

Multiple gastric involvement by myeloid antigen CD13-positive non-secretory plasma cell leukaemia

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Summary. Gastrointestinal tract involvement is a rare complication of plasma cell neoplasia. We present a case of non-secretory type primary plasma cell leukaemia (PCL) with multiple gastric involvement. Dual surface antigen analysis of bone marrow cells revealed that atypical plasma cells coexpressed CD38 and myeloid antigen CD13. Upper gastrointestinal endoscopy disclosed multiple submucosal masses in the body of the stomach. Endoscopic biopsy specimens showed marked infiltration of atypical plasma cells consistent

with a diagnosis of gastric involvement by PCL. Since CD13 antigen is identical to aminopeptidase N, a membrane-bound glycoprotein thought to be involved in the process of tumour invasion, CD13 expression on neoplastic plasma cells may be related to the gastric involvement in this patient.

Keywords: plasma cell leukaemia, gastric involvement, CD13 antigen, aminopeptidase N.

Primary plasma cell leukaemia (PCL) is an unusual manifestation of multiple myeloma. Its incidence is estimated at 1–2% of patients with multiple myeloma (Kosmo & Gale, 1987). The disease is defined as a malignant proliferation of plasma cells involving the peripheral blood, accounting for >20% of the leucocytes or an absolute number exceeding $2 \times 10^9/l$ (Kosmo & Gale, 1987). Involvement of the gastrointestinal tract by plasma cell neoplasia is rare but may be a manifestation of multiple myeloma or extramedullary plasmacytoma (Carlson & Breen, 1986). Its association in PCL is quite uncommon (Sakai *et al.*, 1991). We describe a case of myeloid antigen CD13-positive non-secretory PCL in association with multiple gastric involvement.

CASE REPORT

A 49-year-old man was admitted to hospital in August 1993 because of anaemia and atypical cells in the peripheral blood. 8 months earlier he had been admitted to another hospital because of right putaminal haemorrhage and underwent craniotomy. On admission he was pale and had left

hemiparesis. Haematological findings were Hb 67 g/l; platelets $185 \times 10^9/l$; WBC $7.7 \times 10^9/l$ with 7% plasma cells. A bone marrow aspirate revealed marked hypercellularity, 85.5% atypical large plasma cells with abundant cytoplasm, prominent nucleoli and occasional multinucleated cells, and marked reticulin fibrosis. Subsequent bone marrow aspirates were dry tap and trephine biopsy confirmed secondary myelofibrosis. The cytoplasm of these plasma cells was positive for immunoglobulin (Ig)A by immunohistochemistry. The total serum protein was 64 g/l, and serum protein electrophoresis showed 80.9% albumin and 2.5% gamma-globulin. The serum Ig concentrations were: IgG 1.85 g/l, IgA 0.01 g/l, IgM 0.05 g/l, IgD <0.006 g/l and IgE <5000 U/l. No monoclonal Ig or Bence Jones protein was detected either in serum or $\times 50$ concentrated urine by immunoelectrophoresis. The serum beta-2-microglobulin was elevated to 0.02 g/l. Bone X-rays revealed no manifest osteolytic lesions but bone scintigraphy showed diffuse bony uptake. Abdominal echogram disclosed hepatosplenomegaly. 2 weeks after admission, plasma cells in the peripheral blood reached 39%, and the patient was diagnosed as having non-secretory IgA type PCL. Immunophenotyping of peripheral blood mononuclear cells suggested the coexpression of CD38 and myeloid antigen CD13 on leukaemic plasma cells even in the presence of monocyte contamination. This was confirmed later. Furthermore, Ig heavy chain gene rearrangement (JH),

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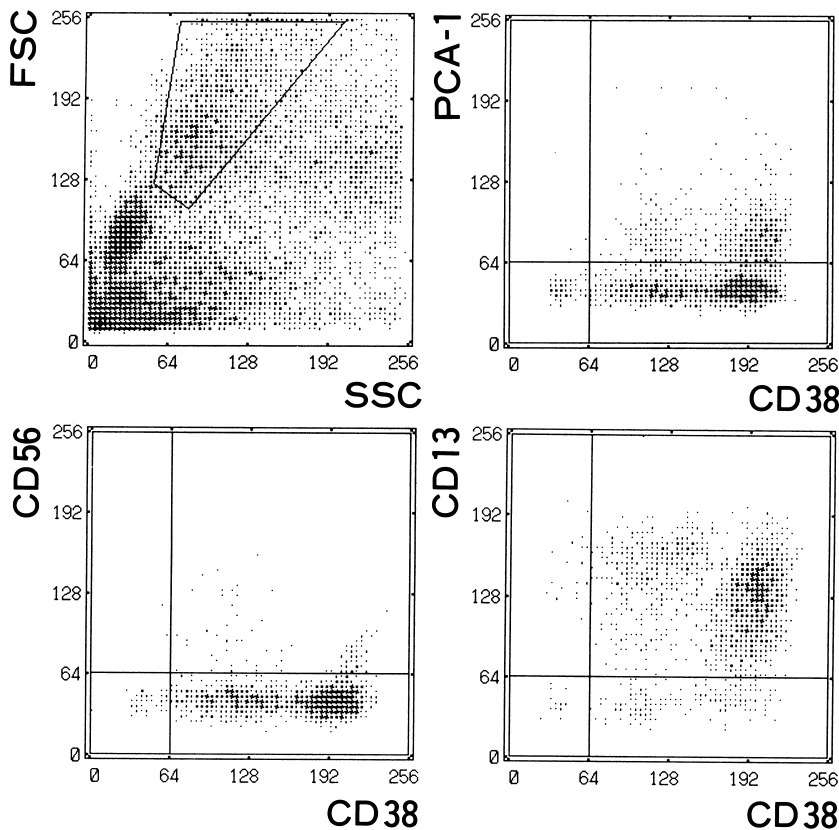


