Clinical Case Report

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Unusual focal keratin expression in plexiform angiomyxoid myofibroblastic tumor

A case report and review of the literature

Giuseppe Quero, MD[a], Teresa Musarra, MD[b], Alfredo Carrato, MD[c], Michelangelo Fici, MD[d], Maurizio Martini, MD, PhD[b], Angelo Paolo Dei Tos, MD[e], Sergio Alfieri, MD[a], Riccardo Ricci, MD, PhD[b,*]

Abstract

Background: Plexiform angiomyxoid myofibroblastic tumor (PAMT), also known as plexiform fibromyxoma, is a rare distinctive benign intramural tumor, typical of gastric antrum, commonly causing mucosal ulceration with upper gastrointestinal bleeding and anemia, effectively treated by complete surgical resection usually accomplished by distal gastrectomy.

Methods and Results: We herein report a 47-year-old man presenting with a syncopal episode, regurgitation and epigastric discomfort, bearing a gastric antral myxoid plexiform tumor positive for α-smooth muscle actin, vimentin and, partially, for caldesmon, desmin, and CD10; CD117, DOG1, CD34, S100, CAM5.2, CK20, CK7, EMA, p53, CDX2, chromogranin A, synaptophysin, anaplastic lymphoma kinase, Melan-A, and HMB-45 were all negative. All these features are typical of PAMT. Of note, focal positivity for AE1/AE3 and pan-CK KL1 was also present.

Conclusions: The finding of a focal keratin expression in PAMT contributes to enlarge the immunophenotypic spectrum of this tumor type and is relevant for avoiding presurgical misdiagnoses which could ultimately lead to inappropriate overtreatment of patients with PAMT.

Abbreviations: CK = cytokeratin, IHC = immunohistochemistry, PAMT = plexiform angiomyxoid myofibroblastic tumor.

Keywords: differential diagnosis, histopathology, immunohistochemistry, plexiform angiomyxoid myofibroblastic tumor, plexiform fibromyxoma

1. Introduction

Plexiform angiomyxoid myofibroblastic tumor (PAMT), also known as plexiform fibromyxoma, is a rare mesenchymal neoplasm, recently characterized by Takahashi et al[1] and Miettinen et al[2] following reports from the preimmunohistochemistry (IHC) era probably concerning the same entity.[3–7] At the best of our knowledge, 59 cases of PAMT (including the present case and 2 uncertain ones) have been reported so far (Table 1).[1,2,8–33] This tumor affects both sexes with a wide age span (7–75 years). It typically arises in the gastric antrum; exceptional extragastric cases have been described in the esophagus, duodenum, jejunum, gallbladder and, possibly, in the colon.[22,26,27,30,33] PAMT characteristically features a plexiform architecture, with myxoid nodules located in the gastric muscularis propria, often ulcerating the overlying mucosa, composed of ovoid cells with indistinct cytoplasm; a prominent capillary network is invariably present. At IHC, PAMT is positive for α-smooth muscle actin (α-SMA) and, sometimes, for desmin and/or caldesmon, consistently with myofibroblastic differentiation. *KIT* and *PDGFRA* are wild type. PAMT pursues a benign course following complete excision by distal gastrectomy. Despite PAMT typical location and plexiform architecture, its rarity and rather vague histology, in a context usually suggestive for GIST (the most frequent gastric mesenchymal tumor[34]), can hinder bioptic attempts to achieve a correct preoperative diagnosis. The latter can be further confused by the exceptional feature we herein describe in a PAMT: cytokeratin expression.

2. Case report

A 47-year-old man presented with a syncopal episode following several months of regurgitation and worsening epigastric discomfort. Routine laboratory tests, electrocardiogram, and chest X-ray were unremarkable. Endoscopy showed a subepithelial lesion in the gastric antrum; the overlying mucosa was focally ulcerated. Endoscopic ultrasound-fine needle tissue acquisition[35] did not yield diagnostic material. Contrast-enhanced computed tomography showed an enhancing 6.5 cm mass bulging into the antral cavity and focally involving the omentum. A distal gastrectomy was performed. Currently, at 10 months' follow-up, the patient is well.

Patient's informed consent was obtained for publication of this case. All the tests performed were part of the diagnostic work-up,

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[a] Department of Surgery, Catholic University, [b] Department of Pathology, Catholic University, Rome, [c] Department of Gastroenterology and Digestive Endoscopy, "A. Cardarelli" Hospital, [d] Department of Radiology, "A. Cardarelli" Hospital, Campobasso, [e] Department of Medicine, University of Padua School of Medicine, Padua, Italy and Department of Pathology, Treviso Regional Hospital, Treviso, Italy.

[*] Correspondence: Riccardo Ricci, Department of Pathology, Catholic University, Largo A. Gemelli, 8, I-00168 Rome, Italy (e-mail: riccardo.ricci@unicatt.it).

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Table 1

Clinicopathologic characteristics of published PAMTs.

