Plasmablastic lymphoma of the stomach. A case report

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ABSTRACT

We report the case of a 53 year-old woman with a gastric tumor showing morphological, phenotypical and molecular features of a plasmablastic lymphoma, a recently recognized subtype of diffuse large B-cell lymphoma. The tumor was composed of plasmablast-like cells, lacked CD45 and B-cell associated antigens, expressed the plasma cell-associated antigen CD38, and showed clonally rearranged IgH genes in the absence of bcl-2 and bcl-6 genes rearrangement.

Key words: plasmablastic lymphoma, stomach, immunophenotype, molecular analysis

The stomach is the most common site of origin of extranodal lymphomas.1 Most of the gastric lymphomas develop from the acquired mucosa-associated lymphoid tissue (MALT),2 and are therefore termed MALT lymphomas (extranodal marginal zone B-cell lymphoma according to the REAL classification).3 They are divided into low-grade and high-grade tumors with a low-grade component. Nevertheless, since a minority of high-grade tumors does not show any low-grade component, the existence of truly primitive gastric diffuse large cell B-lymphomas (DLBCL) is accepted. In 1992 Stein and Dallenbach coined the term plasmablastic lymphoma for rare DLBCL (1.5% of all nodal non-Hodgkin lymphomas) showing the morphological features of immunoblastic lymphoma with plasmacytic differentiation and phenotypical properties of plasmacytoma (CD45 negative, B-cell antigens negative, immunoglobulin positive with light chain restriction, and up to 20% of cytokeratin-expressing cells4). More recently, Delecluse et al. have reported that lymphomas with similar morphological and phenotypical features may develop in the oral cavity of HIV-infected patients.5 We describe the case of a non-immunocompromized patient with a gastric tumor showing morphological, phenotypical and molecular features of plasmablastic lymphoma; so far, only one other case with these features has been described as arising in the stomach.6

Case report

A 53 year-old woman complaining of epigastric distension was admitted to the Emergency Room of the Ospedale Maggiore of Milan. The patient had suffered for ten days from postprandial fullness, left upper quadrant pain and hypochondria with deep asthenia; moreover, she reported a slight fever in the evening, tachycardia and dyspnea. During physical examination, cutaneous pallor was evident and a large abdominal mass in epigastrium was palpable. Blood count showed severe microcytic anemia; serologic test was negative for HIV infection. The electrophoretic pattern of serum proteins was normal. A gastroscopy showed a large gastric polypoid mass from which biopsies were taken. The morphology of the gastric biopsy was in keeping with a high-grade gastric lymphoma. A subtotal gastrectomy and a gastro-jejunal termino-lateral anastomosis were done; 30 centimeters of transverse colon, firmly adherent to the stomach, were also removed. The gastric specimen showed an ulcerating bulky-polypoid large neoplasm measuring 25 centimeters in diameter. Histologically, the tumor was composed of large cells with peripherally located nuclei, one or more basophilic central nucleoli, and abundant strongly basophilic cytoplasm, often containing pale vacuoles, intermingled with plasmablasts (Figure 1A and 1B). Mitotic rate was high (30×10 HPF) and diffuse areas of necrosis were detectable. The normal frame of the gastric mucosa was effaced, without formation of lympho-epithelial lesions. The tumor infiltrated the full thickness of the gastric wall, the adipose tissue of the stomach and transverse colon; the perigastric lymph nodes were free of lymphoma (stage III according to Shimodaira et al.7). Despite extensive sampling, a low-grade component was undetectable. The uninvolved mucosa showed mild chronic non-follicular gastritis. Helicobacter pylori micro-organisms were not detected, neither by light microscopy with
Giems stain, nor with antibodies recognizing Helicobacter-associated antigens. The phenotype was obtained by means of immunohistochemistry (ABC method) and flow cytometry: tumoral cells did not express leukocyte common (LCA), T-cell (CD3, CD5, CD43 and CD45RO) and CD10 antigens. Moreover, they almost completely lacked the B-cell associated antigens CD19, CD20 (Figure 1C) and CD79a, while strongly expressed CD38. Likewise, the neoplastic cells proved to be unreactive to the anti-CD56 antibody. On the other hand, diffuse cytoplasmic IgM and J-chain expression, associated with light chain restriction was detected. A few cells also showed immunoreactivity for antibodies raised against EMA (Figure 1D) and cytokeratin. Moreover, most of them strongly expressed bcl-2 protein, whereas p53 and bcl-6 antigens were lacking. The proliferative rate, as detected by MIB-1 antibody, was about 50%. Molecular analysis was performed as previously described. Southern blot analysis using the JH probe to hybridize EcoRI- and HindIII-digested DNA showed a monoclonal pattern of IgH gene rearrangement. Absence of rearrangement of the bcl-1, bcl-2 and bcl-6 loci was observed in Southern blot analysis. PCR/SSCP analysis of the exons 5 through 9 of the p53 tumor suppressor gene did not detect changes in the normal migrating pattern. Since no lymphoadenopathy was detectable by means of CT scans and ultrasonography of the abdomen, and the bone marrow and liver biopsies were free of lymphoma at histological evaluation, the patient was staged as IE. She was treated with ProMACE-cytaBOM regimen for six courses and is alive and well and free of disease 19 months after diagnosis.

