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Case Report

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Primary multifocal GIST of stomach; a case report

Katarzyna Iwanik, Przemysław Majewski

Department of Clinical Pathology, University of Medical Sciences in Poznań, Poznań, Poland

Summary

Background GISTs are CD 117 positive mesenchymal neoplasms, mainly located in tubular GI tract, frequently with a very similar histologic pattern and different malignancy. They typically occur as solitary lesions, whereas their occurence as disseminated tumours is usually associated with spread from a primary site. GISTs have three kinds of histologic pattern, the most common of which is the spindle cell pattern. The diagnosis of GIST is by positive reaction for CD 117 and the results of other immunohistochemical reactions, mainly for smooth muscle markers, nervous tissue markers also for endothelial cells marker (CD 34).

Aim The aim of this study was to present a case of primary multifocal GIST of stomach.

Case description Two gastric tumours were surgically excised and, after formalin fixation and routine preparation, were tested with antibodies raised against CD 117, desmin, SMA, NSE, S-100 protein, PGP 9.5 and CD 34. The histologic patterns and immunohistochemical results of the two tumours were clearly different.

Conclusions Conclusions despite evident differences in size and location of these tumours in the stomach wall, both lesions can be looked upon as bifocal primary GIST.

Key words **mesenchymal neoplasms of GI tract • GIST • immunohistochemical reactions**

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Author's address: Katarzyna Iwanik, Department of Clinical Pathology, University of Medical Sciences, Przybyszewskiego 49 str., 61-533 Poznań, Poland, e-mail: patomorf@amp.edu.pl

Background

According to a definition suggested by Miettinen, GISTs are KiT-positive mesenchymal tumours with varying malignancy and frequently very similar histologic patterns. They are located throughout and, to a lesser degree, beyond the tubular GI tract, within the abdominal cavity and retroperitoneal space. Their characteristic is a positive reaction for the c-kit oncoprotein (CD 117) [1,2]. Their origin, previously associated with interstitial Cajal cells (peacemaker cells), is currently attributed to multipotential mesenchymal stem cells, which have the ability to differentiate both into interstitial Cajal cells and smooth muscle cells [2,3].

GIST are most frequently occurring mesenchymal neoplasms within this location, mostly affecting the stomach wall and the small intestine, more rarely the colon and the rectum [4]. Sporadically, they develop within the oesophagus, the mesentery, the omentum and in the retroperitoneal space [1]. Typically, they occur as solitary lesions, whereas their occurrence as disseminated intra-abdominal tumours is usually connected with metastasis from the site primarily affecting the GI tract wall [1]. Malignancy is mostly characteristic of small intestine GISTs of more than 5 cm in diameter [5]. However, some cases have been described in which primary multiple GISTs occurred. Some of those are the so-called familial GISTs, with an autosomal dominant pattern of inheritance. In those cases, apart from numerous GISTs affecting much younger persons, there are also other symptoms connected with the KIT gene damage (urticaria pigmentosa and/or cutaneus hyperpigmentation). Primary multiple GISTs are also characteristic of Carney's triad and neurofibromatosis I [1,2,6]. In other cases, inheritance patterns and familial incidence have not been documented. Moreover, in some patients the lesions are so numerous and differing in size that it is impossible to indicate the primary location.

GISTs mainly affect middle-aged and elderly people with a slight majority of men [7]. Clinical symptoms most often include bleeding from the GI tract and stomach ache. In 30% of cases, patients do not report any trouble and the lesion is incidentally detected during an examination for unrelated conditions. [1,6,8].

As they develop, GISTs can affect a part of the GI tract wall, or totally overgrow it, in which case they often show surface ulceration. Sometimes the tumour takes the form of a polyp.

In light-microscope examinations the hypercellularity of GISTs is conspicuous, as is their scanty, but thickly vascularized interstitial layer, often with lymphatic infiltration to various degrees. A significant majority of GISTs have a spindle cell pattern. Epithelioid cells are characteristic for epithelioid GISTs. The presence of both kinds of cells (spindle and epithelioid) are characteristic of the pleomorphic pattern [1,2,9]. Cellular nuclear polymorphism is rare, as is high mitotic activity. Nevertheless, the clinical course can be adverse and the prognosis is uncertain. In GIST diagnostics, apart from the essential positive reaction for CD 117, it is advisable to carry out other immunohistochemical reactions with the use of antibodies raised against smooth muscle markers (desmin, SMA), nervous tissue (NSE, S-100 protein, PGP 9.5), and endothelial cells (CD 34). In most cases, the reaction for desmin is negative and over-expression in the reaction for SMA concerns only about 30% of lesions [1,2]. Reactions for S-100 protein and PGP 9.5 are positive much more often than muscular tissue markers. The reaction for endothelial cells (CD 34) is positive in 60–80% of cases.

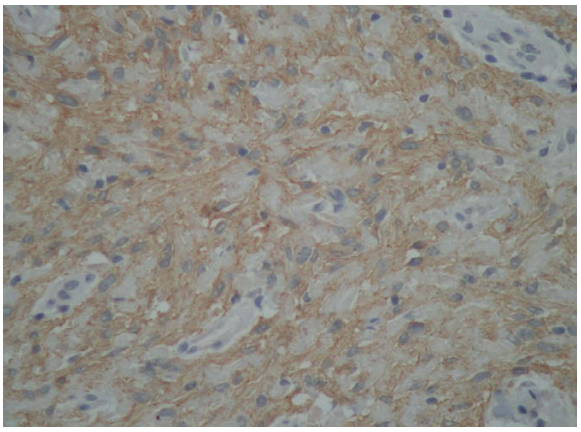

Figure 1. GIST. The tumour of 5 mm in diameter. Positive reaction for CD 117. Magn. 280×.