Fig 1. Coexpression of CD38 and CD13 antigen on marrow plasma cells. Dual surface antigen analysis was performed on 1 September 1994 using flow cytometry and monoclonal antibodies. CD38⁺CD13⁺ cells were 89.1% and CD38⁺PCA-1⁺ cells were 29.1%. CD38⁺ cells were negative for CD56 antigen. The monoclonal antibodies used were anti-CD13 (My-7), anti-CD56 (NKH-1) and anti-PCA-1 (Coulter Immunology, Hialeah, Fla.), and anti-CD38 (Immunotech, Marseille, France).

but no Ig light chain nor T-cell receptor-beta chain gene rearrangement, was found in peripheral blood mononuclear cells (data not shown).

The patient received a VMCP protocol (vincristine, melphalan, cyclophosphamide, prednisolone), followed by VMCAP (VMCP plus doxorubicin), VAD (vincristine, doxorubicin, dexamethasone) and VMD (vincristine, mitoxantrone, dexamethasone). These multiple courses of combination chemotherapy failed to induce complete remission in bone marrow, although plasma cells in the peripheral blood almost disappeared. In September 1994 a bone marrow aspirate was successful and immunophenotyping of bone marrow cells was performed. The immunophenotype of marrow plasma cells was CD38⁺PCA-1⁺CD13⁺CD56⁻CD54⁻CD44⁺. Other myelomonocytic antigens CD15, CD33 and CD14 were negative. Dual surface antigen analysis confirmed the coexpression of CD38 and CD13 antigen on neoplastic plasma cells (Fig 1).

Because of epigastric discomfort, upper gastrointestinal endoscopy was performed on 8 September 1994 and revealed multiple submucosal masses with redness in the body of the stomach. There were irregular-shaped ulcerations on the surface of some gastric masses. Endoscopic biopsy disclosed marked infiltration of atypical plasma cells consistent with a diagnosis of gastric involvement by PCL. Immunohistochemical study of gastric masses showed negative Ig staining. The patient was treated with H₂ receptor antagonists. In October daily administration of oral etoposide was initiated but without success. In December the patient died of cerebral

haemorrhage and renal insufficiency. Autopsy was not performed. Post-mortem bone marrow biopsy revealed diffuse infiltration of atypical plasma cells and reduction of reticular fibrosis.

DISCUSSION

We presented a patient with non-secretory PCL who exhibited uncommon complications: multiple gastric involvement, myeloid antigen CD13 positivity and secondary myelofibrosis. Gastrointestinal tract involvement by plasma cell neoplasia is rare but may be a manifestation of multiple myeloma or extramedullary plasmacytoma (Carlson & Breen, 1986). Primary extramedullary plasmacytoma of the gastrointestinal tract represents <5% of all extramedullary plasmacytomas (Wiltshaw, 1976). Any segment of the gastrointestinal tract may be the site of plasma cell infiltration. The small bowel is the most commonly involved site, followed by stomach, colon and oesophagus (Pimentel & Van Stolk, 1993). Gastric involvement by PCL is quite uncommon, and only a few cases have been reported (Sakai *et al*, 1991).

Malignant plasma cells may coexpress comparable plasma cell antigens and early B-cell antigens as well as myelomonocytic antigens, and its prognostic importance has been described (Durie & Grogan, 1985; Grogan *et al*, 1989; Drach *et al*, 1991). This leads to the hypothesis of pluripotential stem cell involvement in the pathogenesis of multiple myeloma (Barlogie *et al*, 1989). However, Terstappen *et al* (1990) have shown that myeloid-specific antigens such as CD33 and CD13

are expressed on a proportion of plasma cells in normal human bone marrow. Recent studies indicate that a natural killer cell associated antigen (CD56), a molecule identical to neural cell adhesion molecule, is expressed by plasma cells from a subset of multiple myeloma (Van Camp *et al*, 1990; Drach *et al*, 1991). CD56-negative myeloma patients have predominantly aggressive disease and their plasma cells frequently exhibit early B-cell and myeloid antigens. Malignant plasma cells from our patient showed myeloid antigen CD13 expression but no CD56 antigen (Fig 1), and the patient was resistant to multiple courses of chemotherapy.

CD13 antigen is expressed by committed granulocyte-monocyte progenitors (CFU-GM), cells of the granulocytic and monocytic lineages at all morphologically distinct stages of differentiation, and leukaemic blasts of acute myeloid leukaemia (Shipp & Look, 1993). The CD13 cDNA sequence has been found to be identical to that of aminopeptidase N (EC 3.4.11.2), a membrane-bound glycoprotein expressed by the brush borders of the small intestine and renal tubules (Look *et al*, 1989). It also serves as the major receptor for an enteropathogenic coronavirus, transmissible gastroenteritis virus (Shipp & Look, 1993). Furthermore, specific inhibitors or antibodies of aminopeptidase N have been shown to inhibit the penetration of metastatic melanoma cells *in vitro* (Menrad *et al*, 1993), indicating that aminopeptidase N plays a role in the process of tumour invasion. These findings suggest that since gastric involvement by PCL is quite uncommon, CD13 expression on neoplastic plasma cells may be related to gastric involvement in this patient.

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