Discussion

Plasmablastic lymphomas are diffuse large-cell tumours composed by plasmablast-like cells which lack CD20 and CD45, and diffusely express plasma cell-associated antigens. Stein and Dallenbach found that this type of tumor accounts for about 1.5% of nodal non-Hodgkin lymphomas. More recently, Delecluse et al. have reported a series of 16 plasmablastic lymphomas primitively arising in the oral mucosa of HIV-infected patients.

We here describe a case of a tumor with morphological and phenotypical properties of a plasmablastic lymphoma, arising in the stomach of a non-immunocompromized patient. It strikingly dif-

Figure 1.
A: Diffuse proliferation of large cells effacing the normal frame of the gastric wall (hematoxylin-eosin, ×32).
B: The tumor is composed of large cells with peripherally located nuclei, one or more basophilic central nucleoli, and abundant strongly basophilic cytoplasm containing pale vacuoles, intermingled with plasmablasts (arrowheads) and multinucleated giant cells (Giems; ×200).
C: A single cell immunoreactive to anti-CD20 antibody: the overwhelming majority of the tumor is unreactive (ABC method, haematoxylin counterstain, ×80).
D: A few tumor cells are stained with the anti-EMA antibody (ABC method, hematoxylin counterstain, ×80).
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Differentiates from high-grade MALT lymphomas for the absence of a low grade component as well as of any sign of Helicobacter pylori infection, the diffuse plasmablastic differentiation, and the lack of CD45 and CD20 in the presence of strong CD38 expression. Likewise, De Mascarel et al. reported the case of a patient with a gastric large cell lymphoma composed by plasmablasts, which expressed cytokeratin and monotypic IgA but no leukocyte common antigen. These data suggest that plasmablastic lymphoma may develop in extranodal sites different from oral mucosa, and it is not necessarily associated with HIV infection.

The pathogenesis of plasmablastic lymphoma remains to be elucidated: Delecluse et al. found bcl-2 protein overexpression only in a fraction of their cases, and no evidence of bcl-2 gene rearrangement; since all the cases also lacked bcl-6 expression, they concluded that plasmablastic lymphoma probably does not arise from the follicular center cells. In keeping with these data, even the present case did not show evidence of bcl-2 and bcl-6 genes rearrangement.

Clinical features of intestinal lymphomas have been recently reported in this journal. The possibility that plasmablastic lymphoma may develop in the stomach should be kept in mind in order to avoid misdiagnosis, especially on small biopptic specimens: as a matter of fact, the absence of leukocyte-common and B- and T-cell associated antigens, as well as the expression of cytokeratin and EMA might suggest the diagnosis of poorly differentiated carcinoma. For this reason, it is worth noting that parietal cell carcinoma of the stomach (which expresses cytokeratin and lacks LCA) shows a lymphoma-like histologic appearance. These data suggest the usefulness of antibodies which recognize plasma cell-associated antigens, as well as light and heavy immunoglobulin chains, which are almost invariably expressed by plasmablastic lymphoma.

Contributions and Acknowledgments

GP was responsible for the conception of the study, interpretation, and the writing of the paper; GG collected the clinical data and contributed to the execution of the study; LE did the immunohistochemical stainings; LB was the principal clinician involved, did the cytofluorimetric analysis, and was responsible for the ethical approval; AN did the molecular analysis; RB was responsible for the design of the study and for critical reviewing of the data.

All the authors meet the Vancouver definition of authorship. The first two names were reserved to the authors who concepted the study and contributed to its execution (GP, GG). The third name was given to the author who mainly did laboratory analysis (LE). The order of the last three names reflect the degree of involvement in critical reviewing of the data.

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Disclosures

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