients operated in the first trimester of pregnancy without significant impact on the fetus, and without recurrence after 6 years recession [14]. Authors advocated an elective combination of caesarean section and small bowel GIST during the third trimester of pregnancy with satisfactory results [15].

Imatinib treatment protocol provides a remarkable tumor response in 85% to 90% of cases; the evolution without recurrence was shown within 24 months and an overall survival of more than 36 months [16]. Tumor response was significantly correlated with c-KIT mutation occurrence [5]. Adjuvant therapy after complete GIST resection might be useful [7]. Indeed, our patient underwent imatinib chemotherapy after surgery. Data about Imatinib use in pregnant women is limited. Studies demonstrated that imatinib during pregnancy is responsible for spontaneous abortion and fetal congenital abnormalities. Imatinib should not be used during pregnancy unless there is a clear and imminent therapeutical requirement. In case of any use during pregnancy, the fetal potential risk has to be evaluated [1]. Imatinib efficiency in localized or metastatic advanced stromal tumors is at present well established. However, its benefit such as adjuvant or neoadjuvant treatment to surgery is not fully understood [17].

**Conclusion**

Gastrointestinal stromal tumors during pregnancy are extremely rare. The patient care has to involve multidisciplinary team for better treatment options, hence better prognosis. Indeed, this approach allowed favorable outcome for our patient.
List of abbreviations:

- GISTs: Gastrointestinal stromal tumors
- PDGFRA: Alpha-type platelet-derived growth factor receptor
- CD117/Kit: Tyrosine-protein kinase
- MRI: Magnetic Resonance Imaging
- Abdominal CT: Abdominal computed tomography

Consent

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

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

MI, NK, IC, FF, OM and AO treated the patient and wrote the case report; AI supervised the writing. All authors read and approved the final manuscript.
References
Figure 1: Axial view of the stromal tumor in MRI
Figure 2: Sagittal view of the stromal tumor in MRI
Figure 3: Axial view of the stromal tumor in abdominal CT
**Figure 4a**: positive immunohistochemistry for the CD117

**Figure 4b**: positive immunohistochemistry for the CD34
Figure 5a: Macroscopic aspect of the stromal tumor at surgical exploration

Figure 5b: Macroscopic aspect of the stromal tumor after resection of the stromal tumor