Case no.	Author, year	Age, y	Sex	Site	Size, mm	Ulcer	Immunophenotype	*KIT*/*PDGFRA* genotype	Treatment	FU, mo
1, 2	Takahashi et al, 2007[1]	50, 68	M (2)*	A (2)	40, 45	y, n	VIM+; α-SMA+; HHF35+; DES−; CAL+ (focal); CD117−; S100−; NF−; CD34−; CK−	WT (2)	DG, PG	NR, ANED 12
3	Rau et al, 2008[9]	50	F	A	19	y	α-SMA+; HHF35+; DES+ (focal); CD117−; S100−; NSE−; ALK−; β-Catenin−; CD34−	WT	LE	ANED 3
4	Galant et al, 2008[10]	61	M	A	37	n	VIM+; α-SMA+; DES−; CD117−; S100−; EMA−	NR	PG	ANED 6
5, 6	Yoshida et al, 2008[11] Spans et al, 2016[30]	19, 46	F, M	A (2)	45, 35	y, n	α-SMA+; HHF35+; DES+ (focal); CAL+ (partially) (1); CP+ (partially) (1); CD117−; PDGFRA−; S100−; Collagen IV− (1); Laminin− (1); Bcl2− (1); CD34−; AE1/AE3− (1); EMA− (1); CD10−; ER− (1); PR− (1)	WT (2)	DG (2)	ANED 9 and 4
7	Pailoor et al, 2009[12]	23	F	A	80	y	VIM+; α-SMA+; DES+ (focal); CD117−; S100−; CD34−	NR	PG	ANED 2
8–19	Miettinen et al, 2009[2]	7, 16, 21, 30, 33, 38, 43, 50, 56, 62, 65, 75	F (7), M (5)	A (5), AP (2), AB (5)	30, 40, 50 (2), 55 (3), 70, 90, 100 (2), 150	y (8), n (4)	α-SMA+ (8), − (2); DES−; CAL−; CD117−; DOG1−; S100−; CD34−; AE1/AE3− (3); CD10+ (focal) (1), − (2)	WT (3)	DG (5); PG (4); SG; AT; T	ANED 239, 236, 221, 108; ASU 288, 36; DUC 306, 174, 2; LTF (3)
20	Takahashi et al, 2010[13]	23	M	A	140	NR	Data cumulated with other 18 cases; only the following results, common to all cases, can be attributed with certainty to the single previously unreported case: VIM+; HHF35+; CD117−; S100−; NF−; ALK−; CD34−; CK−; EMA−	NR	PG	ANED 12
21	Wang et al, 2010[14]	54	F	GF	15	n	VIM+; α-SMA+; CD117−; S100−; CD34−	NR	ENR	ANED 6
22	Sing et al, 2010[15]	35	F	AP	40	n	α-SMA+; HHF35+; DES+; CAL+; CP+; CD117−; S100−; ALK−; β-Catenin−; CD34−; AE1/AE3−; CD10−; ER−; PR+; ACTH−; GH−	NR	LE	ANED 12
23	Tan et al, 2010[16]	34	M	A	32 (solid) + 245 (pseudo-cyst)	y	α-SMA+; DES+; CD117−; S100−; CD34−; MNF116−	WT	DG	ANED 2
24	Kim et al, 2011[17]	52	M	A	35	y	α-SMA+; DES+ (focal); CD117−; S100−; CD34−	NR	WR	ANED 5
25	Schulz et al, 2012[18]	59	M	P	15	y	α-SMA+; DES−; CD117−; S100−; ALK−; CD34−; panCK−; EMA−	WT	ENR	NR
26, 27	Kang et al, 2012[19]	47, 63	F, M	GB (2)	30, 22	y (2)	α-SMA+; DES−; CD117−; PKCθ− (1); S100−; NF− (1); CD34−; EMA−	WT (2)	WR, ENR	ANED 72, NR
28–30	Bi et al, 2012[20]	31, 42, 47	F (2), M	A (3)	45, 46, 80	y, n (2)	α-SMA+; HHF35+; DES+ (1), −(2); CAL+ (focal); CAM5.2+ (focal) (1), −(2); EMA+ (focal) (1), −(2); CD10+ (1), −(2); PR+ (1), − (2)	NR	NR	NR
31	Li et al, 2014[21]	32	M	A	34	n	VIM+; α-SMA+ (partially); DES+ (partially); CAL+ (partially); CD117−; DOG1−; S100−; ALK−; β-Catenin−; CD34−	NR	PG	ANED 36
32, 33	Duckworth et al, 2014[22]	11, 16	F (2)	E, PD	32, 35	y, n	α-SMA+; DES+ (1), − (1); CP+ (1); Nestin+ (1); CD117−; DOG1− (1); S100−; SYN− (1); CHR− (1); ALK− (1); CD34−; panCK− (1)	NR	Esophageal T, DG	ANED 14 and 15
34	Ikemura et al, 2014[23]	27	F	A	30	y	α-SMA+; DES+ (focal); CD117−; CD34−; CD10+; ER−; PR−; Claudin1−	NR	PG	ANED 40
35	Lee et al, 2014[24]	42	F	A	129	y	α-SMA+; HHF35+; DES−; CD117−; DOG1−; SDHB+; S100−; β-Catenin−; CD34−; MNF116−; CDK4−; MUC4−	NR	DG	ANED 1
36	Sakamoto et al, 2014[25]	60	M	A	20	n	α-SMA−; CD117−; DOG1−; PKCθ−; S100−; CD34−; CD10−	NR	PG	ANED 12
37	Banerjee et al, 2015[26]	19	F	D	138	n	α-SMA−; HHF35−; DES−; CP−; CD117−; DOG1−; S100−; CD34−; CD10−; ER−; HMB45−; Melan A−; prostaglandin receptor+	NR	DG + PDU	ANED 6
38	Lu et al, 2015[8]	26	F	A	NR	n	VIM+; α-SMA+; CD117−; DOG1−; CD34−	NR	DG	NR
39	Fassan et al, 2015[27]	55	F	G	10	n	VIM+; α-SMA+; HHF35+; DES−; CD117−; S100−; GFAP−; Collagen IV+; CD34+; EMA−; CD10−	WT	C	NR
40	Morris et al, 2016[28]	9	F	A	40	y	α-SMA+; DES+ (focal); CP+; CD117−; DOG1−; S100−; GFAP−; ALK−; CD34−; CK−; CD10+ (focal)	NR	P	ANED 4
41	Kane et al, 2016[29]	28	F	A	55	y	α-SMA+; CD117−; DOG1−; S100−; β-Catenin−; CD34−; D2–40−; AE1/AE3−; CD10+ (focal)	NR	DG	ANED 23