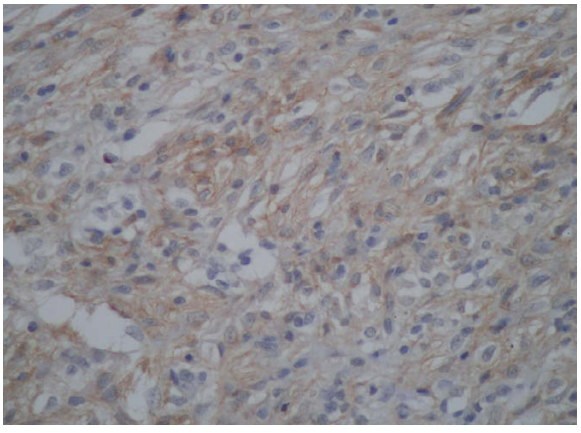

Figure 2. GIST. The tumour of 4, 5 cm in diameter. Positive reaction for CD 117. Magn. 280×.

Aim

The aim of our study was to present a case of primary multifocal GIST.

Case Description

Two gastric tumours were identified in a 62 year old male. The larger tumour was localized in the stomach wall while the smaller was situated between the stomach wall and perigastric fatty tissue. Both lesions were surgically excised after intra-operative examination (frozen section). Tissues were fixed in formalin and embedded in paraffin blocks for routine histopathological and immunohistochemical studies for the presence of CD 117, desmin, SMA, NSE, S-100 protein, PGP 9.5 and CD 34.

Results

Both lesions were GISTs, as confirmed by a positive result for the immunohistochemical reaction with CD 117 (Figures 1,2), however they differed both in morphological

Table 1. The results of immunohistochemical reactions in both gastric GISTs.

Size of tumour	CD 117	NSE	PGP 9.5	S – 100	SMA	Desmin	CD 34
Small (5mm)	+	+	+	+	–	–	–
Large (4,5 cm)	+	+	+	+	+	+	+

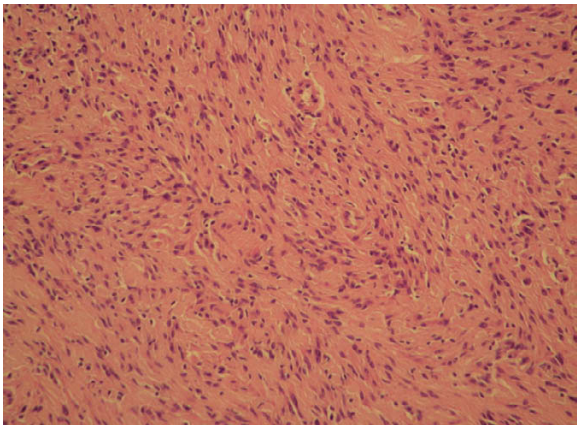

Figure 3. GIST. The tumour of 5 mm in diameter. HE. Magn. 140×.

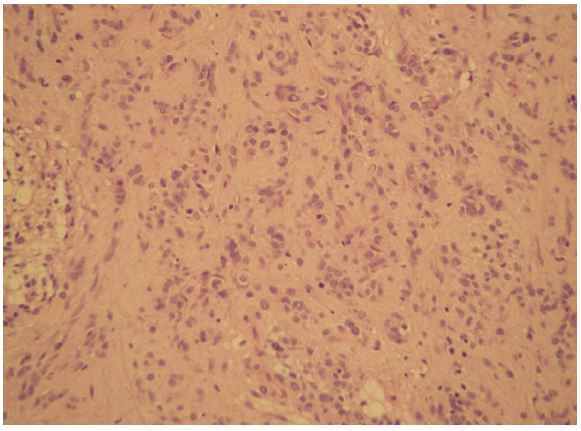

Figure 4. GIST. The tumour of 4, 5 cm in diameter. HE. Magn. 140×.

pattern and in other immunohistochemical reactivity. The tumour of 5 mm in diameter, situated between the gastric wall and the perigastric fatty tissue, had a positive reaction with NSE, S –100 protein, PGP 9.5 and negative results for reactions with desmin, SMA and CD 34 (Table 1). Its histological structure was of a spindle cell pattern (Figure 3). The tumour of 4,5 cm in diameter, situated in the gastric wall, had a strong positive reaction to all the above mentioned antibodies (Table 1). Moreover, under the light microscope, the lesion had a pleomorphic pattern of a mainly epithelioid pattern (Figure 4). The mitotic activity of both tumours was low and had 0–1 mitosis/50 HPV.

Discussion

Generally, in cases of malignant neoplasms, metastases foci are histologically similar to the primary lesion. It seems that the same rule should also apply to GISTs. This, however, has not been described in the literature. Thus, we have assumed that the presence of two lesions of clearly different histological structure in the gastric wall can serve as proof of their independent origins. This view has been strengthened by differences in the results of immunohistochemical examinations in both tumours. Moreover, during physical examination, no skin lesions were detected (urticaria pigmentosa, cutaneus hyperpigmentation). Familial inquiries could not confirm the presence of similar tumours in other members of the patient's family, which enabled us to rule out familial GISTs [1,2,6]. Low mitotic activity, the tumours' diameter, and their location in the gastric wall were additional proofs against malignancy and thus confirmed their independent origin [1,5].

Conclusions

Despite differences in size and location of these tumours within the stomach wall, the lesions can be looked upon as two independent, primary GISTs.

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