

## CASE REPORT

## Primary gastric plasmacytoma: a rare entity

Rui Caetano Oliveira,<sup>1</sup> Pedro Amaro,<sup>2</sup> Maria José Julião,<sup>1</sup> Maria Augusta Cipriano<sup>3</sup><sup>1</sup>Department of Pathology, Hospitais da Universidade de Coimbra, Coimbra, Portugal<sup>2</sup>Department of Gastroenterology, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal<sup>3</sup>Pathology Department, University Hospital Center of Coimbra, Coimbra, Portugal**Correspondence to**

Dr Rui Caetano Oliveira, ruipedrocoliveira@hotmail.com

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**SUMMARY**

Extramedullary plasmacytomas (EP) are tumours composed by a monoclonal population of plasma cells that arise in extraosseous tissues, comprising <5% of all plasma cell neoplasms. Usually, EP arise in the head and neck region, and the stomach is the second most common location—gastric plasmacytoma (GP). Clinical and radiological manifestations are unspecific and may mimic other tumours like gastric adenocarcinomas, gastric stromal tumours and lymphomas, mainly marginal cell lymphoma (MALT lymphoma) and usually definitive diagnosis is provided by pathological evaluation. We present a case of primary GP, discovered incidentally as a polypoid lesion. Tumour was composed by sheets of mature and immature plasmocytes positive for CD138 on immunohistochemistry, without *Helicobacter pylori* identification. The patient is alive 6 years later and without tumour relapse.

**BACKGROUND**

This case was written due to its rarity and in order to increase awareness of the entity. Gastric plasmacytomas (GP) are very rare but with good prognosis, with non-specific clinical and radiological presentations that may mislead the clinician into a diagnosis of a more aggressive tumour. Pathological examination usually provides the diagnosis, but sometimes it may not be obvious and extensive immunohistochemistry panel has to be employed as in our case.

Knowledge of GP characteristics might improve disease approach with quick and accurate diagnosis.

**CASE PRESENTATION**

A man aged 61 years recurs to the emergency department with symptoms of upper gastrointestinal bleeding.

Personal background included tongue carcinoma surgically removed 4 years before, alcoholic cirrhosis, type II diabetes mellitus, arterial hypertension, atrial fibrillation, congestive heart failure, chronic gastritis, obesity and prostate benign hyperplasia. Familiar background revealed grandmother with breast cancer and aunt with head and neck cancer.

Regular medication was pantoprazole, warfarin, amiodarone, spironolactone, furosemide, insulin, metformin, candesartan, digoxin and finasteride.

**INVESTIGATIONS**

An upper endoscopy was promptly performed and showed a 40 mm gastric lobulated sessile polypoid lesion (type 0-Is, Paris classification) on the greater curvature of the distal body, lined by mucosa with ulcerated areas (figure 1). Patient status and characteristics of the lesion allowed endoscopic intervention, and a piecemeal endoscopic mucosal



**Figure 1** Endoscopy showed polypoid lesion on the greater gastric curvature, with ulceration.

resection (inject and cut technique) was performed. The procedure underwent uneventfully.

Histological examination was performed on H&E-stained slides observed in light microscope—Nikon Eclipse 50i, and images obtained using a Nikon-Digital Sight DS-Fi1 camera.

The endoscopic mucosectomy fractioned specimen was composed of three fragments, the larger with polypoid configuration measuring 2.5 cm. Externally, it had a dark brown rough surface and on cut section showed a brownish tissue with white firm areas.

Histologically, the bigger fragment revealed in the lamina propria (figure 2A) a dense proliferation forming a cohesive sheet of medium and large cells (figure 2B) with eosinophil cytoplasm of undefined boundaries and pleomorphic nuclei with grumpy chromatin. In some areas, it was possible to identify mature and immature plasmocytes. No lymphoepithelial lesions were seen. Mitotic activity was frequent (26 mitoses/10 high-power-fields) (figure 2C, D). The lesion had a polypoid growth, partially ulcerated and covered by granulation tissue, and showed in the periphery hyperplastic gastric mucosa. The margin did not show signs of involvement by the lesion and the remaining two fragments were composed of normal oxyntic gastric mucosa. *Helicobacter pylori* infection was ruled out by Whartin Starry stain.