Case no.	Author, year	Age, y	Sex	Site	Size, mm	Ulcer	Immunophenotype	*KIT*/*PDGFRA* genotype	Treatment	FU, mo
42–55	Spans et al, 2016[30]	18, 19, 28, 29, 30, 36, 44, 47, 51, 58, 62, 63, 65, 76	F (11), M (3)	S (4), GB, A (8), J	10, 20, 35, 40, 43, 45 (2), 55, 65, 80, 90, NR (3)	NR	α-SMA+; CD117−; DOG1−; S100−; ALK−; β-Catenin+ (cytoplasmic); CD34− EMA−	WT (2)	NR	NR
56	Dixit et al, 2016[31]	51	F	A	84	y	α-SMA+; CAL−; CD117−; S100−; ALK−; β-Catenin−; CD34−	NR	DG	NR
57	Present case, 2016	47	M	A	60	y	VIM+; α-SMA+; DES+ (partially); CAL+ (partially); CD117−; DOG1−; S100−; SYN−; CHR−; ALK−; CD34−; AE1/AE3+ (focal); CAM5.2−; panCK+ (focal); CK20−; CK7−; EMA−; CD10+ (partially); CDX2−; p53−; MelanA−; HMB45−	WT	DG	ANED 10
58 (uncertain)	Fukunaga, 2004[32]	75	M	GF	270	n	α-SMA−; HHF35−; DES−; CD117−; S100−; NSE−; CD34+; CD31−; CAM5.2−	NR	PG	ANED 20
59 (uncertain)	Daum et al, 2010[33]	44	F	Cecum	50	n	VIM+; α-SMA+; DES−; CD117−; S100−; GFAP−; CD34−; AE1/AE3−; CAM5.2−; EMA−	WT	NR	NR

A = gastric antrum, ALK = anaplastic lymphoma kinase, ANED = alive, no evidence of disease, AP = antrum/pylorus, ASU = alive disease status unknown, AT = antrectomy, C = cholecystectomy, CAL = h-caldesmon, CHR = chromogranin, CK = cytokeratin, CP = calponin, D = duodenum, DES = desmin, DG = distal gastrectomy, DUC = dead of unknown cause, E = esophagus, EMA = epithelial membrane antigen, ER = estrogen receptor, ENR = endoscopic resection, F = female, FU = follow-up, G = gallbladder, GB = gastric body, GF = gastric fundus, GFAP = glial fibillary acidic protein, J = jejunum, LE = local excision, LTF = lost to follow-up, M = male, n = no, NF = neurofilment, NR = not reported, P = polipectomy, PAMT = plexiform angiomyxoid myofibroblastic tumor, PD = pylorus/duodenum, PDU = proximal duodenectomy, PG = partial gastrectomy, S = stomach, SG = subtotal gastrectomy, SMA = smooth muscle actin, SYN = synaptophysin, T = tumorectomy, VIM = vimentin, WR = wedge resection, WT = wild type, y = yes.

* Whenever data are drawn from papers reporting more than 1 PAMT, a number in brackets represents the number of cases with the indicated feature if >1; with regard to immunophenotype, the number in brackets refers to the number of cases with the reactivity referred to only if detailed and different with respect to the total number of the reported cases.

and followed standard laboratory procedures. This case is not part of a clinical trial or research study. The declaration of Helsinki is thus not applicable and approval of the ethics committee is not required.

