Plasma Cell Granuloma of the Sigmoid Colon Associated with Diverticular Disease and Accompanying IgM-Type Monoclonal Gammopathy

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Abstract

Plasma cell granuloma is a pseudoneoplastic lesion composed of reactive plasma cells of a polyclonal nature and must be distinguished from plasmacytoma. We report a case of plasma cell granuloma in the sigmoid colon associated with diverticulosis. In this case, the lesion consisted of multiple submucosal tumors with prominent infiltration of polyclonal plasma cells. Although the patient exhibited IgM-type monoclonal gammopathy, the expression of a monoclonal immunoglobulin was not detected in the sigmoid colonic lesion, but in the bone marrow cells. Plasma cell granuloma in the lower alimentary tract has been rarely reported. Recurrent inflammatory process with diverticular disease was considered as a pathogenesis of the pseudoneoplasm and a possible cause of monoclonal proliferation of IgM-producing lymphoid cells in this case.

Key words: plasma cell granuloma, sigmoid colon, monoclonal gammopathy

Introduction

Plasma cell granuloma is a non-malignant lesion composed of reactive plasma cells with a polyclonal nature and must be distinguished from plasmacytoma, which presents a monoclonal proliferation of plasma cells (1). The lesion is most frequently reported in the lung and bronchus, and the occurrence in the lower gastrointestinal tract is rare. Herein, we report a case of plasma cell granuloma involving the sigmoid colon associated with diverticular disease. As the patient also presented a monoclonal gammopathy, the clonality was analyzed in the sigmoid colonic lesion and the bone marrow cells.

Case Report

An 82-year-old woman was admitted because of lower abdominal pain and melena. She had a ten-year history of colonic diverticular disease with recurrent diverticulitis as well as hypertension, diabetes mellitus, bronchial asthma and old tuberculosis. Routine laboratory test presented no remarkable abnormalities except for slight anemia (hemoglobin 11.1 g/dL) and hypoalbuminemia (albumin 3.2 g/dL). Blood examination showed slight elevation of serum IgM (645 mg/dL) without decrease of immunoglobulin level of the other classes. Serum electrophoresis presented an M-peak, which was ascertained as IgM-kappa type monoclonal protein by immunofixation study (Fig. 1). A radiological examination revealed the tumor lesions in the sigmoid colon and the fistula formation in the descending colon, in addition to the multiple diverticular formations (Fig. 2). Computed tomography (CT) scan revealed the thickness of the sigmoid colonic wall, but no abnormalities or mass lesions in other sites were identified.

Colonoscopy showed the multiple submucosal tumors in the sigmoid colon (Fig. 3). Pathological examination of endoscopic biopsied specimen from a tumor in the sigmoid co-
Figure 1. Detection of the monoclonal immunoglobulin. A) Serum electrophoresis. The arrow shows the M-peak. B) Serum immunofixation. The arrow indicates the M-band by the IgM-kappa M-protein.

Figure 2. Radiological examination using diatrizoate meglumine and diatrizoate sodium (Gastrografin®, Bracco Diagnostics, Inc., Princeton, NJ) showing diverticular disease and a stricture involving the sigmoid colon.

Figure 3. Colonoscopy showing multiple submucosal tumor lesions in the sigmoid colon.

Ion presented the marked proliferation of mature plasma cells in an edematous and highly vascular granulomatous matrix (Fig. 4A). The plasma cell nature of the cellular infiltrate was confirmed immunohistochemically by CD138 positivity (Fig. 4B). These plasma cells were considered to be of polyclonal nature, as there was no restriction for IgG, IgA and IgM heavy chains and kappa and lambda chains by intracellular immunostaining (Figs. 4C, 4D). A diagnosis of plasma cell granuloma was made based on these histological and immunohistochemical findings.

Bone marrow aspirate presented a normal number of plasma cells (1.0%) and no infiltration of lymphoplasmacytic or lymphoma cells. After informed consent, RNA was extracted from cells in the sigmoid colonic lesion and bone marrow mononuclear cells and was subjected to reverse-transcription polymerase chain reaction (RT-PCR) analysis for the expression of the rearranged immunoglobulin (Ig) heavy chain gene. As shown in Fig. 5, a monoclonal band was detected in the bone marrow, but not in the sigmoid colonic lesion, using primers amplifying the third complementarity determining region (CDR3) (2). Thus, it was confirmed that the sigmoid colonic lesion was not a producing site of the monoclonal Ig. As no tumors other than the colonic lesion or symptoms attributable to M-protein were identified, a diagnosis of IgM monoclonal gammopathy of undetermined significance (MGUS) was made according to the criteria (3).

