IgG Lymphoplasmacytic Intestinal Lymphoma: A Case Report

Heidrun Z. Rotterdam
Sheldon C. Sommers

Follow this and additional works at: https://scholarlycommons.henryford.com/hfhmedjournal

Part of the Life Sciences Commons, Medical Specialties Commons, and the Public Health Commons

Recommended Citation
Available at: https://scholarlycommons.henryford.com/hfhmedjournal/vol27/iss3/5

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.
IgG Lymphoplasmycatic Intestinal Lymphoma: A Case Report
Heidrun Z. Rotterdam, MD* and Sheldon C. Sommers, MD*

We describe a rare case of a localized primary small intestinal lymphoma with features of both the Mediterranean and the Western type. This case demonstrates the need to regard intestinal lymphoma as a spectrum of diseases with the Mediterranean and the Western types at opposite ends and many variants in between. The role of the plasma cell infiltrate has been interpreted as reactive as well as neoplastic. In our case, both lymphocytic and plasmacytic proliferations spread widely in the intestinal submucosa, extended into muscularis propria and subserosal fat, and involved mesenteric lymph nodes. Direct immunofluorescence demonstrated IgG-kappa both in plasma cells and within the lymphocytic infiltrate. We conclude that both cell types were neoplastic and the lymphoma was of a mixed lymphocytic-plasmacytic type. We also discuss the possibility of a common B cell origin for both cell types and the significance of the production of different immunoglobulins by different intestinal lymphomas.

Primary intestinal lymphoma is divided into two main groups on the basis of pathologic and clinical features (1-6). The Mediterranean type (MTL) is predominantly but not exclusively found in young Arabs or Jews from North Africa or the Middle East. It presents most frequently with malabsorption and abdominal pain and is characterized pathologically by diffuse or multifocal involvement of the small intestine by lymphoma and a pronounced plasma cell infiltrate. It may be associated with the production of excessive amounts of IgA heavy chains, which can be demonstrated in the circulation in 36% of cases (alpha chain disease) (5). The more common Western type (WTL) often causes obstructive symptoms, involves mainly the distal small intestine, forms a localized mass, and shows no plasma cell infiltrate on histological examination. An association with alpha chain disease has not been reported.

Although the significance of the plasma cell infiltrate in the MTL is not clear, it has been variously interpreted as an inflammatory process (3) or as the premalignant phase of lymphoma (2). Its confinement to the mucosa and submucosa without infiltration of the muscularis propria, the absence of cytologic atypia, and the lack of gross tumefaction all favor a benign reactive process. The theory of premalignancy gains support from the observation that plasmacytic infiltration often precedes the development of lymphoma (3) and from the histologic finding of transitional forms between plasma cells and lymphoma cells, as expressed in such hybrid terms as “plasmacytoid histiocyte” (2) and “plasmacytic reticulum cell sarcoma” (7).

If the plasma cell infiltrate were to develop toward malignant neoplasia, the resulting tumor would be a plasmacytoma. However, the most commonly reported histologic type in MTL has been histiocytic lymphoma (2), a “pleomorphic lymphoma” that cannot be classified further (3), or an immunoblastic lymphoma (6). When 125 cases of primary intestinal lymphoma in England were reclassified, a surprising 39% incidence of plasmacytomas was found, most of which had previously been classified as Hodgkin’s disease or reticulum cell sarcoma (8).

Significantly, histiocytic lymphomas of nodal origin are also being reclassified by cytochemical, histochemical and immunohistochemical studies (9,10) that show most to be derived from B lymphocytes. Since plasma cells have the same origin, this reclassification of some intestinal histiocytic lymphomas as plasmacytic tumors is not surprising. Investigators in Iraq, where intestinal lymphoma is common, have also interpreted many lymphomatous proliferations as plasmacytic and suggested the term “lymphoplasmacytic lymphoma” (11).

Recently, we studied a case of intestinal lymphoma with marked plasma cell infiltration by immunofluorescence. Our findings support the notion that the plasma cells are neoplastic and an intrinsic part of the lymphomatous process.
Case Report

Clinical history
A 55-year-old, well-nourished North American Jewish man was hospitalized for recurrent abdominal pain that had become increasingly frequent during the past three years. An upper GI series three years earlier had shown an ileal stricture, interpreted as ischemic, and a repeat X-ray study six months later had been interpreted as normal. There was no history of travel to Mediterranean countries. On admission, a small bowel X-ray series demonstrated segmental narrowing and thickening of mucosal folds of the distal ileum, but there was no evidence of malabsorption. All laboratory data were normal. Serum protein electrophoresis yielded high normal values for alpha 2 and beta components, normal gamma globulins, and total serum protein. Immuno-electrophoresis was not done.