**DIFFERENTIAL DIAGNOSIS**

The lesion architecture and morphology were unspecific and a first panel of immunohistochemistry was performed on the basis of a first approach to diagnosis: lymphoma seemed more probable, followed by carcinoma and melanoma or, in lower probability, neuroendocrine carcinoma.

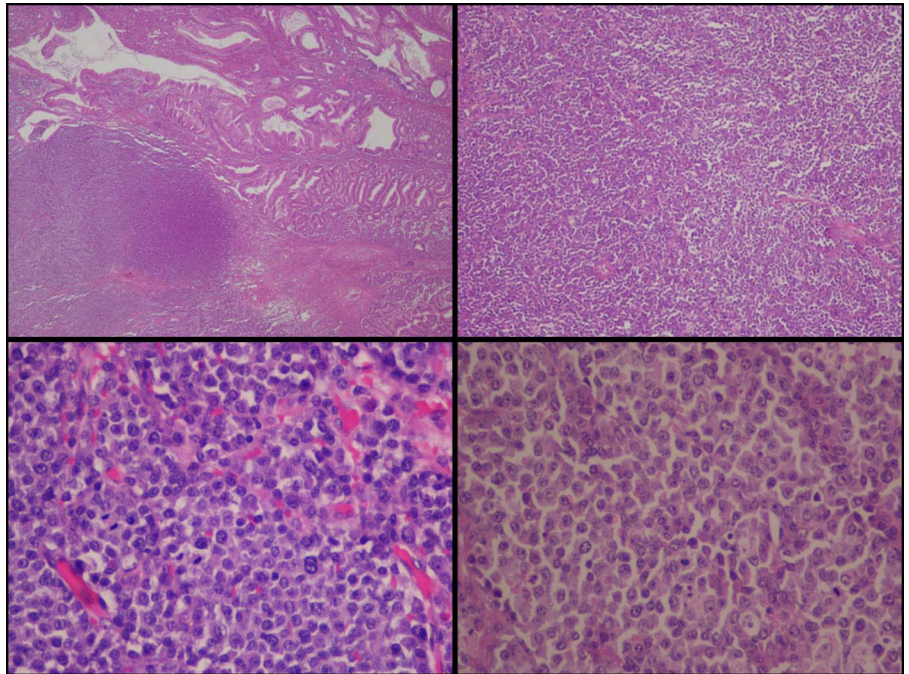
Immunohistochemical studies were performed on one representative block of the lesion, resorting to



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**Figure 2** H&E examination revealed a dense proliferation in the lamina propria (A,  $\times 40$ ) forming a cohesive sheet of medium to large cells (B,  $\times 100$ ) with eosinophil cytoplasm of undefined boundaries and pleomorphic nuclei with mitotic activity (C,  $\times 400$ ) and mature and immature plasmacytes (D,  $\times 400$ ).



avidin-biotin-peroxidase complex detection system and performed on Ventana Marker Platform Bench Mark ULTRA IHC/ISH using the following antibodies: AE1/AE3 (PCK26, Ventana, Arizona, USA), Bcl-2 (124, Ventana), Bcl-6 (GI191E/A8, CellMarque, California, USA), CD3 (2VG6, Ventana), CD5 (SP19, Ventana), CD10 (SP67, Ventana), CD20 (L26, Dako, Denmark), CD43 (cL60, Ventana), CD45/LCA (2B11&PD7/26, Ventana), CD79a (SP18, Ventana), CD138 (BA-38, CellMarque), chromogranin A (LK2H10, Ventana), cyclinD1 (SP4-R, Ventana), epithelial membrane antigen (EMA, E29, Ventana), IgA (polyclonal, CellMarque), IgG (polyclonal, CellMarque), IgM (polyclonal, CellMarque), Ki67 (30-9, Ventana), Kappa chain (polyclonal, Ventana), Lambda chain (polyclonal, Ventana), LMP1 (CS1-4, CellMarque), PAX5 (SP34, Ventana), melanoma A (A103, Ventana), melanosome