Surgical resection of the lesion was not performed as her pulmonary function was reduced because of old tuberculosis and bronchial asthma. The patient is doing well for 2 years after the diagnosis except for two episodes of melena which recovered by conservative treatment. Follow-up CT scan showed slight improvement of the thickness of the sigmoid colonic wall. Serum IgM level was not significantly changed to date.

Discussion

Plasma cell granuloma, also called inflammatory pseudotumor or inflammatory myofibroblastic tumor, is a rare non-neoplastic lesion characterized by a proliferation of inflammatory cells with a predominance of mature polyclonal plasma cells in a fibrovascular background (1). This lesion may mimic true neoplasm and should be distinguished from the malignant plasma cell tumor, plasmacytoma, which presents as a monoclonal plasma cell proliferation. Immunohistochemical study staining intracellular Igs, especially kappa and lambda light chains, is necessary to confirm the polyclonal nature of plasma cells.

Plasma cell granuloma is most frequently reported in the lung and bronchus, but rarely found in extrapulmonary sites. To our knowledge, fourteen cases with plasma cell granu-
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Figure 4. Histology of the sigmoid colonic lesion. A: Prominent infiltration of mature plasma cells (Hematoxylin and Eosin staining; ×400). B-D: Immunohistochemical staining showing a positive reaction for CD138 (B), kappa (C) and lambda (D) chains (×400).

Figure 5. Reverse-transcription polymerase chain reaction (RT-PCR) analysis. RNA was extracted from sigmoid colonic lesion and bone marrow mononuclear cells in this case and reverse transcribed. cDNA was amplified using the VH-consensus primer (5'-CTGTCGACACGGCCGTGTATTACTGTG-3') corresponding to 3' end of FR3 of VH and the JH-consensus primer (5'-AATCAGAGGAGACGGTGACC-3') and electrophoresed through 4.0% agarose gel. These primers were designed to amplify CDR3 of the rearranged IgH according to the previous report (2) with slight modifications. cDNA was also amplified using GAPDH primers. RNA from CD138-positive bone marrow plasma cells in a patient with multiple myeloma was similarly analyzed. Monoclonal bands (indicated by arrow) were detected in the myeloma cells (lane 1), and in the patient’s bone marrow cells (lane 3), but not in the sigmoid colonic lesion (lane 2).

Plasmacytoma, inflammatory pseudotumor or inflammatory myofibroblastic tumor presenting involvement in the large intestine have been reported to date in the English language literature (4-14). The clinical behaviors in these cases were various (Table 1). In six adult cases, four presented intraluminal polypoid or spherical tumors, two of which caused the colonic obstruction. In the present case, the lesion did not present a solitary mass, but multiple submucosal tumors in a segment of diverticular disease with stricture formation accompanying bleeding.

Although the exact pathogenesis of plasma cell granuloma remains uncertain, it is considered to be inflammatory in nature. In this case, chronic inflammatory stimulation by diverticulitis would lead to the formation of the lesion. Two cases with inflammatory pseudotumor in the urinary bladder associated with sigmoid colonic diverticulitis were reported (8, 15). Formation of invasive pseudotumors induced by chronic inflammation should be recognized as a complication with diverticular disease in the high prevalence of the disease in the population.

In the present case, plasmacytoma was initially suspected based on the predominant plasma cell infiltration and the presence of monoclonal gammapathy. However, the immunohistochemical study showed the polyclonal nature of the infiltrating plasma cells and the RT-PCR analysis confirmed that the monoclonal Ig was expressed in the bone marrow cells, but not in the sigmoid colonic lesion. In addition to the serum monoclonal IgM concentration, the absence of symptoms attributable to tumor infiltration or monoclonal protein led us to the diagnosis of IgM MGUS (3). Produc-
A high volume of inflammatory cytokines such as interleukin (IL)-1 beta and IL-6 have been demonstrated in a case with plasma cell granuloma in the lung with systemic symptoms (16). In the present case, the persistent production of cytokines by inflammatory stimulation associated with diverticular disease might have induced the systemic monoclonal proliferation of IgM-producing B-lymphoid cells as well as the reactive infiltration of polyclonal plasma cells in the lesion, although no treatment for monoclonal gammopathy was necessary. This case emphasized the significance of clonality analysis of the plasma cell proliferative lesion to attain an accurate diagnosis and avoid unnecessary radiotherapy or chemotherapy.

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References


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