Extranodal Lymphoplasmacytoid Lymphoma (Immunocytoma) Presenting as Small Intestinal Obstruction

A Case Report and Review of the Literature

Monica A. Recine, MD; Maria T. Perez, MD; Beria Cabello-Inchausti, MD; Rogerio C. Lilenbaum, MD; Morton J. Robinson, MD

A 57-year-old woman presented with intermittent symptoms of intestinal obstruction. Workup provided nondiagnostic radiologic studies. An exploratory laparotomy revealed a segmental dilatation in the proximal ileum, which showed diffuse thickening of the intestinal wall. Microscopic examination of the affected area disclosed a diffuse transmural infiltrate composed of small lymphocytes, mature plasma cells, and lymphoplasmacytoid cells in different stages of maturation associated with extracellular periodic acid-Schiff–positive material. In addition, serum protein electrophoresis showed a monoclonal immunoglobulin M κ paraprotein. Postoperative workup did not demonstrate evidence of systemic involvement. The morphologic features and immunohistochemical and molecular analyses were consistent with lymphoplasmacytoid lymphoma (immunocytoma). We report an unusual case of primary extranodal immunocytoma involving the small intestine and discuss its clinicopathologic features.

(Arch Pathol Lab Med. 2001;125:677–679)

Lymphoplasmacytic/plasmacytoid lymphomas (immunocytomas) are low-grade small cell lymphomas with plasmacytic/plasmacytoid differentiation with predominant nodal involvement. The frequent association of this tumor with hyperviscosity symptoms due to the presence of monoclonal serum gammopathy, usually of the immunoglobulin M type, is clinically important. Although the plasmacytic differentiation is not a unique feature of the immunocytomas and can be seen in other low-grade lymphomas, including mucosa-associated lymphoid tissue lymphomas and follicular lymphoma, the differential diagnosis has important clinical implications.

Primary extranodal lymphoplasmacytoid lymphoma occurs less commonly than its nodal counterpart. To our knowledge, involvement of the small intestine as a primary and only site of disease has not been reported previously in the English literature.

REPORT OF A CASE

A 57-year-old white woman presented with a 15-month history of recurrent abdominal pain associated with nausea, vomiting, and a 4.5-kg weight loss. Upper gastrointestinal and small intestinal radiographic series demonstrated a normal mucosal pattern with no evidence of intrinsic lesions or external mass effect. Computed tomographic scan of the abdomen was unremarkable. An exploratory laparotomy revealed a thickened and nodular segment of ileum and adjacent mesentery. An intraoperative pathologic consultation disclosed a lymphoproliferative process involving the intestinal wall. The patient had an uncomplicated recovery. A significant postoperative laboratory finding was the presence of a small monoclonal band identified as IgM-k by immunofixation. Immediate postoperative follow-up with radiologic studies and bilateral bone marrow biopsies did not reveal systemic involvement. No additional therapy was given. Subsequent serum protein immunofixations revealed a normal protein profile without evidence of monoclonal gammopathy. There was no evidence of recurrent local or systemic disease 17 months after surgery.

MATERIALS AND METHODS

Four-micrometer-thick, formalin-fixed, paraffin-embedded tissue sections were stained with hematoxylin-eosin, periodic acid–Schiff, Giemsa, Congo red, and crystal violet for light microscopic examination. Additional sections were stained with a series of monoclonal antibodies using the standard avidin-biotin complex immunoperoxidase technique directed against CD20 (L26, 1:100, Dako Corporation, Carpinteria, Calif), CD5 (1:10, Novocastra Laboratories Ltd, Newcastle Upon Tyne, United Kingdom), IgM (Cell Marque, Austin, Tex), and κ and λ light chain (Cell Marque) cell antigens. Additionally, mononuclear cell suspensions of the tumor were analyzed by flow cytometry immunophenotyping using the Becton-Dickinson (San Jose, Calif) FACS Calibur with a standard lymphoma panel. Gene rearrangement studies by polymerase chain reaction were performed on paraffin-embedded tissue using primers directed at the V_{\text{\gamma}} and J_{\text{\gamma}} regions for the T-cell receptor γ chain and the V_{\text{\alpha}} and J_{\text{\alpha}} regions of the B-cell immunoglobulin heavy-chain genes.

PATHOLOGIC FINDINGS

The resected specimen consisted of a 30-cm-long segment of small intestine, which showed an 8-cm fusiform...
dilatation in the midportion of the intestinal segment accompanied by indurated mesenteric fat. Cut section of the dilated area revealed marked thickening of the intestinal wall with attenuation of the mucosal folds and a “fish-flesh” appearance.

Histologic examination of the area of thickening showed a diffuse transmural infiltrate composed of small lymphocytes, some mature plasma cells, and numerous plasmacytoid lymphocytes with occasional Dutcher bodies (Figures 1 and 2), which extended into the mesentery fat. Neither lymphoepithelial lesions nor reactive lymphoid follicles showing colonization were present. Pools of extracellular periodic acid-Schiff–positive material, which were negative for crystal violet and Congo red, were present among the neoplastic cells (Figure 3). Immunohistochemical stains showed strong positivity of the tumor cells with CD20, confirming the B-cell differentiation of this lymphoma. In addition, numerous plasmacytoid lymphocytes showed strong cytoplasmic staining for IgM and κ light chains and negative reaction for λ light chains. CD5 expression was not significant. Flow cytometric immunophenotyping revealed predominance of B cells expressing CD19, CD20, CD22, and HLA-DR and lacking expression of CD5 and CD10. The expression of CD38 was 25.56%. Gene rearrangement studies also supported a monoclonal B-cell process with heavy-chain rearrangement. Based on these findings, this lymphoma was classified as lymphoplasmacytoid lymphoma (immunocytoma).