Sections from formalin-fixed, paraffin-embedded tumor were stained with hematoxylin and eosin or alcian blue. Pathology revealed a 60-mm reddish gelatinous lobulated antral mass (Fig. 1A), involving submucosa, muscularis propria, and subserosa; the overlying mucosa was ulcerated. Histology showed a plexiform tumor composed of cells with ovoid nuclei, indistinct cytoplasms and, occasionally, clear halos, in a myxoid, alcian-positive matrix, sometimes with tiny collagen bundles, with arborizing capillary vessels (Fig. 1B and C). Tumor cells were positive for α-SMA (Fig. 1D), vimentin (not shown) and, partially, for caldesmon (Fig. 1E), desmin and CD10 (not shown); moreover, focal positivity for AE1/AE3 (Fig. 1F) and pan-CK KL1 (not shown) was detected. CD117, DOG1, CD34, S100, CAM5.2, CK20, CK7, EMA, p53, CDX2, chromogranin A, synaptophysin, Melan-A, HMB-45, and anaplastic lymphoma kinase (ALK) were all negative (not shown). *KIT* (exons 9, 11, 13, and 17) and *PDGFRA* (exons 12, 14, and 18), amplified using the same primers and polymerase chain reaction conditions described elsewhere,[35] were wild type. These findings rule out GIST, the most common mesenchymal tumor of stomach,[34] and carcinoma, because of both morphology and inconsistent immunophenotype; conversely, they are typical of PAMT, with the exception of the focal CK (AE1/AE3 and KL1) expression, exceptional in this tumor type.

3. Discussion

In this study, we report the exceptional occurrence of CK expression in a typical PAMT. PAMT, also known as plexiform fibromyxoma, is a myofibroblastic tumor recently fully characterized.[1,2] Probably the same tumor had been previously signaled several times in the pre-IHC era.[3–7] At the best of our knowledge, 59 PAMTs (including the present case and 2 uncertain ones) have been described in the literature (Table 1).[1,2,8–33] With the caveat due to the limitations in both number of cases and follow up, PAMT appears a benign entity; in fact, neither metastases nor relapses after complete surgical resection have been signaled so far. PAMT is capable of smooth muscle differentiation, as shown by the possible focal expression of caldesmon and desmin.[1,21,22,28]As such, PAMT can be expected to occasionally express CKs, since both myofibroblastic and smooth muscle tumors are known to be sometimes able to express these markers.[36] A restrict number of mesenchymal tumors (i.e., synovial sarcoma and epithelial sarcoma) display a true epithelial differentiation, with expression of both low- and high-molecular weight CK isoforms and of other epithelial markers, such as desmoplakins and occludin. Unlike these sarcomas, CK expression found in smooth muscle and myofibroblastic tumors is anomalous and does not reflect genuine epithelial differentiation, involving only a subset of neoplastic cells, mostly with IHC staining limited to a portion only of the cytoplasm, sometimes in a dot-like pattern.[37] This is the case of the herein reported PAMT (Fig. 1F). Coherently with the lack of a true epithelial differentiation, EMA IHC resulted negative, as happened in all PAMTs previously tested for this marker[10,11,13,18,19,27,30] with the exception of a focal positivity in a single case reported in the Chinese literature.[20] The presence of a hybrid epithelial–mesenchymal phenotype (so-called "amphicrine pattern") is a feature of epithelial-to-mesenchymal

