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Report of a giant tumor with a rare histological pattern.

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Gastrointestinal stromal tumor of the gastric serosa protruding to the greater omentum. Report of a giant tumor with a rare histological pattern.

We report an unusual case of a 76 year old woman admitted to our hospital for investigation of anemia and palpable epigastric mass. Intraoperatively a huge (19 cm), well defined tumor was found adhering to the stomach wall, protruding into the greater omentum and compressing the transverse colon. A tumorectomy was performed and the greater omentum was removed due to its close relation. Pathology revealed a high risk Gastrointestinal Stromal tumor of the gastric serosa. Histologically the tumor was of mixed type (spindle and epitheliod cells) with hemangiopericytomatoid pattern peripherically, variably myxoid stroma, central necrosis and cytologic pleomorphism. On immunohistochemical examination there was a consistent positivity for c-kit (CD-117) and CD-34, but without myogenic or neural differentiation. We consider this case unusual because of its huge size, its gastric serosal location and its extremely rare histological pattern.

KEY WORDS: C-kit, Gastrointestinal stromal tumor, Gastric serosa, Interstitial cells of Cajal, Imatinib mesylate.

Introduction

Gastrointestinal Stromal Tumours (GIST) are the most frequent form of mesenchymal tumours of the Gastrointestinal Tract [1,2]. Although still confusing, concerning their clinical behavior, they have recently been elucidated as distinct clinical and pathological entities. These neoplasms, previously regarded as myogenic tumours (leiomyoma, leiomyoblastoma, leiomyosarcoma) or neural tumors (schwannoma), are now well defined, based on their histological pattern as spindle or epithelioid cell lesions arising in the wall of the Gastrointestinal tract and on their immunophenotype as specific c-kit expressing and kit signaling driven mesenchymal tumours, most of which have kit-activating mutations [2,3]. We describe herein an unusual case of GIST, due to the combination of morphological and pathological features.

Case report

A 76 year old woman was initially admitted to our hospital for investigation of anemia and of an intra-abdominal tumor, which had been identified on physical examination.
On admission the patient was well nourished. The presenting symptoms were weakness and constipation for

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the last 25 days. Physical examination was unremarkable except for the signs of anemia of the palpebral conjunctivae and the distended abdomen with a palpable epigastric mass. The peripheral blood cell count showed moderate anemia with a blood cell count of 3, 1 x 10^6 /mm^3 (HGB: 8,09 g/dl, MCV 85,7 fl). The serum tumor markers revealed an increased CA 125 (210 U/ml). Gastroscopy showed that the anterior gastric surface in the region of the pyloric antrum was compressed extraluminary without mucosal abnormalities. Abdominal ultrasonography and computed tomography (Fig. 1) revealed a well defined sizeable mass of heterogenous density, 19cm in diameter lying below the left lobe of the liver, in front and adjacent to the stomach and the transverse colon. Free fluid was apparent in the perihepatic and Douglas regions.

At laparotomy, a well defined tumor was found adhering to the stomach wall, protruding into the greater omentum and compressing the transverse colon. On frozen sections a mesenchymal tumor with myxoid degeneration was revealed. A tumorectomy was performed without difficulty. The greater omentum was also removed due to its close relation with the tumor.

On macroscopic examination, the tumor measured 19x14x3 cm, had a multilobal external surface and central cystic hemorrhagic degenaration. On cut surface the cystic wall 2,7 cm thick, nodular with elastic and focally myxoid consistency.

Histologically, the tumor exhibited a mixed cell pattern (spindle and epithelioid). Peripherally, the lesion showed hemangiopericytomatoid pattern with spindle-shaped or ovoid cells with focally nuclear palisading and variably prominent myxoid stroma (Fig. 2). In this area smooth muscle bundles were entrapped, probably from the gastric wall. An abrupt or gradual transition, between spindle cells arranged in short fascicles or whirls and sheets of epithelioid cells, was apparent. In these areas abundant collagenous stroma surrounded nodules or isolated neoplastic cells. Stromal bheeding was extensive, especially in the central areas of the neoplasm. Cytologic pleomorphism was also noted. The mitotic rate was 6-9/ 50 H.P.F. Invasion of the greater omentum was not observed.

Immunohistochemical examination showed positivity for C-kit (CD-117) in >50% of the tumor cells with variable intensity (Fig. 3), 10-100% positivity for CD34 in different sections and 20-30% positivity for SMA. Most of the tumor cells expressed an intensive positive immunoreactivity for Vimentin but no immunoreactivity for Desmin, HHF-35, EMA, S-100 protein and Cytokeratines 8, 18, 19, and 10, 14. The Ki-67 (MIB-1); proliferation index was 2-10%.

