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Case Report

Gastrointestinal stromal tumor as cause of acute abdominal pain in a patient with neurofibromatosis type 1: case report and literature review

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ABSTRACT

Acute abdomen is a common and sometimes dramatic clinical condition, which can be fatal if diagnosis is not made in time. There are many etiologies for acute abdominal pain; therefore, the diagnostic approach should be based on clinical assessment, including laboratory and image studies. Neurofibromatosis 1 (NF1) is an autosomal dominant condition, characterized by cutaneous pigmentation and tumor formation along nerves in the brain, skin and other organs, the gastrointestinal stromal tumors are rare mesenchymal neoplasms associated with NF1. The close correlation between both pathologies is well known, and the clinical relevance relies on the different pathogenesis from sporadic gastrointestinal stromal tumor (GIST), with important therapeutic implications as the use of imatinib prior or after surgery, regarding the individual context of the patient. This case report illustrates the management of an NF1 patient presenting with acute abdomen to the emergency room and follow-up.

Keywords: GIST, Neurofibromatosis, Acute abdomen

INTRODUCTION

According to Ferner et al, neurofibromatosis type 1 (NF1) is a common autosomal dominant neurocutaneous disorder associated with an increased risk of benign and malignant tumor formation. This disorder affects specifically nervous system, bone and skin, but the there are other variable complications that can manifest in other body parts. NF1 differs from NF2, a rare disorder where bilateral vestibular schwannomas and benign tumors localized in the nervous system are the main characteristic.[1]

Neurofibromas can manifest in all the body and the plexiform variant can be find internally with a high risk of becoming a malignant peripheral nerve sheath tumor (MPNST). We must differentiate MPNST from gastrointestinal stromal tumors (GIST) which are another, but not so frequently, cause of gastrointestinal tumors in these patients. GIST are characterized by being located in the small bowel causing bleeding, anemia and positive fluorodeoxyglucose (FDG)-positron emission tomography (FDGF PET CT).[1]

These types of tumors have a mesenchymal origin, with an incidence of 6,000 cases annually. Most tumors have KIT gain-of-function mutations or other receptor kinases. Currently, molecular subgroups must be identified in order to offer opportune management according to the tumor that they have.[2] Surgery is the cornerstone in the treatment of localized disease. According to the context of each patient, gastrointestinal stromal tumors benefit from the use of tyrosine kinase inhibitors in both neoadjuvant and adjuvant protocols.[2]

We present here the management and follow-up given to a 54-year-old woman with prior diagnosis of neurofibromatosis an acute abdominal pain caused by a GIST at ileum.

CASE REPORT

This is the case of a 54 years - old women, with clinical record of NF1 and systemic arterial hypertension. She starts with 24-hour evolution abdominal pain, colic type, located in mesogastrium, migrating to lower right quadrant, intensity 6/10 in numeric analog scale (NAS) associated with anorexia, nausea and hyaline emesis, without fever, nausea or urinary nor gynecological symptoms. She states taking symptomatic and analgesic treatment without clinical improvement. Due to persistence of symptoms she arrives to emergency department for evaluation. Vital signs were normal. Physical examination revealed disseminated neurofibromas, abdominal with normal peristalsis, with localized pain in the right iliac fossa at deep palpation, McBurney, Rovsing, talopercussion and obturator signs are positive (Figure 1a and b). The blood test showed leukocytosis with 85% of neutrophils. An abdominal ultrasound with scanning of right iliac fossa was ordered reporting a 44×32 mm hypoechoic solid lesion suggestive of a probable plastron (Figures 2a and b).

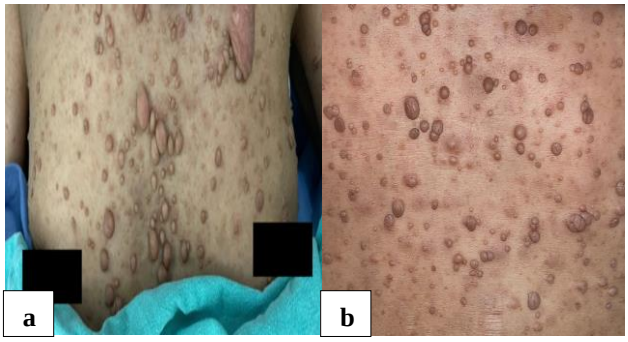

Figure 1: (a) and (b) Neurofibromas in anterior and posterior thorax.