COMMENT

Lymphoplasmacytic/plasmacytoid lymphoma (immunocytoma) is a low-grade B-cell lymphoma characterized by a proliferation of small and plasmacytoid lymphocytes as well as plasma cells, containing monoclonal intracytoplasmic immunoglobulins. The term immunocytoma from the Kiel classification has been mainly used in the European literature and is synonymous with small lymphocytic-plasmacytoid lymphoma in the Working Formulation and with lymphoplasmacytoid lymphoma in the revised European-American Lymphoma (REAL) classification.

In the original Kiel classification, this lymphoma was divided into 3 subtypes: (a) lymphoplasmacytic type, characterized by a predominance of mature plasma cells; (b) lymphoplasmacytoid type, in which plasmacytoid lymphocytes predominate; and (c) polymorphic type, with a considerable number of immunoblasts. In the updated Kiel classification, the polymorphic subtype is no longer recognized.

More recently, lymphoplasmacytoid lymphoma has been defined by the REAL classification as a low-grade B-cell lymphoma composed of small lymphocytes, lymphoplasmacytoid lymphocytes, and mature plasma cells and lacking features of other low-grade B-cell neoplasms. This entity accounts for approximately 5% of all non-Hodgkin lymphomas and occurs in the same age group population as B-cell chronic lymphocytic leukemia, with males being affected slightly more frequently than females.

Lymph node involvement is seen more commonly than primary extranodal presentation. In most patients, the lymphadenopathy develops slowly and affects many regions. Occasionally, splenomegaly is the first sign of disease. This lymphoma is often associated with a monoclonal paraprotein, frequently of the IgM type, which may cause hyperviscosity symptoms (Waldenström macroglobulinemia).

Primary extranodal involvement has been described in a variety of tissues, including skin, lung, eye, urinary bladder, and prostate. In 1981, Lennert published a study based on a total of 181 biopsies of extranodal immunocytoma and reported the following distribution:
skin, 22%; eye, 21%; gastrointestinal tract, 20%; and other sites, 37%. The distribution within the gastrointestinal tract was not specified in that study. Although case reports of immunocytoma involving rectum and stomach have been documented, to our knowledge, no previous cases of primary immunocytoma of the small intestine as the only site of disease have been reported in the English literature.

From the pathologic standpoint, these lymphomas are characterized by a diffuse proliferation of small lymphocytes, plasmacytoid lymphocytes, and plasma cells. It is not unusual to encounter variable amounts of extracellular periodic acid-Schiff-positive material representing pools of Ig. Occasionally, the lymphoplasmacytoid lymphocytes may contain intranuclear pseudoinclusions with similar tinctorial qualities (Dutcher bodies). The differential diagnosis for this entity in the gastrointestinal tract includes other low-grade lymphomas, especially mucosa-associated lymphoid tissue lymphoma, which is characterized by a diffuse lymphoid infiltrate composed of centrocyte-like cells, monocytoid B cells, and small lymphocytes. One third of the cases show plasma cell differentiation. Lymphoepithelial lesions and reactive lymphoid follicles showing follicular colonization, almost constant features of mucosa-associated lymphoid tissue lymphoma, especially in the stomach, are not present in lymphoplasmacytoid lymphomas. Follicular center lymphoma rarely involves the gastrointestinal tract, but may occur in the small intestine, especially in the terminal ileum. It is characterized by a proliferation of cleaved and noncleaved follicular center cells growing in follicular (nodular) or diffuse patterns. Plasmacytic differentiation is seen in the minority of cases. Although the differentiation of lymphoplasmacytoid lymphoma from other low-grade lymphomas is based predominantly on morphologic criteria, immunohistochemical studies may contribute to the diagnosis. Lymphoplasmacytoid lymphoma is a CD10-negative, monoclonal B-cell proliferation demonstrated by the expression of pan-B-cell markers (CD19, CD20, and CD22). Positive reaction for CD5 has been reported in most cases of the lymphoplasmacytoid subtype, whereas reactivity for CD5 in the plasmacytoid variant is usually negative. The lymphoplasmacytoid lymphocytes contain monocytoid cytoplasmic Ig of the same isotype as the surface Ig expressed by the small lymphocytes. Mucosa-associated lymphoid tissue lymphomas are usually CD5-negative, CD10-negative monoclonal B-cell neoplasms. Follicular lymphomas, on the other hand, express CD10 but lack CD5 expression.

It is important to make the pathologic distinction from other low-grade B-cell lymphomas because lymphoplasmacytoid lymphoma carries different clinical implications. Because of the high association of this lymphoma with monoclonal gammopathies, and in particular with Waldenström macroglobulinemia, its diagnosis should alert the clinician to the possibility of serum paraproteinemia, with or without clinically evident hyperviscosity symptoms. Another important clinical association is that this type of lymphoma may develop in patients with longstanding autoimmune disease. In addition, lymphoplasmacytoid lymphoma (immunocytoma) is considered by some authors to be a more aggressive lymphoma compared to other low-grade lymphomas (eg, chronic lymphocytic lymphoma), since it often presents with more rapid lymph node enlargement, higher incidence of constitutional symptoms, and marked anemia, which result in the need for earlier therapy. The 5-year survival rate has been reported to be 59%. However, localized extranodal disease seems to have a more favorable prognosis and may be treated conservatively with surgery alone, as in our case.

References