Case report

Plexiform angiomyxoid myofibroblastic tumour of the stomach: A rare, recently described gastric antral tumour

PN Amarabandu, J LCYong, L D Santos

Introduction

Plexiform angiomyxoid myofibroblastic tumour (PAMT) of the stomach is a rare submucosal tumour of the stomach (1-3). It occurs mostly in the gastric antrum and histologically characterised by a plexiform growth pattern, proliferating bland spindle cells in a myxoid stroma rich in small blood vessels (1-8). Microscopic differential diagnosis includes Gastrointestinal Stromal Tumour (GIST), which should be excluded since there is a specific treatment, gastric schwannoma, myxoid leiomyoma, leiomyosarcoma, inflammatory myofibroblastic tumour (IMT) and inflammatory fibroid polyp (IFP). According to the current published data the tumour behaves in a benign manner (1-8). We reported two cases of PAMT.

Case 1

Case History

A forty-year-old-lady presented with a history of upper abdominal discomfort and a clinical query of GIST. On investigation, imaging

studies confirmed a distal gastric mass. She underwent partial gastrectomy two weeks after the FNAC which yielded insufficient material.

Pathology

The specimen composed of distal stomach with a globular tumour, 16g and measuring 105 x 97 x 55mm. The cut surface revealed a submucosal myxoid, yellowish, glistening soft tumour measuring 76 x 52 x 40mm (Fig.1.a). The lesion macroscopically appeared to be surrounded by a thin delicate capsule. The overlying mucosa was unremarkable. The muscularis propria appeared stretched but not infiltrated by the tumour. Surgical margins were clear by 9mm.

Microscopy revealed a submucosal tumour of the gastric wall. The tumour was composed largely of diffuse proliferation of spindle cells in myxoid stroma with a rich arborizing network of small blood vessels (Fig.1.b). Tumour cells were regular with no mitosis or necrosis. There was an inflammatory infiltrate composed of eosinophils, mast cells and scattered mononuclear cells. The

Department of Anatomical Pathology, Sydney South West Area Health Service, Australia

Correspondence: P N Amarabandu, Base Hospital, Tangalle, Sri Lanka.

Email: pnamarabandu@gmail.com

tumour focally stretched the mucosa causing focal ulceration. The muscularis mucosa was disrupted with smooth muscle cells incorporated into the tumour. Vascular invasion was not seen.

Immunoperoxidase (IPX) showed the tumour cells were negative for CD 117(c-kit), S-100, CD34 and desmin. Vimentin was positive (Fig.1.c). Some cells were positive for smooth muscle actin (SMA). Reticulin and Masson's stains showed a rich elastic and collagen network.

Fig.1a. Gross appearance of the dissected gastric tumour

Fig.1b. Submucosal proliferation of spindle cells in a myxoid stroma (H &E x40)

Fig.1c. The neoplastic cells show positive staining for vimentin (x200).

Case 2

Case History

A thirty-year-old man presented with a history of an abdominal mass with accompanying abdominal discomfort and loss of appetite. Imaging studies confirmed a distal gastric mass. The patient underwent distal gastrectomy.

Pathology

An ulcerated, light grey, polypoid and myxoid lesion 35x 34x 25mm located on the posterior wall of the stomach wall involving the full thickness of the wall was received. It was continuous with a sac like structure 25 x 75 x 145 mm which had a haemorrhagic inner wall with multiple perforations. Microscopically, the tumour was composed of bland spindle cells with round to oval nuclei separated by abundant myxoid stroma rich in small blood vessels (Fig.2.a).

Fig.2a. There is a diffuse proliferation of bland spindle cells in a myxoid stroma rich in small blood vessels. (H&E x 40)

There was no evidence of necrosis, significant atypia or mitosis. The myxoid stroma showed positive staining for Alcian blue and

colloidal iron and was negative for Periodic–Acid-Schiff (PAS). The tumour cells were positive for SMA (Fig.2.b) and desmin and were negative for c-kit, MNF116, S-100 and CD34. The Ki-67 proliferation index was less than 2%. Ultrastructurally, the tumour cells were oval to spindle in shape and widely spaced in a myxoid

Fig.2b. The neoplastic cells show positive staining for SMA (x200)

Fig.2c. Electron microscopy - Spindle shaped cells with peripheral cytoplasmic filament bundles.

stroma containing Type 1 collagen (Fig.2 c). The cells had dilated rough endoplasmic reticulum and cytoplasmic filament bundles with dendrites. The cells appeared to be myofibroblastic in origin. No mutations were identified in c-kit and PDGFR gene studies.

Discussion

PAMT is a multinodular myxoid tumour involving gastric antrum (1-9). It was first reported in 2007 and only 18 cases have been confirmed by immunohistochemistry in the literature (1-5).