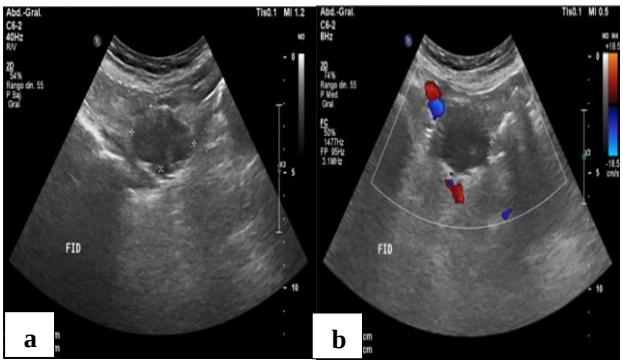

Figure 2: (a) and (b) Abdominal ultrasound showing right iliac fossa lesion suggestive of plastron due to acute appendicitis, doppler vision of the identified lesion.

The patient was taken to the operating room for an exploratory laparotomy, with the finding of a 3.6×5.1 cm ileum-dependent tumor 60 cm from the ileocecal valve (Figure 3a and b). We performed an ileum resection and manual entero-entero termino-terminal anastomosis in two planes, drainage was placed towards the anastomosis site and we follow the post operative period in the hospitalization floor. Patient was discharged after 4 days without complications.

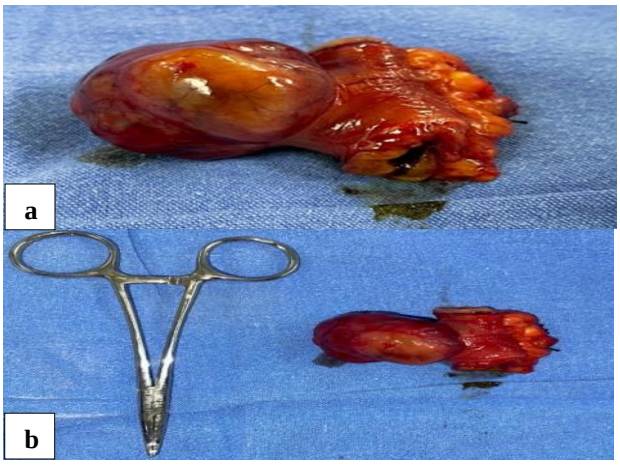

Figure 3: (a) and (b) Ileum-dependent tumor of 3.6×5.1 cm at 60 cm from the ileocecal valve.

Pathology study reported in the macroscopic description a 3.6×5.1 cm segment of the ileum, smooth brown serosa, a whitish wall tumor of 2.9 cm in its long axis with a medium consistency, 0.8 cm from the closest surgical edge and green mucosa with preserved folds, microscopic description of subepithelial mesenchymal neoplasia.

Ileum mucosa: adjacent puzzle pattern with neoplasia evidence with spindle cell pattern of long intersecting moderately cellular bundles and vascular congestion. Magnification at 40×: elongated cells, moderate eosinophilic cytoplasm, elongated regular contours, fine chromatin without apparent nucleoli (Figure 4a-b).

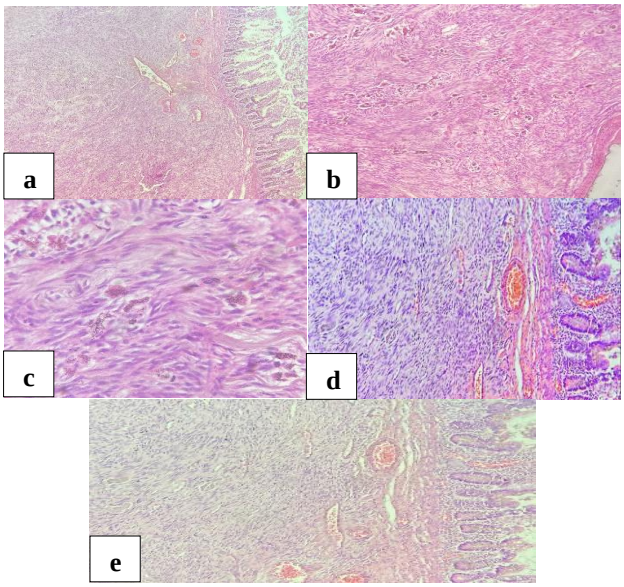

Figure 4: (a)-(b) Microscopic view of subepithelial mesenchymal neoplasia.