The diagnosis of high risk, mixed cell type, Gastrointestinal Stromal Tumor of the gastric serosa was confirmed.

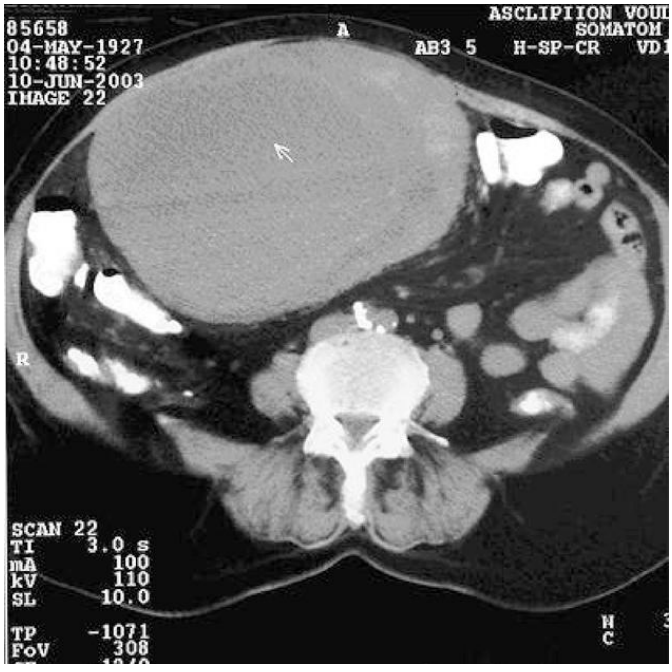

Fig. 1: Computed Tomography. Sizeable mass lying below the left lobe of the liver; in front and adjacent to the stomach and the transverse colon.

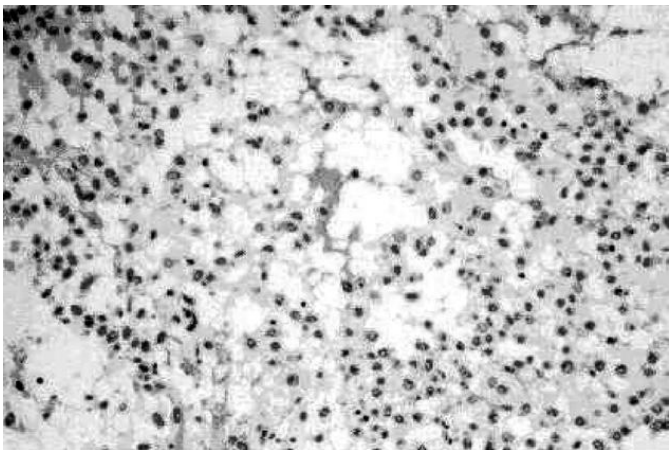

Fig. 2: Hemangiopericytomatoid pattern with spindle-shaped or ovoid cells with focally nuclear palisading and variably prominent myxoid stroma. H/E 10X.

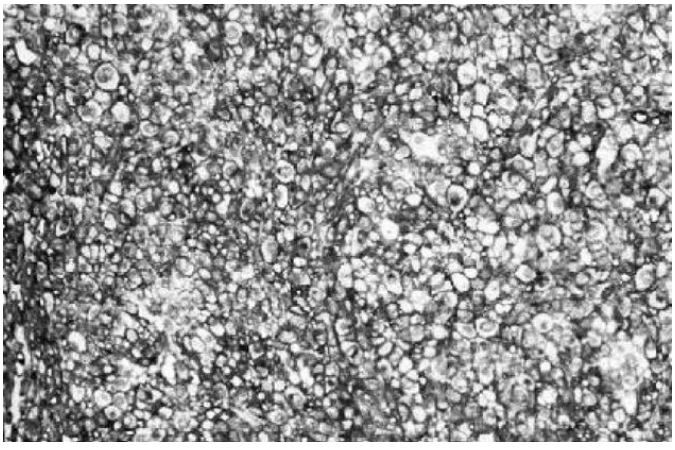

Fig. 3: Intense C-kit (CD-117) positivity. 20X.

The patient was discharged a few days later, after an unventful postoperative course. Due to the high risk potential and although no clinical trial has yet assured the benefit of antitumor therapy with Imatinib mesylate (synthetic tyrosine kinase inhibitor) after complete surgical excision, the patient was assigned to receive the drug (400mg/day orally).
The follow up 6 and 12 months later was unremarkable. The anemia and the assosiated symtoms had retrieved (HGB: 12,2 g/dl, MCV: 83,5 fl), while the tumor serum markers returned to normal (CA 125: 3,9 U/ml). Constipation was also eliminated. The CT scan using IV contrast, the barium meal and gastroscopy showed no signs of tumor recurrence.