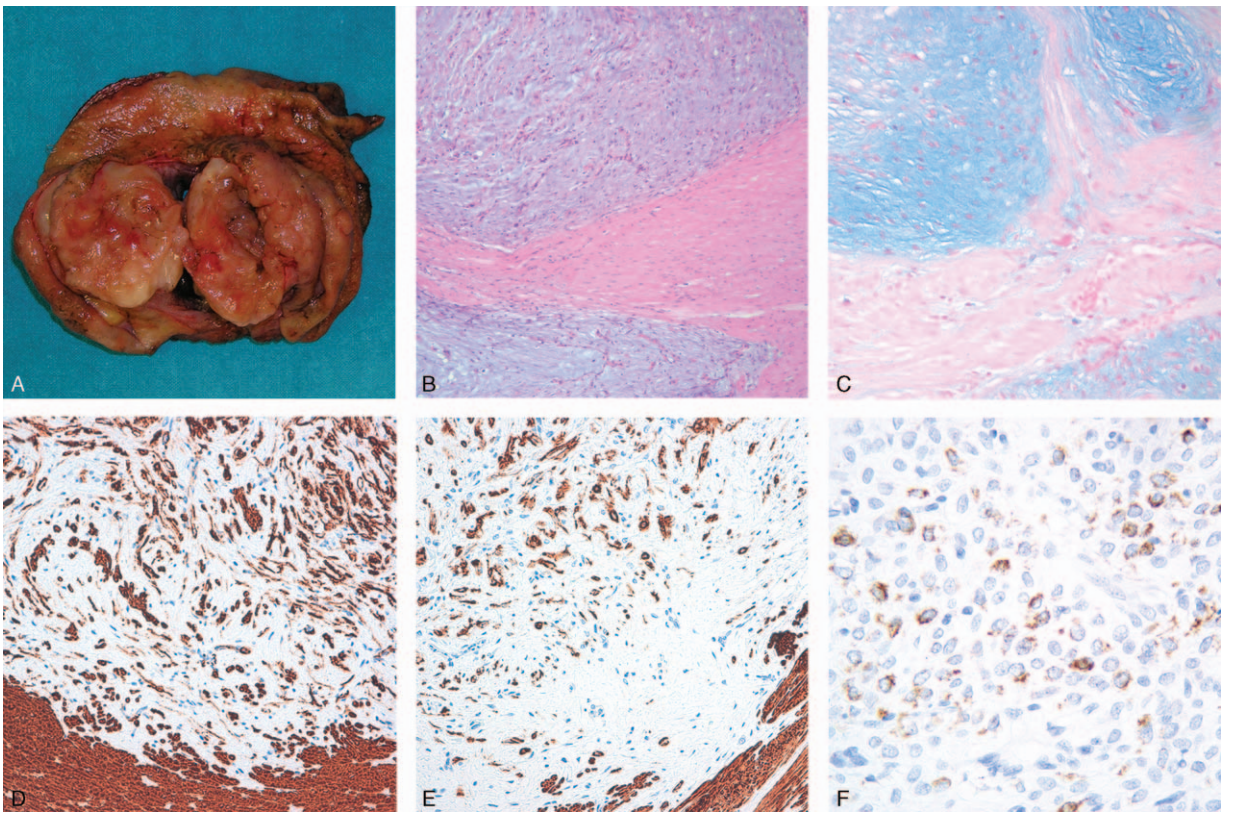

Figure 1. Pathological findings of the resected mass. (A) The resected specimen revealed a 60 mm lobulated intramural antral mass with a reddish gelatinous cut surface. (B, C) Histology of the tumor showed a plexiform intramural neoplasm displaying an alcian-positive myxoid matrix, with an arborizing capillary network (B, hematoxylin and eosin; C, alcian blue). (D–F) Immunohistochemistry of the tumor showed expression of α-smooth muscle actin (D) and partial positivity for caldesmon (E) (note the positive control of the intensely stained muscularis propria—bottom in D, bottom right in E), and focal positivity for cytokeratins AE1/AE3, sometimes with a perinuclear or a dot-like pattern (F).

and mesenchymal-to-epithelial cell transitions (MET), phenomena which can be found either in organ development or tumors. With regard to gastrointestinal (GI) mesenchymal tumors, MET has been described in GISTs, apparently with a favorable prognostic role.[38] Given the lack of aggressive behavior in the hitherto reported PAMTs, there is no room for a similar biological role of MET in these tumors.

The morphology of the herein reported PAMT (as happens with PAMT as a whole) does not support a diagnosis of carcinoma, although some carcinomas may show myxoid features.[39] In particular, its typical discohesive architecture excludes most carcinomas with the possible exceptions of poorly cohesive gastric carcinoma and gastric metastasis from a lobular breast cancer. However, the former is ruled out by the lack of atypia in the overlying mucosal epithelium and the latter by the clinical context of the reported tumor (lobular breast cancer is very rare in males). Furthermore, both of these neoplasms are excluded by the detected tumoral immunohistochemical profile.

PAMT must be distinguished from other mesenchymal tumors which can be found in the GI tract. GISTs (which can display myxoid or plexiform features) are typically CD117+ and DOG1+, express CD34 in about 2/3 of cases and mostly bear an activating mutation in either *KIT* or *PDGFRA*.[34] Inflammatory fibroid polyps, although often arising in the gastric antrum, rarely grow deeper than submucosa, typically feature CD34+ spindle cells arranged in an onion-skin pattern around blood vessels, are rich in eosinophils and are often *PDGRA* mutant.[40] Schwannomas, although often displaying areas with a loose texture (so-called "Antoni B areas") and sometimes featuring a plexiform architecture, often exhibit peripheral lymphoid aggregates and are consistently intensely and diffusely S100+. Inflammatory myofibroblastic tumors feature a relevant inflammatory infiltrate which, together with the loosely arranged myofibroblasts in an edematous myxoid background, simulates granulation tissue; moreover, about half of cases display cytoplasmic positivity for ALK protein.[41] Abdominal desmoid-type fibromatoses feature myofibroblasts arranged in long sweeping bundles, set in a collagenous stroma and, although sometimes showing myxoid change, lack a plexiform architecture and are mostly β-catenin positive at nuclear level.[42] Perhaps the gastric mesenchymal tumor which can be more easily confused with PAMT is myxoid leiomyoma, given its positivity for α-SMA, desmin, and caldesmon; however, it usually arises in the cardias or fundus, and is composed of cells with relatively abundant, intensely eosinophilic cytoplasm, with blunt-ended nuclei and intensely and diffusely desmin+ and caldesmon+.[43,44] In females, PAMT must be distinguished from metastatic low-grade endometrial stromal sarcoma (ESS); in fact, progesterone receptor positivity has been exceptionally reported in 2 PAMTs,[15,20] while ESS displays CD10 positivity, can be myxoid and can metastasize to the GI tract; a clinical history negative for gynecological neoplasms and the lack of estrogen and progesterone receptors exclude this entity.[11]Table 2 summarizes the differential diagnosis of PAMT.