Macroscopic size varies from 30 to 150mm and is variably intraluminal, intramural and externally bulging (2). All the reported cases were found in the gastric antrum or pylorus. The tumour usually has transmural or muscularis propria involvement (3).

Microscopically, PAMT is characterised by a plexiform nodular growth of cytologically bland spindle cells with oval nuclei and variably eosinophilic cytoplasm in an abundant myxoid extracellular matrix. The matrix is Alcian blue positive (at pH 2.5) and hyaluronidase sensitive (1-5). Some nodules demonstrate a dense collagen matrix. Fascicular or palisading arrangement is usually not seen (1). Mitotic figures are scanty [4/50 high power fields (HPF)] (1-2). Eosinophils are rare (5). Sometimes a more cellular, non plexiform spindle cell proliferation can be observed (2). Nuclear atypia is limited.

Tumour necrosis is not usual but haemorrhage, necrosis and cystic degeneration has been observable in certain cases (1). A prominent arborising network of capillaries is often present (2). A fibro-collagenous matrix is observed only in some cases (3).

Immunohistochemically, tumour cells are positive for vimentin and SMA, and negative for CD117, CD34, S-100, cytokeratin, ALK, EMA and NF (1-4, 6-7). Ki-67 labeling index is usually less than 1% (1). Myofibroblastic cells are positive for SMA and negative for Desmin, where as fibroblasts are negative for SMA. Immunohistochemistry suggests that PAMT is a myofibroblastic tumour (1).

However in some instances, PAMT are not purely myofibroblastic in nature and shows morphological features of both smooth muscle and/or fibroblastic differentiation containing both smooth muscle cells and fibroblasts (1). Bland spindle cells, absence of atypia and very low mitotic count are evidence for benign nature of PAMT. Neither recurrence nor metastases have been documented in the literature.

Main histological differential diagnoses include GIST (specially the myxoid variant), myxoid leiomyoma, myxoid leiomyosarcoma, schwannoma, IFP and IMT. GIST is composed of spindle and / or epithelioid cells. Spindle cells are oval to elongate and contain blunt ended nuclei with eosinophilic fibrillary cytoplasm (10-13). The stroma may be myxoid and contain

skenoïd fibres (10-11). Spindle cells are arranged in whorls, palisades and in a herringbone pattern. Almost 90% of the GISTs express CD117 which can be focal or diffuse, strong or weak (10-15). These features with near consistent expression of CD117 (>90%) helps to differentiate GIST from PAMT.

In the gastrointestinal tract (GIT) leiomyomas occur commonly in the oesophagus and extramurally in the colon (12). Myxoid leiomyomas may reveal a plexiform tortuous architecture (2). However, myxoid leiomyoma shows typical solid areas showing a fascicular growth pattern (2). Immunohistochemically, leiomyomas are SMA and desmin positive (2, 12). Leiomyosarcomas, on the other hand, exhibit nuclear atypia and mitosis, including atypical figures.

Myxoid gastric schwannomas histologically differ from soft tissue schwannomas. The former is composed of wavy spindle cells arranged in palisades with a rim of lymphocytes (16). Antoni type A and B areas are not seen in GIT schwannomas (10). Gastric schwannomas are strongly positive for S-100. Presence of a lymphoid rim, wavy spindle cells and immunohistochemical expression of S-100 protein differentiates them from PAMT.

Inflammatory fibroid polyp (IFP) is an uncommon tumour in the GIT, the commonest site being the stomach (17). It is grossly polypoid or sessile and appears to arise in the submucosa. It is composed of mononuclear spindle cells with eosinophilic cytoplasm arranged in a

perivascular pattern (onion skin pattern), resembling granulation tissue (17). Inflammatory cells are invariably present, usually composed of lymphocytes and eosinophils. Numerous small to medium sized blood vessels are present (17). Immunohistochemically, the neoplastic cells are positive for vimentin and show variable expression of actin and histiocytic markers. Although immunohistochemical findings may overlap with PAMT, the presence of onion skin and absence of plexiform growth pattern excludes IFP from PAMT.

Inflammatory myofibroblastic tumour (IMT) of the stomach on the other hand has infiltrative margins as opposed to PAMT. Histologically, fascicle-like growth pattern with vascular, myxoid, inflamed stroma resembles PAMT (12). Abundance of plasma cells, lymphocytes and ALK positivity readily distinguish this entity from PAMT.

Summary

PAMT is a distinct new entity. It is characterised by a proliferation of bland spindle cells in a plexiform growth pattern. The stroma is myxoid and rich in small blood vessels. Immunoperoxidase studies and ultrastructural studies favour a myofibroblastic origin. The absence of atypia, rarity of mitosis and low Ki-67 favour benign tumour.

However, it should be always differentiated from GIST and other rare myxoid mesenchymal tumours of the stomach.

