Malignant gastrointestinal stromal tumor of the ampulla of Vater presenting with obstructive jaundice

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ABSTRACT

Malignant gastrointestinal stromal tumor (GIST) consists a rare neoplasm, developing in small intestine and stomach. The presenting manifestations include weakness, weight loss, nausea, melena and anaemia. The present case refers to a 65 years old female patient with a GIST of the ampulla of Vater presenting with obstructive jaundice. Diagnosis was achieved pre-operatively by biopsies collected through diagnostic ERCP. The tumour was locally excised, with preservation of the ampulla. The histological analysis suggested low grade GIST positive for both CD 117 (c-kit) and CD34. Two years after the surgery the patient remains free of disease. Malignant GIST of the ampulla of the Vater is extremely rare as only few similar cases have been described in the literature. This is the first time a GIST being presented as obstructive jaundice ever reported. Despite the unavailability of EUS-FNA, the diagnosis was set preoperatively and the tumor was resected.

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the gastrointestinal tract, which are usually located in the small intestine and the stomach. Most authors suggest that GISTs are derived either from smooth muscle cells and neuronal elements, or by differentiation of the interstitial cell of cajal.[1] The incidence of GIST ranges from 0.1 to 3% of all gastrointestinal tumors. Duodenal GIST is even rarer representing only the 4% of these tumors.[2] GIST of the ampulla of Vater is an extremely scarce entity, as only four cases have been described to date in literature.[14] Recent studies suggest that GISTs can be diagnosed preoperatively by Endoscopic ultrasonography (EUS) and Fine needle aspiration (FNA), although in centres that do not perform EUS, the diagnosis is established mainly postoperatively by histological examination of the excised material.

The most common manifestations of GIST of the ampulla of Vater include asthenia, weight loss, nausea, melena and anaemia. The tumor may exhibit central ulceration or bleeding.[7] Obstructive jaundice as the presenting symptom of this entity has not been previously described.

Case History

A 65-years-old female patient presented to the emergency department with complaints of for 24 hours, jaundice for 48 hours and weakness and fatigue for the past 2 months. The patient’s medical record showed a history of chronic lymphocytic leukaemia (10 years ago), which was treated successfully and a duodenal ulcer (6 months ago), for which a proton pump inhibitor lansoprazol (20 mg bid) along with diet management were advised. The patient denied the use of NSAIDs for the last two months.

On admission, blood pressure was 110/80 mmHg, the heart rate was 72/min the axillary temperature was 36.5°C. The physical examination revealed jaundice. A blood cell count revealed low hematocrit (25%), while the peripheral blood smear was suggestive of hypochromic microcytic anemia. All other studies, including biochemical parameters, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (Ca 19-9) were within normal values, except for total and direct bilirubin levels which were 8.9 mg/dl and 7.2 mg/dl respectively. Gastroduodenal endoscopic study, revealed a large
oval-shaped submucosal tumour, with a central oozing ulceration. Multiple biopsies were collected from the lesion endoscopically. Attempted cholangiography and pancreatography through ERCP, for both diagnostic and therapeutic reasons, failed due to bleeding from the tumor after the collection of biopsies. The bleeding was treated conservatively with transfusion of 3 blood units and 4 plasma units. The patient stabilized two days later [Figure 1]. The unavailability of EUS in the hospital prevented the medical team from using this technique for the collection of biopsy specimens.

Computed tomography (CT scan) revealed a uniformly enhanced smooth outlined solid mass (5 x 6 cm) of the 2nd part of the duodenum (in the ampulla of Vater) with a central niche, which partially obstructed the duodenal lumen. The tumour covered the distal end of the common bile duct and was clearly separated from the pancreatic head and the inferior vena cava; with no evidence of peritoneal or liver disease [Figure 2]. The histological examination of the biopsies suggested malignant GIST. Microscopic examination of the tumor revealed large spindle-shaped and epithelioid tumor cells with cellularity and increased mitotic range. Immunohistochemical studies of the tumor were positive for CD 117 (c-kit) in >50% of the malignant cells at variable intensity, CD34, actin, cytokeratin, vimentin and S-100. The above picture suggested malignant GIST of intermediate malignancy supporting and confirming the endoscopical gross macroscopic diagnosis [Figure 3].