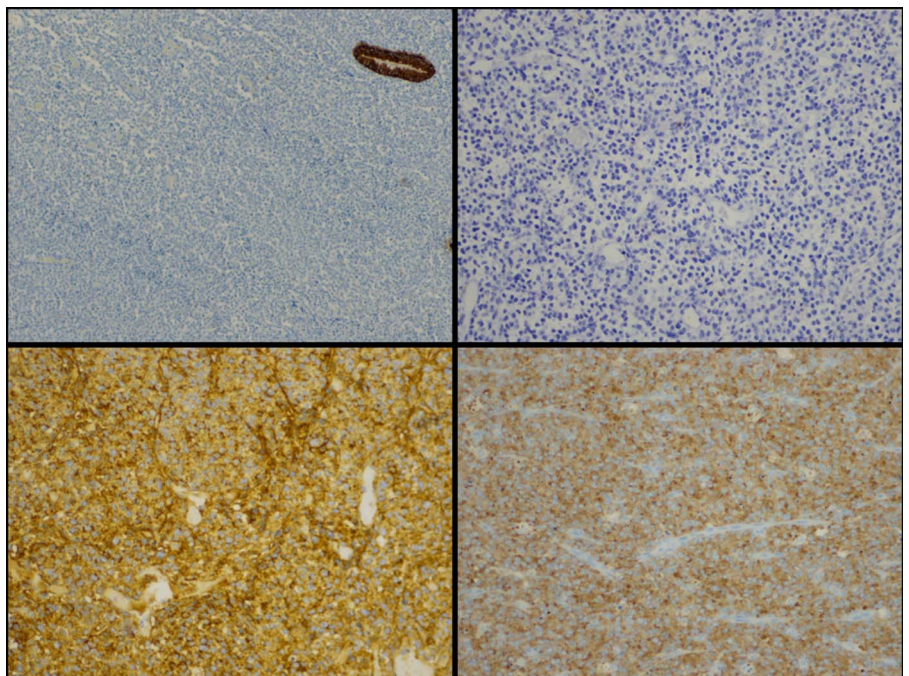
(HMB45, Ventana), MUM1 (MRQ-43, CellMarque), myeloperoxidase (polyclonal, CellMarque), synaptophysin (MRQ-40, CellMarque), S100 protein (S100, 4C4.9, Ventana) and vimentin (V9, Ventana).

The initial study was negative for AE1/AE3 (figure 3A), CD45 (figure 3B), Melan A, HMB45, S100, chromogranin A and synaptophysin; positivity for vimentin was registered.

Incorporating the results with tumour morphology, we thought of plasmablastic lymphoma, plasmacytoma/multiple myeloma, MALT lymphoma with marked plasmacytic differentiation and Castleman's disease, plasma cell type.

A second panel of immunohistochemistry was negative for CD20, CD79a, Bcl6, PAX5, CD3, CD5, CD10, cyclinD1 and LMP1; Bcl2 and CD43 were positive and the Ki67 proliferative index was near 60%.

**Figure 3** Immunohistochemistry was negative for AE1/AE3 (A) and for LCA (B), with positivity for CD138 (C) and Lambda chains (D).



Rethinking our possibilities and once again conjugating with morphology, especially taking into account the presence of mature and immature plasmacytes in the periphery, the possibility of plasmacytoma/multiple myeloma was considered and on a third immunohistochemical panel, we obtained positivity for CD138 (figure 3C), EMA and MUM1; there was evidence of lambda chain restriction (figure 3D), demonstrating a clonal population. A diagnosis of GP/involvement by multiple myeloma was made. The differential diagnosis between these entities needs extra workup, namely bone marrow biopsy to evaluate for plasma cell, assessment of plasmacytic skeletal lesions, tumour serological markers and immunoglobulins as well as protein electrophoresis.

Laboratory exams did not show any alterations, despite mild anaemia. Tumour serological markers were normal as well as immunoglobulins. Protein electrophoresis was normal and bone marrow biopsy showed no involvement.

## TREATMENT

Treatment consisted of endoscopic polypectomy without radiation. Since no *H. pylori* was identified, eradication was not performed.

## OUTCOME AND FOLLOW-UP

The patient was discharged with no further therapeutic. One year after polypectomy, prostate cancer was diagnosis by serum PSA elevation—prostate biopsy showed Gleason 6 (3+3) adenocarcinoma—and treated with radiotherapy.

