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CASE REPORT

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Coexisting primary early gastric plasmacytoma and sarcoidosis with hypercalcaemia

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Abstract We report on a 61-year-old woman with coexisting early stage primary gastric plasmacytoma and sarcoidosis with hypercalcaemia. Laboratory data on admission showed hypercalcaemia, with 12.8 mg/dl, parathyroid hormone-related peptide (PTHrP) 1.2 pmol/l, C-PTHrP 69.5 pmol/l, and 1,25-dihydroxyvitamin D3 46.7 pg/ml. Neoplastic plasma cells proliferated in the propria mucosa of the stomach, showed a monoclonal immunoglobulin of cytoplasmic IgA (lambda light chain) and were positive for leucocyte common antigen and epithelial membrane antigen on paraffin section prepared from a stomach biopsy specimen. Russel bodies were present, as were crystals. Abundant sarcoid granulomas were observed in many of the regional lymph nodes around the stomach and in the dermis of a skin nodule. The patient underwent subtotal gastrectomy with administration of antimyeloma chemotherapy. We suggest that the hypercalcaemia in this patient was due to PTHrP production by neoplastic plasma cells.

Key words Primary gastric plasmacytoma · Sarcoidosis · Hypercalcaemia · Parathyroid hormone-related peptide

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Introduction

The incidence of gastric plasmacytoma is about 0.07% (3 of 4199) of malignant tumours of the stomach [16]. Most extramedullary plasmacytomata occur in the upper respiratory tract, and gastric plasmacytoma constitutes only 5% of all extramedullary plasmacytomata [4]. The frequency of malignant lymphoma and lung cancer is significantly higher in patients with sarcoidosis [2], and hypercalcaemia is a prominent feature of this disease [3].

We report on a 61-year-old woman with coexisting early stage primary gastric plasmacytoma and sarcoidosis with hypercalcaemia.

Case report and pathological results

A 61-year-old woman noticed subcutaneous nodules, ranging up to the size of the tip of the little finger, on the forehead, right cheek and lower left eyelid, and below the nose on 8 June 1994. However, she did not seek any advice on these. She consulted our hospital on 20 September 1995, for general fatigue, anorexia, weakness of the lower extremities and nausea, and was found to have hypercalcaemia (12.8 mg/dl). She did not have malabsorption with chronic diarrhoea and abdominal pain. Laboratory studies on admission showed the following values in serum; total protein 6.3 g/dl with globulin 2.5 g/dl, Na 142 mEq/l, K 2.7 mEp/l, and Ca 6.9 mEq/l (normal range 4.2–5.4), P 2.5 mEq/l (2.7–4.5), C-parathyroid hormone (PTH) 0.3 ng/ml (normal range under 0.5), PTH-related peptide (PTHrP) 1.2 pmol/l (under 0.6), C-PTHrP 69.5 pmol/l (13.8–55.3). calcitonin 16 pg/ml (29.7–45.9), and angiotensin-converting enzyme (ACE) 34.2 IU/l (8.3–21.4). The PTH levels were measured by radioimmunoassay using commercially available kits. β2-Macroglobulins were 9.3 mg/l (1.0–1.9) in blood and 3210 μg/l (under 230) in urine. Bence-Jones protein was not detected, and no monoclonal gammopathy was observed in the serum.

IIc-like lesions were observed on the anterior wall of the antrum. In 6 of 9 biopsy specimens resected from the stomach on 26 September 1995, plasmacytoid cells proliferated diffusely in the propria mucosa of the stomach (Fig. 1). Russel bodies were present, as were crystals. The crystals appeared to be needle-like, rhomboidal, and rectangular. Dutcher bodies were not observed. Neoplastic plasma cells showed monotypic immunoglobulin of cytoplasmic IgA (lambda light chain) (Fig. 2a, b) and were positive for LCA (leucocyte common antigen, CD45) and EMA (epithelial membrane antigen), but negative for cytoplasmic kappa light chain

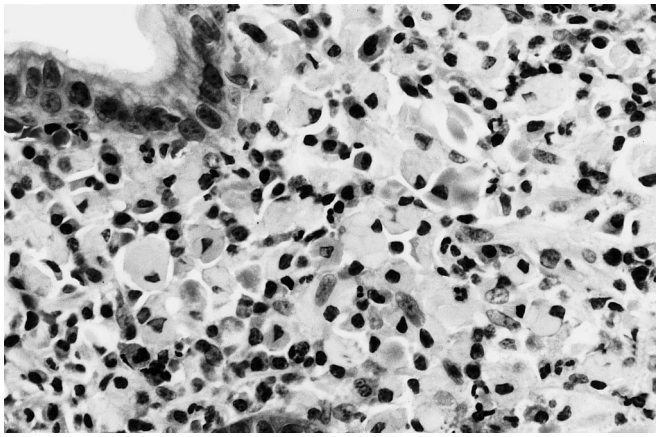

Fig. 1 Many plasmacytoid cells proliferated diffusely in the propria mucosa of the stomach. Russel bodies were present, as were crystals. Haematoxylin and eosin, ×400

(Fig. 2c), L26 (CD20), Ber-H2 (CD30) on paraffin sections. There was no proliferation of centrocyte-like cells, monocytoid B-cells or small lymphocytes, and nor were lymph-epithelial lesions with neoplastic cells present.