The patient did not consent pancreatoduodenectomy, which was initially proposed under the prospect of a more radical procedure. Thus, the patient underwent a wide local resection of the tumor via duodenotomy, with preservation of the ampulla and the third part of the common bile and pancreatic duct. A local wide excision was considered as a good alternative as the size of the lesion and the histological findings suggested a tumor of an intermediate malignancy. The tumor did not invade the ampulla and the jaundice was caused by compression. Neither peritoneal was liver metastases nor invasion of regional lymph nodes invasion noted during the laparotomy. Nine regional lymph nodes sent for histopathological examination were negative for malignant disease. The patient was discharged 10 days later after an uneventful postoperative course. The histological examination of the excised specimen was similar to the the initial one, suggesting a malignant gastrointestinal stromal tumor.

At two years follow up, the patient remains free of any sign of tumour recurrence or metastasis.

Discussion

Gastrointestinal stromal tumors constitute the largest group of the stomach and small intestine’s primary non-epithelial neoplasms, although they represent only a small percentage (0.1-3%) of the gastrointestinal malignancies. The tumor occurs usually between 5th to 7th decades of the life and there appears to be no gender predilection. The large majority of the GIST are located in the stomach and the small intestine.
and only 4% of them occur in the duodenum.\(^1\text{,}^4\text{,}^5\)

The present case is unique in its location at ampulla of Vater and presenting symptom, obstructive jaundice.

Endoscopic ultrasonography (EUS) is a reliable and robust tool, through guidance of fine needle aspiration (FNA) in a technique known as EUS-FNA, enhances the possibilities for early diagnosis of GIST. Despite the fact that EUS-FNA is considered to be the first choice in these cases, several limitations regarding the difficulties encountered even by specialists in collecting adequate amount of tissue samples during the process, often postpones the diagnosis postoperative period.\(^1\text{,}^8\)

Immuno-histochemical studies are essential for the tumor classification into four subtypes: (a) smooth muscle type, (b) neural type, (c) dual differentiation type (with characteristics from both smooth muscle and neural types) and (d) uncommitted types (lack of differentiation towards a specific cell type).\(^1\text{,}^9\) The immuno-histochemical expression of CD-117 (a proto-oncogene protein) is the most important defining feature and probably the gold standard for diagnosing GISTs. The CD-117 expression pattern led to the adoption of the current subclassification of gastrointestinal mesenchymal tumors into GISTs (CD-117 positive), true smooth muscle tumors and true Schwann cell tumors. Moreover, CD-34 was found to be expressed in 60-80% of GISTs whereas a correlation with the tumor serum marker CA125 probably exists. Preoperative diagnosis remains difficult and many times controversial, requesting a high degree of suspicion and the potent involvement of advanced medical techniques like EUS-FNA.\(^1\text{,}^10\)

The immunohistochemical data of the present case suggested the presence of a GIST consisted of interstitial cell of Cajal (ICC)-like cells immunoreactive for both CD34 and CD117 (c-kit), excluding a smooth muscle cells or a nervous elements origin.\(^1\text{,}^4\text{,}^6\)

The tumour size and the malignant cells mitotic rate have been suggested as prognostic factors regarding the aggressiveness of the malignancy. In detail, tumour size larger than 5 cm and mitotic rate higher than 2 mitoses per HPF has been proposed to correlate with aggressive clinical behaviour.\(^1\text{,}^6\) In the present case, although the characteristics of the tumour indicated potent aggressiveness (intermediate malignancy), the clinical course of the patient was proved to be mild and uncomplicated at least at the 2 year follow up.

In cases of malignant gastrointestinal stromal tumours, most authors suggest radical procedures, including Whipple. Due to the scarcity of GISTs, all available data are primarily from case series and individual case reports, attributing a grade E according to evidence-based medicine to the above. The present case underlines the possibility that more conservative procedures, as local wide excision, could be considered in cases of small tumours (< 5 cm) with intermediate malignancy. Nevertheless, the outcome of this approach might be well compromised by the evolution of loco-regional recurrence or distant metastases at least in some cases. Thus, larger clinical studies are needed to confirm the role of surgical treatment of GISTs.\(^1\text{,}^5\text{,}^6\)

### References