Currently, the patient is alive and has been on clinical follow-up for 6 years, without signs of plasmacytic tumour relapse.

## DISCUSSION

Plasma cell neoplasms are defined as mature B-cell neoplasm according to the World Health Classification<sup>1</sup> and may be divided into four categories: multiple myeloma, plasma cell leukaemias, solitary plasmacytomas of the bone and extramedullary plasmacytomas (EP); the latter are tumours composed by a monoclonal and localised proliferation of plasma cells that arise in extraosseous tissues.<sup>2</sup>

EP are rare, comprising <5% of all plasma cell neoplasms and normally presents as localised lesions, usually in the head and neck region, being the stomach the second more common location—GP.<sup>3</sup>

Biologically, GP seem distinct from their bone counterpart and plasma cell myeloma and some authors believe that there is an association with marginal zone lymphoma and *H. pylori* infection.<sup>4</sup>

Clinically, GP are more frequent in men, with a median age of 55 years,<sup>2,3</sup> but some rare cases have been described in adolescents;<sup>5</sup> symptoms are usually non-specific and include weight loss, epigastric pain/discomfort or gastrointestinal bleeding.<sup>6</sup> Radiology is also vague in diagnosing GP, showing a polypoid lesion or homogeneous concentric gastric wall thickening in computerised tomography, generally interpreted as gastrointestinal stromal tumour or lymphoma; due to mucosal/submucosal origin of GP endoscopy may only show a protruding gastric wall and be misjudged as adenocarcinoma,<sup>7</sup> but represents a good approach since allows tissue biopsy/tumour excision—essential for diagnosis,<sup>4</sup> as in our case—the tumour presented as sessile polypoid lesion, which enable endoscopic mucosectomy.

The tumour morphology, with sheets of mature and immature plasmacytes in the lamina propria, with high mitotic count and absence of lymphoepithelial lesions raised as main differential

diagnosis: GP, MALT lymphoma with marked plasmacytic differentiation, Castleman disease plasma cell variant, plasmablastic lymphoma and diffuse large B-cell lymphoma anaplastic variant, but the morphological findings associated with a correct immunohistochemistry panel (CD20, CD79a, CD10, Bcl-2 negatives; CD138, EMA, MUM1 positives and lambda chain restriction) provided the correct diagnosis.<sup>2,3</sup>

However, pathology diagnosis, despite accurate for assessing a monoclonal proliferation of plasma cells, is not synonym of GP, since extramedullary involvement by multiple myeloma may occur in up to 20% of the patients, and GP may be the initial manifestation of a multiple myeloma, with some reports in the literature.<sup>8,9</sup>

Therefore, the patient must undergo systemic evaluation to exclude bone marrow involvement and there must not be clinical or laboratory evidence of myeloma—low or absent M-protein concentration, no hypercalcaemia and absence of kidney failure.<sup>2,3,7</sup> Our patient fulfilled all these criteria—it had not bone marrow involvement, no plasmacytic bone lesions and serological markers and protein electrophoresis were normal.

Similar to other gastric tumours like gastric adenocarcinoma and MALT lymphoma, a putative relation with *H. pylori* has been postulated, especially in cases with concomitant infection; however, some GP cases did not have *H. pylori* infection; despite there is not a definitive association, *H. pylori* eradication may be considered as therapeutic option in these cases.<sup>10,11</sup> In the reported case, *H. pylori* was not present, so eradication was not performed.

Surgery, with or without radiation, is the treatment of choice, normally with good results.<sup>2,3</sup> Follow-up usually is favourable, with good disease-free survival at 10 years.<sup>6</sup>

## Learning points

- ▶ Gastric plasmacytoma are rare entities comprising about 5% of all plasma cell neoplasms.
- ▶ Final diagnosis is provided by pathological examination, after extensive differential of hypothesis, supported by immunohistochemistry.
- ▶ Multiple myeloma must be excluded with bone biopsy and clinical/laboratory tests.
- ▶ Surgical excision normally is the treatment of choice, with good results.
- ▶ Follow-up is favourable with long disease-free survival.

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**Patient consent** Obtained.

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