We diagnosed this as a case of primary gastric plasmacytoma. Toluidine blue staining and *Heliobacter pylori* immunostaining were negative in the mucous coat and on the surface of the foveolar epithelium of the stomach.

A forehead nodule was biopsied on 29 September 1995. Many noncaseating epithelioid cell granulomas with scattered multinucleated giant cells were observed in the dermis (Fig. 3). Subtotal gastrectomy with lymph node resection was performed on 27 November 1995. Neither nodules nor ulcers were observed in the resected stomach. Clusters of plasmacytoid cells with cytoplasmic inclusions were scattered throughout the muscularis propria mucosa of the gastric body, including the antrum. They did not extend into the submucosa or spread to the serosa and were nonulcerating lesions of the superficially spreading type of gastric plasmacytoma. Regional lymph nodes were swollen and ranged from the size of a soybean to the tip of a forefinger. Noncaseous epithelioid cell granulomas were involved in 26 of 60 resected lymph nodes. However, no atypical plasmacytoid cells were observed in any lymph node. We diagnosed the skin nodule and regional lymph nodes around the stomach of this case as sarcoidosis. Neither lymphadenopathy (hilar or superficial)

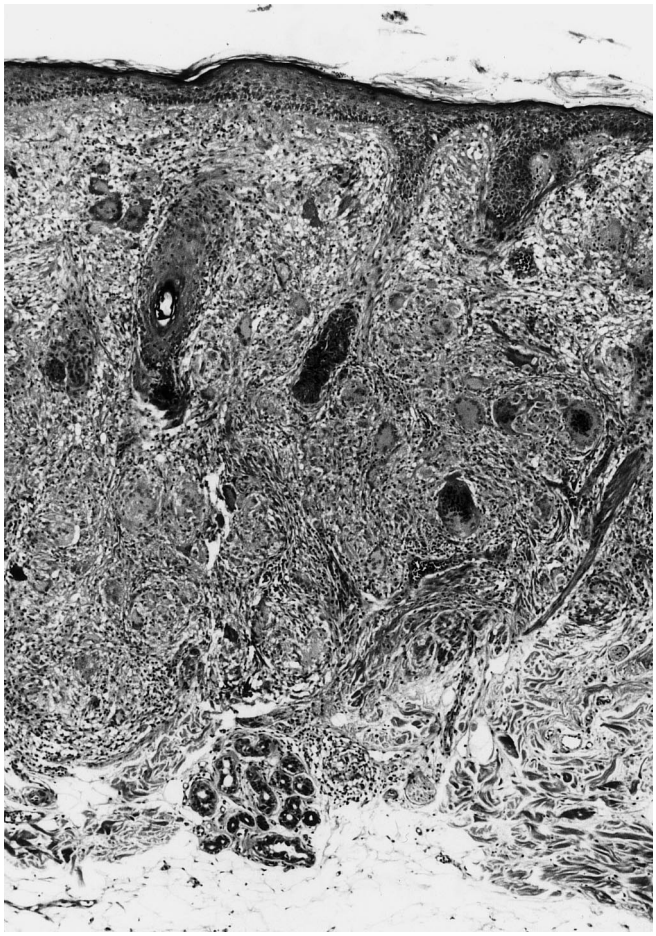

Fig. 3 Many noncaseating epithelioid cell granulomas with scattered multinucleated giant cells were observed in the dermis. Haematoxylin and eosin, ×200

nor lung involvement was visible on chest roentgenogram. There was no involvement of the eye, salivary gland, liver, or spleen. The patient showed loss or negativity of the skin test to tuberculin; 3×3 mm, and the Kveim test was not performed. Bone marrow aspiration bi-

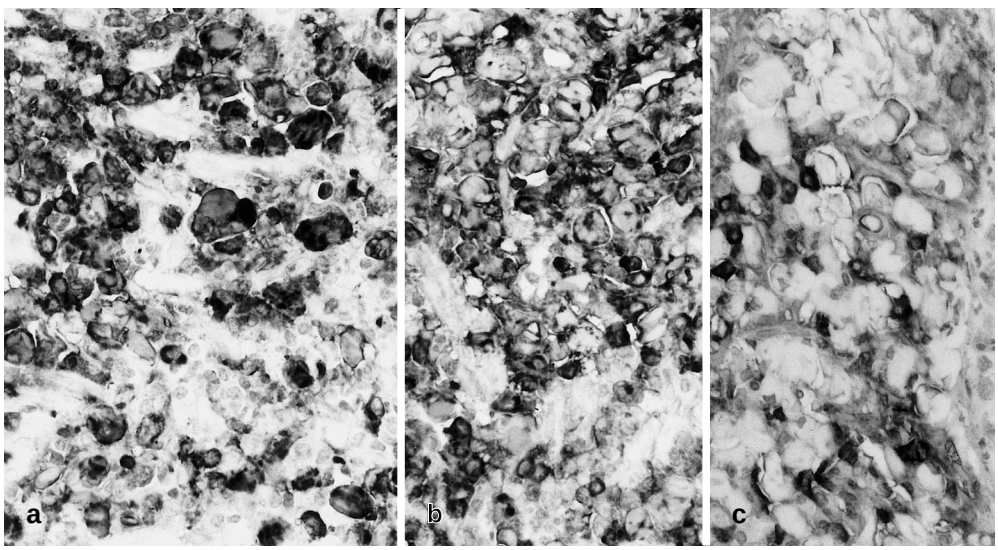

Fig. 2 Neoplastic plasma cells had a monotypic immunoglobulin of cytoplasmic IgA (**a**, *left*) and lambda light chain (**b**, *centre*) and showed the negative reaction for kappa light chain (**c**, *right*). Immunostaining, ×400

