

CASE REPORT

A RARE CAUSE OF RECURRENT IRON DEFICIENCY ANAEMIA

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Abstract

Gastro intestinal Stromal Tumours (GISTs) are a rare neoplasm of the gastrointestinal tract. They often grow silently and present late when surgical cure is not possible. Chemo and radiotherapy have a very poor success rate. We present a case of successful surgical removal of a gastrointestinal stromal tumour in a patient who presented with GI bleeding and a recurrent microcytic anaemia.

Introduction

Microcytic anaemia is a vague presenting sign of many pathological conditions and has the potential to cause severe symptoms including fatigue, dyspnoea and even heart failure [1]. Iron deficiency is the commonest microcytic anaemia and may be secondary to a variety of pathologies including GI malignancies [2]. Unfortunately in cases of chronic or slowly developing conditions such as gastrointestinal stromal tumours (GISTs) of the small bowel, the cause may not be apparent at the time of first presentation. Appropriate management can therefore be challenging and delay effective treatment.

Case Report

A 69 year old man initially presented to the gastroenterologists in 2003 with symptomatic microcytic anaemia, shortness of breath and melaena. His past medical history included Type II diabetes mellitus and hypertension, but there was neither relevant personal gastrointestinal (GI) history nor a family history of malignancy. Investigations including colonoscopy, small bowel meal and abdominal CT scan were reported as normal. He was managed symptomatically with oral ferrous sulphate and repeated blood transfusions.

He represented as an emergency in 2005 with a haemoglobin of 6.5g/dl and a mean corpuscular volume of 79.5 fL. Physical examination was normal apart from pale conjunctivae. Upper and lower gastrointestinal endoscopy were both normal but an abdominal CT scan revealed a central abdominal mass (Figure 1) which was confirmed as extra-colonic on a subsequent CT pneumocolon (Figure 2). On this second CT the mass was found lying in the pelvis suggesting it to be mobile and therefore a likely small bowel mass. The differential diagnosis included primary small bowel adenocarcinoma or lymphoma or an inflamed Meckels diverticulum. At laparotomy, the mass in the distal small bowel was the only finding of note. A small bowel resection with and end to end anastomosis was performed and the resected specimen sent for histological examination (Figure 3). Histology confirmed complete excision of the mass, identified as a GIST by CD117 positivity on immunohistochemistry. The tumour was graded as having an intermediate risk of malignancy on the basis

of having 5 mitoses/50 HPF (high power fields). His post-operative recovery was uneventful and he was discharged 10 days after his surgery. After discussion at the GI MDT it was decided that he needed no further treatment. At one year follow up he remained well with a normal haemoglobin.



Figure 1. CT scan demonstrating a small bowel mass (yellow circle). A benign cyst can also be seen on the left kidney.



Figure 2. CT pneumocolon demonstrating the small bowel mass (yellow circle) now lying in the pelvis.

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Figure 3. Surgical specimen excised at laparotomy showing solid mass attached to small bowel.

Discussion

Microcytic anaemia is a common condition and iron deficiency is the commonest cause, affecting between 2-5% of adult males and post-menopausal females in the developed world [3]. The causes and relative frequency of iron deficiency are listed in Table 1 and these data inform the order and extent of investigation which aim to exclude the common conditions first [2]. A thorough history and examination including a menstrual history in pre-menopausal females may reveal indicators of the likely source of the iron deficiency such as non-steroidal anti-inflammatory drug usage, excessive alcohol consumption, a family history of bleeding diathesis or the buccal discolorations of Peutz – Jehgers disease. Initial blood tests should confirm an iron deficiency anaemia (low haemoglobin, MCV and ferritin with normal B12 and folate) and exclude coeliac and thyroid diseases. If there are no pointers to either an upper or lower GI cause, both upper and lower GI endoscopy should be performed. If both are normal then there is no indication for further investigation unless the anaemia is transfusion dependent, as the yield from further investigations in such cases is very low [4]. If there is an indication for further investigation then the small bowel may be imaged by barium studies, CT scanning with contrast or Video Capsule Endoscopy [2].

Small bowel lesions are a rare cause of both iron deficiency anaemia and symptoms in general. The differential diagnosis includes a variety of neoplasms and a Meckel's diverticulum, a congenital remnant of the vitellointestinal duct commonly containing active ectopic gastric mucosa. Small bowel carcinoids usually present by virtue of the increased serotonin activity with abdominal cramping, flushing, diarrhoea and heart failure [5]. Lymphoma of the small bowel are typically Non-Hodgkin type and may be B or T cell variants – T cell lymphomas are associated with coeliac disease [6]. GISTs account for only 1% of all gastrointestinal tumours and have an estimated incidence of 15 per million population per year [7]. They encompass those tumours previously described as leiomyomas, leiomyosarcomas, leiomyoblastomas and schwannomas but they are now considered to arise from gastrointestinal pacemaker cells known as the interstitial cells of Cajal [8]. Two thirds occur in the stomach, with small bowel accounting for most of the remainder

– colorectum and oesophagus are implicated in only 10% of GISTs [9]. GISTs may behave in either a benign or malignant fashion, although there is no clear demarcation between the two. The risk of malignant behaviour increases with tumour size, mitotic activity and location [10,11]. Tumours <2cm in size are usually benign whilst those >5cm in diameter are almost always malignant [11]. Similarly, more than five mitoses per high powered field on light microscopy is considered diagnostic of malignancy [11]. The more distal in the GI tract the GIST is located, the greater the the risk of malignant behaviour. They may be an incidental finding or present with abdominal pain, nausea, overt upper GI haemorrhage or anaemia. Commonest presentations are in the 5th and 6th decades of life [8].

GISTs are resistant to both chemotherapy and radiotherapy, curative surgical resection is the treatment of choice [11]. GIST cells contain the mutated KIT proto-onco gene which codes for a transmembrane glycoprotein tyrosine kinase that is responsible for cell growth and differentiation. The mutation results in uncontrolled cellular proliferation [12]. Ninety five percent of GISTs are positive for KIT receptor tyrosine kinase (CD117 antigen) on immunohistochemistry [13]. This presents a target for immunological management and the use of the tyrosine-kinase inhibitor Imatinib (Glivec®, Novartis, Basel, Switzerland) has revolutionised the treatment of residual, recurrent, metastatic or unresectable GISTs. Imatinib has improved the two year survival rate of patients with metastatic GISTs from 26% to 76% [14]. Resistance to Imatinib can develop and alternative tyrosine kinase receptor inhibitors such as Sumatinib (Pfizer Inc, New York) may then be effective [15].

Conclusion

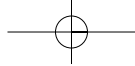
Iron deficiency anaemia has a wide range of causes and may represent the first sign of a developing malignancy, so requires thorough investigation. In post-menopausal women and adult men gastrointestinal neoplasms are the most common underlying pathologies. Although GISTs are an uncommon tumour of the GI tract they characteristically develop unnoticed by the patient and often present when curative resection is no longer possible. They should therefore be considered as a potential cause of unexplained transfusion dependent iron deficiency anaemia.

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Occult GI Blood Loss	Non-GI Blood Loss	Malabsorption
<ul style="list-style-type: none"> Aspirin/NSAID use 10-15% Colonic carcinoma 5-10% Gastric Carcinoma 5% Oesophagitis 2-4% Small Bowel Tumour 1-2% 	<ul style="list-style-type: none"> Menstruation 20-30% Haematuria 1% Epistaxis <1% 	<ul style="list-style-type: none"> Coeliacs Disease 4-6% H.pylori colonisation <5% Gut resection <1%

Table 1. Causes of Iron deficiency anaemia [2].



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