Although the PAMT CK expression we report is thus not surprising, given the tissue lineage of this neoplasm, our finding

Table 2

Features of tumors entering in the differential diagnosis of plexiform angiomyxoid myofibroblastic tumor.

Lesion	Morphology	Immunophenotype of spindle cells										*KIT*/*PDGFRA* genotype
		α-SMA	Desmin	H-caldesmon	CD117	DOG1	CD34	S100	ALK	β-catenin	PR	
GIST	Usually centered in the muscularis propria. Spindle and/or epithelioid cells with mildly eosinophilic, often vacuolated, cytoplasm. Variable, mostly low mitotic activity	+ (~40%)	− (5% to 10%+, mostly gastric epithelioid)	+ (~50%)	+	+	+ (~70%)	− (5% to 10% +, so-called "GANT")	−	−	−	*KIT* (75% to 80%) or *PDGFRA* (5% to 8%) mutant
Inflammatory fibroid polyp	Usually centered in the submucosa, often polypoid. Spindle-to-ovoid cells in short fascicles, often around blood vessels (usually numerous) in an onion skin pattern; leukocytic infiltrate rich in eosinophils. Low mitotic activity	+	−	−	−	−	+ (often − in intestinal cases)	−	−	−	NA	*PDGFRA* mutant (50-70%)
GI schwannoma	Unencapsulated. Elongated cells; tapered spindled nuclei; ample, ill-delimited eosinophilic cytoplasm; mostly in sheets and interlacing fascicles; palisading; prominent thick-walled/hyalinized blood vessels; lymphoid cells aggregates at the periphery and perivascular; foamy macrophages. Low mitotic activity	−	−	−	−	−	−	+	−	−	−	WT
Inflammatory myofibroblastic tumor	Myofibroblasts and inflammatory infiltrate (plasma cells, lymphocytes, and eosinophils) in 1 of the following patterns: plump or spindled cells loosely arranged in an edematous myxoid background, with abundant blood vessels; compact fascicular spindle cell proliferation with ganglion-like cells with vesicular nuclei and eosinophilic nucleoli in myxoid or collagenized areas, with inflammation diffuse or in small aggregates; scar-like plate-like collagen with low cellularity and relatively sparse inflammatory infiltrate. Low mitotic activity	+ (~90%)	+ (10% to 70%)	−	−	−	−	−	+ (50% to 60%)	−	−	WT
Abdominal desmoid-type fibromatosis	Poorly circumscribed, infiltrative proliferation of elongated, slender, spindle-shaped uniform cells, without atypia, in long sweeping bundles in a collagenous stroma with variably prominent often slit-like blood vessels; microhemorrages. Variable mitotic activity	+	− (5% +)	−	− (reported +, depending on technical artifacts)	−	−	−	−	+ (70% to 75%)	−	WT
Smooth muscle tumors	Spindled to slightly epithelioid cells with intensely eosinophilic, sometimes vacuolated, cytoplasm, and uniform blunt-ended, cigar-shaped nuclei in intersecting fascicles; leiomyoma mostly paucicellular; may be myxoid change. Significant atypia in leiomyosarcoma. Mitotic activity low in leiomyoma, often high in leiomyo sarcoma	+ (~100% leiomyoma, ~70% to 100% leiomyosarcoma)	+ (~100% leiomyoma, ~50% to 90% leiomyosarcoma)	+ (~100% leiomyoma, ~50% to 95% leiomyosarcoma)	−	−	−	−	−	−	− (may be + in females)	WT
Low-grade endometrial stromal sarcoma, metastatic	Infiltrating masses of uniform, mostly oval small cells resembling endometrial stroma, surrounding small vessels; foci of hyalinization and foamy cells. Possible prominent myxoid change	+	− (sometimes focally +)	−	− (+ ~5% of cases, focal)	−	−	−	−	+ (40%)	+	WT

ALK = anaplastic lymphoma kinase, GANT = gastrointestinal autonomic nerve tumor, GI = gastrointestinal, GIST = gastrointestinal stromal tumor, NA = not assessed, PR = progesterone receptor, SMA = smooth muscle actin, WT = wild type.

nevertheless contributes to enlarge the known immunophenotypic spectrum of this tumor. In fact, at the best of our knowledge, all PAMTs so far immunohistochemically tested for CK expression resulted negative[1,2,11,13,15,16,18,22,24,28,29] with the exception of the report of focal positivity in a single case from the Chinese literature.[20] But, beyond its descriptive value, the awareness of a possible CK positivity in PAMT is relevant for avoiding possible misinterpretations of PAMT biopsies, especially when dealing with suboptimal amounts of tissue. In fact, under these circumstances, there is the risk of misdiagnosing PAMT as poorly cohesive gastric carcinoma, a neoplasm which can be extensively infiltrative in spite of mucosal lesions endoscopically elusive, potentially leading to dramatic consequences in the management of patients with PAMT.