Immunohistochemistry was performed in order to rule out gastrointestinal stromal tumor based on clinical history, reporting CD117+, DOG1+, AML negative, S100 negative, desmin negative, CD34+, correlated with a fusocelular type gastrointestinal stromal tumor, mitotic index: 2 mitoses in 50 fields (Figure 5). The follow-up was continued in relation to low-risk ileum GIST with imaging studies, without adjuvant schemes.

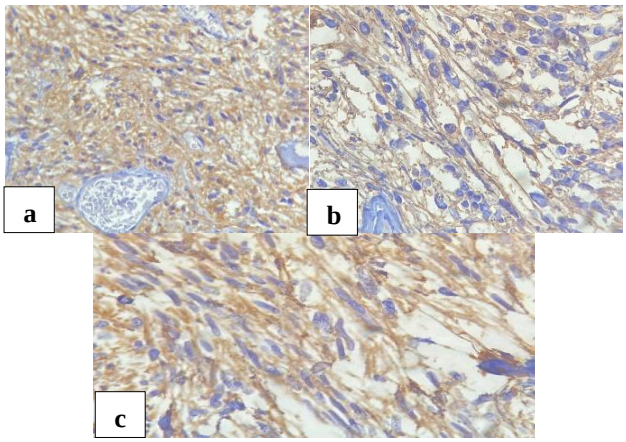

Figure 5: Immunohistochemical markers in the diagnostic work-up of GIST (a) CD117, (b) CD34, and (c) DOG1.

DISCUSSION

Gastrointestinal stromal tumors derive from mesenchymal cells. In the intestine, these are found as interstitial cells of Cajal, located between the longitudinal and circular muscular layers. They present as subserous or submucosal lesions, located in stomach (50-60%), ileum and jejunum (20-30%), duodenum (3-5%), rectum and anus (2-4%).[2] Histologically, the most common pattern is fusiform (70%), followed by epithelioid (20%) and they represent approximately 1-2% of primary gastrointestinal cancers. Most cases present in patients between the age of 60-69. The incidence of GIST ranges between 7 to 8 cases per million population per year and although a majority of GISTs are sporadic, approximately 5% of patients have an associated genetic syndrome.[6]

Most GISTs harbor characteristic mutations in KIT or platelet-derived growth factor receptor PDGFRA; almost all GISTs express CD117, a transmembrane glycoprotein codified by KIT proto-oncogene. The expression of KIT occurs in 95%, DOG1 in 98%, PDGFRA in 80% and CD34 in 70-80%. Currently immunohistochemistry and genetic approach of molecular markers without part of the approach in order to provide timely and individualized management.[2]

Up to 30% of GISTs develop metastases, so models have been designed to predict the risk of recurrence and identify groups that benefit from the use of multiple kinase inhibitors. The risk is determined considering the size of the tumor, mitotic index and location, in addition, the tumor rupture must be assessed in the pathology studies to stratify the risk (Table 1).[2,3]

Surgery is an opportune treatment in small and accessible lesions, with resection of the lesion without lymph node dissection in case of negative nodes. Even gastric lesions smaller than 2 cm may benefit from follow-up. In the case of lesions larger than 2 cm or non-resectable at diagnosis, a neoadjuvant scheme with imatinib can be offered and the response evaluated to consider tumor resection (Figure 6).[2]