opsy was performed on 8 January 1996, and the clot section showed no plasma cell proliferation. 1,25-Dihydroxyvitamin D3 in serum was 46.7 pg/ml (normal range 20–60 pg/ml on 14 June 1996. The patient then received antimyeloma chemotherapy, but was not given any therapy for sarcoidosis. Immunostaining for PTHrP and 1,25-dihydroxyvitamin D3 was not performed on the biopsy specimens. The laboratory data (serum levels) on 10 March 1997 were: Ca, 4.4 mEq/l; PTHrP, under 0,2 pmol/l; C-PTHrP, 44.3 pmol/l. In November 1997, the patient was alive and in a good general condition.

Discussion

We diagnosed our case as gastric plasmacytoma from the clinical, morphological and immunohistochemical findings. The illness differed from extranodal marginal B cell lymphoma of mucosa-associated lymphoid tissue (MALT) type and immunoproliferative small intestinal disease (IPSID, alpha heavy chain disease). Extranodal marginal B cell lymphoma of MALT type is characterized by the proliferation of centrocyte-like cells, small lymphocytes, monocytoid B cells, and transformed blasts and also by lymph-epithelial lesions with neoplastic cells and follicular colonization [10, 17]. Plasma cell differentiation is present in approximately one-third of the lymphoma [10]. IPSID is a disorder of IgA (alpha)-heavy chain-producing cells without either kappa and lambda light chains; it occurs mainly in young adults, most commonly in the Mediterranean area, presenting with profound malabsorption and characterized by massive infiltration of the lamina propria of the intestine by plasma cells, centrocyte-like cells, and transformed blasts [5, 7, 11]. Issacson et al. proposed that IPSID and extranodal marginal B cell lymphoma of MALT type both originate from MALT [10].

Several reports have indicated that *Helicobacter pylori* infection may be a cause of primary gastric lymphoma [6, 23]. *Helicobacter pylori* was not associated with this gastric plasmacytoma.

Primary gastric plasmacytoma is rare, and most cases are not diagnosed until an advanced stage. Reports of cases at an early stage have been published by several groups [8, 9, 13, 14]. Ishido et al. previously reported on 5 cases of gastric plasmacytoma found among 38 cases with primary gastric malignant lymphomas [9]. They concluded that plasmacytoma might not be as rare in the stomach as elsewhere [8, 9, 19], and that it was necessary to differentiate plasmacytoma from reactive lymphoid cell hyperplasia or extranodal marginal B cell lymphoma of MALT type by means of plasma cell differentiation [8, 9].

There is only one other reported case similar to ours. Karakantzna et al. [12] reported that a mesenteric mass (10×5 cm), histologically demonstrating diffuse infiltration by plasma cells expressing kappa light chain and consistent with a diagnosis of extramedullary plasmacytoma, developed 27 years after the diagnosis of sarcoidosis. The concept of a sarcoidosis–lymphoma syndrome was proposed on the basis of various immunological features [1]. Brincker [1] suggested that lymphopenia and treatment with steroids are predisposing factors for the development of lymphoma. Masuda et al. [15] also reported a 65-year-old woman who was diagnosed with systemic sarcoidosis 15 years prior to the development of malignant lymphoma of the stomach. The relationship between sarcoidosis and lymphoma has not yet been defined; potential links remain controversial. We considered that the coexisting plasmacytoma and sarcoidosis in our case developed simultaneously.

Hypercalcaemia is common in adult T-cell leukaemia (ATL) and multiple myeloma, but very rare in malignant lymphoma or leukaemia. Hypercalcaemia in ATL was ascribed to the humoral hypercalcaemia of malignancy (HHM) [18], while hypercalcaemia in multiple myeloma was thought to be local osteolytic hypercalcaemia (LOH). Hypercalcaemia, which may be a prominent feature of sarcoidosis, is considered to be the result of increased absorption of intestinal calcium due to accelerated 1,25-dihydroxyvitamin D3 production by sarcoid granuloma [20, 21]. Hypercalcaemia in malignant disease without evidence of bone destruction is thought to be attributable to PTHrP production by malignant cells [22]. In this patient, after subtotal gastrectomy and administration of antimyeloma chemotherapy, the calcium, PTHrP, and C-PTHrP in serum normalized. Since the patient did not receive therapy for sarcoidosis, hypercalcaemia can be ascribed to PTHrP production by neoplastic plasma cells.

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