In conclusion, we demonstrate the possible expression of CK in PAMT, an exceptional finding which, although not surprising considering the tissue lineage of this tumor, can be very relevant in the routine practice of pathologists for avoiding possible misdiagnoses with heavy clinical consequences.

References

[1] Takahashi Y, Shimizu S, Ishida T, et al. Plexiform angiomyxoid myofibroblastic tumor of the stomach. Am J Surg Pathol 2007;31:724–8.

[2] Miettinen M, Makhlouf HR, Sobin LH, et al. Plexiform fibromyxoma: a distinctive benign gastric antral neoplasm not to be confused with a myxoid gist. Am J Surg Pathol 2009;33:1624–32.

[3] Carpanelli JB, Sarra L. Gastric fibromyxoma. Prensa Med Argent 1959;46:1049–52.

[4] Rizzo F. Fibromyxoma of the stomach: clinical and anatomopathological contribution. Ann Ital Chir 1959;36:161–81.

[5] Rossi F. Contribution to the study of gastric myxoma. Friuli Med 1960;15:619–30.

[6] Strat V, Diaconescu MR, Georgescu S, et al. Gastric myxoma. Rev Med Chir Soc Med Nat Iasi 1986;90:523–4.

[7] Hull MT, Jesseph JE. Ultrastructure of gastric myxofibroma with intracytoplasmic collagen. Ultrastruct Pathol 1982;3:25–30.

[8] Lu B, Ye W, Liu H. A rare gastric tumor in a young woman. Gastric plexiform angiomyxoid myofibroblastic tumor. Gastroenterology 2015;149:294–5.

[9] Rau TT, Hartmann A, Dietmaier W, et al. Plexiform angiomyxoid myofibroblastic tumour: differential diagnosis of gastrointestinal stromal tumour in the stomach. J Clin Pathol 2008;61:1136–7.

[10] Galant C, Rousseau E, Duc DKHM, et al. Re: Plexiform angiomyxoid myofibroblastic tumor of the stomach. Am J Surg Pathol 2008;32: 1910author reply 1912–1913.

[11] Yoshida A, Klimstra DS, Antonescu CR. Plexiform angiomyxoid tumor of the stomach. Am J Surg Pathol 2008;32:1910–2. author reply 1912–1913.

[12] Pailoor J, Mun KS, Chen CT, et al. Plexiform angiomyxoid myofibroblastic tumour of the stomach. Pathology 2009;41:698–9.

[13] Takahashi Y, Suzuki M, Fukusato T. Plexiform angiomyxoid myofibroblastic tumor of the stomach. World J Gastroenterol 2010;16: 2835–40.

[14] Wang WY, Li JN, Li GD. Plexiform angiomyxoid myofibroblastic tumour of the gastric fundus: successful diagnosis and treatment by endoscopy. J Clin Pathol 2010;63:569–70.

[15] Sing Y, Subrayan S, Mqadi B, et al. Gastric plexiform angiomyxoid myofibroblastic tumor. Pathol Int 2010;60:621–5.

[16] Tan CY, Santos LD, Biankin A. Plexiform angiomyxoid myofibroblastic tumour of the stomach: a case report. Pathology 2010;42:581–3.

[17] Kim A, Bae YK, Shin HC, et al. Plexiform angiomyxoid myofibroblastic tumor of the stomach: a case report. J Korean Med Sci 2011;26:1508–11.

[18] Schulz T, Drgac J, Chmelar C, et al. Plexiform angiomyxoid myofibroblastic tumour of the stomach. Pathologe 2012;33:65–9.

[19] Kang Y, Jung W, Do IG, et al. Plexiform angiomyxoid myofibroblastic tumor of the stomach: report of two cases and review of the literature. Korean J Pathol 2012;46:292–6.

[20] Bi R, Yin W, Liu XL, et al. Plexiform angiomyxoid myofibroblastic tumor of stomach. Zhonghua Bing Li Xue Za Zhi 2012;41:756–60.

[21] Li P, Yang S, Wang C, et al. Presence of smooth muscle cell differentiation in plexiform angiomyxoid myofibroblastic tumor of the stomach: a case report. Int J Clin Exp Pathol 2014;7:823–7.

[22] Duckworth LV, Gonzalez RS, Martelli M, et al. Plexiform fibromyxoma: report of two pediatric cases and review of the literature. Pediatr Dev Pathol 2014;17:21–7.