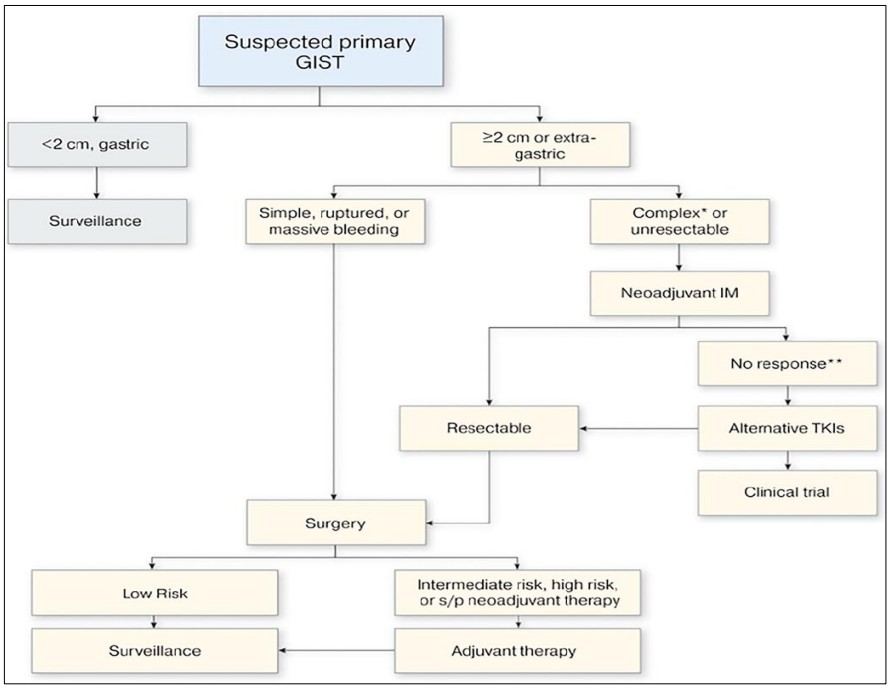

Figure 6: Treatment algorithm for the management of primary GIST.

Table 1: Armed forces institute of pathology criteria assessment in gastrointestinal stromal tumor.

Tumor group	Tumor size in cm	Tumor mitotic rate (per 50 HPFs)	Risk of progressive disease (GIST) %			
			Gastric	Jejunal and ileal	Duodenal	Rectal
1	≤2	≤5	0 (none)	0 (none)	0 (none)	0 (none)
2	>2 to ≤5	≤5	1.9 (very low)	4.3 (low)	8.3 (low)	8.5 (low)
3a	>5 to ≤10	≤5	3.6 (low)	25 (moderate)	34 (high)	57 (high)
3b	>10	≤5	12 (moderate)	52 (high)		
4	≤2	>5	0	50		54 (high)
5	>2 to ≤5	>5	16 (moderate)	73 (high)	50 (high)	52 (high)
6a	>5 to ≤10	>5	55 (high)	85 (high)	86 (high)	71 (high)
6b	>10	>5	86 (high)	80 (high)		

After surgery, the risk of recurrence should be assessed according to current models for adjuvant schemes with imatinib in intermediate and high-risk groups for at least 3 years. It can be extended for 5 years for tumors with a high mitotic index or tumors that have ruptured before or during surgery. The use of imatinib for 3 years has been identified with an impact on overall survival.[2,3] GIST associated with neurofibromatosis usually don't have KIT or PDGFRA mutations, therefore there's no benefit using it for their treatment nowadays.[4]

In the case of our patient, a history of neurofibromatosis is considered as a risk factor for GIST located in the small intestine with fusiform pattern. In addition, it should be noted that she is a patient with a low risk of recurrence estimated at 8.3%, as it is a 2.9-cm ileum tumor with a mitotic index of less than 5 in 50 fields. In this case, according to the management guidelines, it is advisable to continue active surveillance without the need for adjuvant treatment with a tyrosine kinase inhibitor due to its ineffectiveness in stromal tumors related to neurofibromatosis.[5]

CONCLUSION

The timely diagnosis and treatment of acute abdomen is the cornerstone that defines the evolution of the patient during the hospital stay. A complete and extensive anamnesis of the patient must be carried out, as well as a correct interrogation of relevant antecedents that could be related to the clinical scenario. It can be difficult to consider GIST as a probable etiology of acute abdomen, however, it should be considered in patients with risk factors for it. The follow-up offered to this type of patient relies on the risk of recurrence, bases on the characteristics of the tumor. The follow-up must be individualized in order to achieve an integral and complete management.

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