Acknowledgement

The authour wishes to thank Mrs Sandra Pereira, Mrs Stephanie Harvey, Associate Professor Shantay Ryan, Associate Professor Murray Killingsworth, Dr Sanaz Sasani, Dr Tao Yang, Dr Shashank Sharma, and Dr Kasim Ismail of Department of Anatomical Pathology, Liverpool Hospital, Sydney, NSW, Australia, for the support given in various ways.

References

1. Takahashi Y, Suzuki M, Fukusato T. Plexiform angiomyxoid myofibroblastic tumour of the stomach. *World J Gastroenterology* 2010; 16(23):2835-2840.
2. Miettinen M, Makhoul H. R, Sobin L .H, Lasota J. Plexiform fibromyxoma A distinct benign gastric antral neoplasm not to be Confused with a myxoid GIST. *American Journal of Surgical Pathology* 2009; 33(11):1624-1632.
3. Wang W, Li J, Li G. Plexiform angiomyxoid myofibroblastic tumour of the gastric fundus: successful diagnosis and treatment by endoscopy. *Journal of Clinical Pathology* 2010; 63: 569-570.
4. Takahashi Y, Shimizu S, Ishida T, Aita K, Toida S, Fukusato T, Mori S. Plexiform Angiomyxoid Myofibroblastic Tumour of the Stomach. *American Journal of Pathology* 2007; 31(5): 724-728.
5. Sing Y, Subrayan S, Mqadi B, Ramdial P. K, Reddy J, Moodley M.S, Bux S. Case Report: Gastric plexiform angiomyxoid myofibroblastic tumour. *Pathology International* 2010; 60: **621-625**.
6. Galant C, Rousseau E, Duc D.K.H.M, Pauwels P. Letter to editor Plexiform angiomyxoid myofibroblastic tumour of the Stomach. *American Journal of Pathology* 2009; 32(12): 1910-1912.
7. Pailoor J, Mun K, Chen C.T, Pillay B. Correspondence Plexiform angiomyxoid myofibroblastic tumour of the stomach. *Pathology* 2009; 41(7): 698-699.
8. Rau T.T, Hartmann A, Dietmaier W, Schmitz J, Hoenberger W, Hofstaedter F, Katenkamp K. Case report Plexiform angiomyxoid myofibroblastic tumour: differential diagnosis of gastrointestinal stromal tumour in the stomach. *Journal of Clinical Pathology* 2008; 61: 1136 – 1137.
9. Rous R.V. Surgical Pathology Criteria . Gastric plexiform fibromyxoma . Stanford school of Medicine. *Stanford University Medical Centre*. (A web page).
10. Campbell F, Lauwers G.Y, William G.T. Tumours of the oesophagus and stomach. In: Fletcher C.D.M. Diagnostic Histopathology of Tumours. Vol 1, 3rd edn. Churchill Livingstone Elsevier, 327-378.
11. Rosai J Rosai and Ackerman's Surgical Pathology. Vol 1, 9th ed. Mosby: Edinburg, 2004; chapter 11, Gastrointestinal tract.
12. Montgomery M, Fisher C. Gastrintestinal Mesenchymal Tumours: In Lacouzio- Donhue C.A, Montgomery E, Gouldblum J .R. Gastrintestinal and Liver Pathology, A volume in the series: Foundation in Diagnostic Pathology. Churchill Livingstone:Elsevier. 204-234.

13. Owen D. A. The Stomach: In Mills S.E, Carter D, Greenson J.K, Reuter V. E, Stoler M.H. Sternberg's Diagnostic Surgical Pathology ,Vol 2, 5th ed. Wollers kluwer Lippincott Williams and Wilkins Philadelphia . Baltimore. New York. London. Buenos Aires. Hong Kong. Sydney. Tokyo. 1279-1312.
14. Miettinen M, Lasota J. Gastrointestinal stromal tumours Review on morphology, molecular pathology, prognosis, and differential diagnosis. *Archives in Pathology and laboratory Medicine* 2006; 130: 1466-1478.
15. Trupiano J.K, Srewart R.E, Misick C, Appelman H.D, Goldblum J.R. Gastric Stromal Tumours. A clinicopathological study of 77 Cases with correlation of features with nonaggressive and aggressive clinical behaviours. *Aerican Journal of Surgical Pathology* 2002; 26(6): 705-714.
16. Hou Y.Y, Tan Y.S, Xu J. F, Lu S H, Ji Y, Wang J& Zhu X Z. Schwannoma of the gastrointestinal tract:: a clinicopathological , immunohistochemical and ultrastructural study of 33 cases . *Histopathology* 2006, 48: 536-545.
17. Ozolek J.A, Sasatomi E, Swalsky P.A, Rao U, Krasinskas A, Finkelstein S.D. Inflammatory fibroid polyp of the gastrointestinal tract : Clinical , pathologic, and molecular characteristics. *Applied Immunohistochemistry and Molecular Morphology* 2004; 12(1):59-66