[23] Ikemura M, Maeda E, Hatao F, et al. Plexiform angiomyxoid myofibroblastic tumor (PAMT) of the stomach. A case report focusing on its characteristic growth pattern. Int J Clin Exp Pathol 2014;7: 685–9.

[24] Lee PW, Yau DT, Lau PP, et al. Plexiform fibromyxoma (plexiform angiomyxoid myofibroblastic tumor) of stomach: an unusual presentation as a fistulating abscess. Int J Surg Pathol 2014;22:286–90.

[25] Sakamoto K, Hirakawa M, Atsumi K, et al. A case of gastric plexiform fibromyxoma: radiological and pathological findings. Jpn J Radiol 2014;32:431–6.

[26] Banerjee N, Gupta S, Dash S, et al. Plexiform angiomyxoid myofibroblastic tumour of the duodenum: a rare entity. BMJ Case Rep 2015;doi: 10.1136/bcr-2015-210004.

[27] Fassan M, Salmaso R, Saraggi D, et al. Plexiform fibromyxoma of the gallbladder. Pathologica 2015;107:181–4.

[28] Morris MW, Sullivan L, Sawaya DE, et al. Gastric plexiform fibromyxoma tumor in a child—case report and review of the literature. J Pediatr Surg Case Rep 2016;4:38–41.

[29] Kane JR, Lewis N, Lin R, et al. Plexiform fibromyxoma with cotyledon-like serosal growth: a case report of a rare gastric tumor and review of the literature. Oncol Lett 2016;11:2189–94.

[30] Spans L, Fletcher CD, Antonescu CR, et al. Recurrent MALAT1-GLI1 oncogenic fusion and GLI1 upregulation define a subset of plexiform fibromyxoma. J Pathol 2016;doi: 10.1002/path.4730.

[31] Dixit JD, Sharief SA, Goyal MK, et al. Plexiform angiomyxoid myofibroblastic tumor (PAMT) of stomach with synchronous bilateral cystic ovarian neoplasms, a rare case presentation. Indian J Surg Oncol 2016;7:82–5.

[32] Fukunaga M. Gastric fibromyxoma, a distinct entity of pure fibroblastic tumor—an ultrastructural study. APMIS 2004;112:304–8.

[33] Daum O, Jirasek T, Grossmann P, et al. Plexiform fibroma of the colon. Appl Immunohistochem Mol Morphol 2010;18:483–4.

[34] Ricci R, Tos APD, Rindi G. GISTogram: a graphic presentation of the growing GIST complexity. Virchows Arch 2013;463:481–7.

[35] Ricci R, Chiarello G, Attili F, et al. Endoscopic ultrasound-guided fine needle tissue acquisition biopsy samples do not allow a reliable proliferation assessment of gastrointestinal stromal tumours. Dig Liver Dis 2015;47:291–5.

[36] Miettinen M. Immunohistochemistry of soft tissue tumours—review with emphasis on 10 markers. Histopathology 2014;64:101–18.

[37] Folpe AL, Gown AM. Weiss SW, Goldblum JR. Immunohistochemistry for analysis of soft tissue tumors. Soft tissue tumors 5th Ed.Philadelphia: Mosby, Elsevier; 2008. 129–74.

[38] Gurzu S, Turdean S, Kovecsi A, et al. Epithelial-mesenchymal, mesenchymal-epithelial, and endothelial-mesenchymal transitions in malignant tumors: an update. World J Clin Cases 2015;3:393–404.

[39] Gurzu S, Szentirmay Z, Bara T, et al. Myxoid variant of adrenocortical carcinoma: a report of two illustrative cases and a brief review of the literature. Pathology 2014;46:83–5.

[40] Martini M, Santoro L, Familiari P, et al. Inflammatory fibroid polyp of the gallbladder bearing a platelet-derived growth factor receptor alpha mutation. Arch Pathol Lab Med 2013;137:721–4.

[41] Coffin CM, Fletcher JA. Fletcher CDM, Bridge J, Hogendoorn PCW, et al. Inflammatory myofibroblastic tumour. WHO classification of tumours of soft tissue and bone 4th Ed.Geneva:WHO Press; 2013. 72–3.

[42] Goldblum J, Fletcher JA. Fletcher CDM, Bridge J, Hogendoorn PCW, et al. Desmoid-type fibromatosis. WHO classification of tumours of soft tissue and bone 4th Ed.Geneva:WHO Press; 2013. 72–3.

[43] Lee HH, Hur H, Jung H, et al. Analysis of 151 consecutive gastric submucosal tumors according to tumor location. J Surg Oncol 2011; 104:72–5.

[44] Miettinen MM, Quade B. Fletcher CDM, Bridge J, Hogendoorn PCW, et al. Leiomyoma of deep soft tissue. WHO classification of tumours of soft tissue and bone 4th Ed.Geneva:WHO Press; 2013. 110–1.