Discussion

Mazur and Clark introduced the term "stromal tumor" in 1983 referring to a group of mesencymal neoplasms that lacked the immunophenotypic features of smooth muscle differentiation[4]. The demonstration of CD-34 expression by many GISTs suggested a specific entity distinct from smooth muscle tumors [5]. It was the subsequent observation of CD117 expression that ultimately led to the current acceptance that gastrointestinal, mesenchymal, tumors can be divided into GISTs (CD-117 positive), true smooth muscle tumors and true schwann cell tumors [6]. We now know that GIST cells demonstrate characteristics similar to those of the interstitial cells of Cajal, or pacemaker cells, which control gut motility [1].
The annual incidence of all GISTs is around 16-20 cases per million [7,8]. About 60-70% of GISTs occur in the stomach, 20-30% in the small intestine and 10% or less in the oesophagus, colon and rectum [9,10,11,12,13]. Extragastrointestinal stromal tumors, similar to GISTs may arise in the omentum, mesentery, or retroperitoneum. [14,15]
Histologically GISTs appear in 3 types: spindle cell type (70%), epithelioid type (20%), or mixed type. Only 5% of lesions show a variably prominent myxoid stroma and only a very small minority of cases (<2%) show notable cytologic pleomorphism [16].
Immunohistochemically the expression of CD-117 (a protooncogene protein) is the most important defining feature and probably the gold standard for diagnosing GISTs. CD-34 is expressed in 60-80% of GISTs.
Preoperative diagnosis remains controversial, difficult and needs a high degree of suspicion. Interestingly, reviewing the literature [17] and considering this case and other GISTs we have encountered, a correlation with the tumor serum marker CA125 probably exists.
Prognostically GISTs are categorized into low, intermediate and high risk tumors based on an estimation of their potential for reccurence and metastases. They are all potentially malignant [3]. High risk tumors are considered those 1) larger than 10cm in size, 2) larger than 5 cm in size with more than 5/50 HPF mitosis count and 3) with more than 10/50 HPF mitosis count.
Treatment of choice remains the complete surgical excision. Targeted therapy with Imatinib mesylate a synthetic tyrosine kinase inhibitor is considered to be the drug of choice for metastatic and inoperable GIST. The efficacy of Imatinib after surgical excision as a protective agent for reccurence or metastases has not yet elucidated.
Of those GISTs that undergo resection, about half will recur or metastasize and half will not [9].

Conclusions

Our case represents an unusual mixed cell type GIST, due to its size and pathological findings. The cystic degeneration with central necrosis, the hemangiopericytomatoid component, the mixoid stroma and the cytologic pleomorphism compose a rare histologic pattern. According to the statistics presented above this case is estimated to be less than 1% of the reported ones and less than 8 cases per 10^8 of population, meaning that in our country (approximately 10^6 citizens) this case might be unique. Suprisingly, despite the poor prognostic factors (size 19 cm, mitotic rate 9/50 HPF) no metastases were apparent. Although still controversial, the use of Imatinib was considered essential due to the high potential of malignancy. The 12 month follow up has showed no signs of recurrence or metastases, thus enforcing our surgical and medical intervention.

Riassunto

Gli autori presentano l'inusuale di una donna 76enne, ricoverata nel nostro ospedale per accertamenti, data la presenza di una massa in sede epigastrica, bene evidente e palpabile, associate ad una netta anemia.
Intraoperativamente è stata scoperta una massa tumorale ben circoscritta, di enormi dimensioni (diametro di 19 cm) aderente alla parete gastrica e protrudente nel grande omento, con compressione a livello del colon trasverso. Fu eseguita una tumorectomia allargata, con asportazione insieme alla massa tumorale anche il grande omento, direttamente coinvolto per infiltrazione da parte del tumore in questione.
Dall'esame citoistologico della massa asportata gli Anatomopatologhi hanno identificato un tumore gastrointestinale stromale della sierosa gastrica ad alto rischio (cellule fusate ed epitelioidi).
Istologicamente il tumore si dimostrò a struttura mista, con aspetto emangiopericitomatoide perifericamente, uno stroma variabilmente mixoide, una zona di necrosi centrale ed infine un intenso pleiomorfismo citologico.
All'esame immunoistochimico è stata rilevata una consistente positività per i noti oncogeni c- kit (CD – 117)

e CD – 34, senza però che coesistesse una ben documentabile differenziazione miogenica oppure neurale. Consideriamo il caso da noi riportato, inusuale, a causa: A) della enorme dimensione della massa tumorale, B) della non frequente localizzazione del tumore alla sierosa parietale gastrica ed infine C) dell' estremamente raro corredo istocitologico del tumore .

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