A laparotomy revealed segmental thickening and rigidity of the distal ileum. Draining mesenteric lymph nodes were enlarged. Peri-aortic nodes appeared normal. Fifty cm of small intestine and attached mesentery were resected. Serum immunoelectrophoresis showed normal values for IgG and IgA and slightly elevated IgM (390 mg/dl; normal: 75-270 mg/dl).

Pathologic findings
Gross examination revealed a rigid 5 cm long segment of ileum that measured 1 cm in thickness as compared to 0.3 cm thickness of the remaining intestinal wall (Fig. 1). Firm gray tissue distended the submucosa. The mucosa was flattened but intact (Fig. 2). Enlarged mesenteric lymph nodes were measured up to 1.5 cm in diameter. On microscopic examination mucosa and submucosa were densely infiltrated by lymphocytes and plasma cells. Small lymphocytes aggregated into ill-defined nodular masses, and mature plasma cells with pale cytoplasm were packed into solid bands which surrounded the lymphocytic infiltrate (Fig. 3). Intermediate forms between lymphocytes and plasma cells were rare. Atypical plasma cells with enlarged nuclei and scanty cytoplasm were present. Lymphocytic and plasmacytic infiltrates rarely mingled; rather they formed separate but closely juxtaposed masses of approximately equal volumes best seen with reticulin staining. The nodules of lymphocytes contained few reticulin fibers and stood out clearly from the denser network of reticulin fibers in the plasma cell infiltrate (Fig. 4). Mucosal villi were lost, and crypts were shortened and spread apart, although none of the epithelial changes described in cases of Mediterranean lymphoma (2) were seen. The mucosa away from the lymphomatous infiltrate had a normal villous pattern and normal crypts. The lymphocytic and plasmacytic infiltrates extended focally into the muscularis propria (Fig. 5) and spread widely in the subserosal fat (Fig. 2). In these deep locations lymphocytes predominated. Mesenteric lymph nodes were diffusely infiltrated by the same type of pale plasma cells as seen in the submucosa and mucosa of the ileum. Plasma cells spread mainly in the medulla and between preserved cortical follicles. Capsule and perinodal fat were invaded (Fig. 6).

Immunofluorescent findings
Deparaffinized sections of the Bouin's fixed tissue from ileum and mesenteric lymph node were studied by direct immunofluorescence, according to the method developed in our laboratory by Dorsett and Loachim (12). Sections were stained with fluorescein-isothiocyanate (FITC) labeled monospecific goat antihuman antisera directed against IgG, IgM, IgA, IgD, IgE, kappa and lambda chains, and viewed through a Leitz Ortholux microscope equipped with a Phloxin incident-light illumination system. Plasma cells in the ileal submucosa and mesenteric lymph node showed bright cytoplasmic fluorescence with anti-IgG and anti-kappa sera only (Fig. 7). Lymphocytes in the nodular infiltrates showed weak staining of the same kind with rare, single, brightly staining cells.

Electron microscopic findings
Fresh tissue was fixed for more than 24 hours in 0.075 M cacodylate-buffered glutaraldehyde followed by two hours in Veronal acetate-buffered osmium tetroxide. It was dehydrated in graded alcohols and embedded in Epon. Sections were cut on a Porter-Blum microtome II, stained with uranyl acetate and lead hydroxide, carbon filmed, and viewed in an Elmiskop 101 electron microscope operating at 80 kv. Cells in the lymphocytic infiltrate had round or oval nuclei with prominent heterochromatin and occasional small nucleoli. Plasma cells had slightly irregular nuclei with occasional large nucleoli. The cytoplasm contained abundant, often distended, granular endoplasmic reticulum and a prominent Golgi apparatus (Fig. 8).

Follow-up
The patient received postoperative radiotherapy and has been followed for two years without recurrence. One year after the ileal resection, a laparotomy for cholecystitis revealed intestines and mesenteric lymph nodes that appeared grossly normal. Immuno-electrophoresis one year later showed normal values for IgG and IgA and slightly elevated IgM (350 mg/dl; normal: 75-290 mg/dl).

Discussion
This case is unusual in three respects: the lymphoplasmacytic histopathology, the extensive plasma cell proliferation, and the monospecific IgG immunofluorescence of both cell types. The clinical features of obstructive symptoms, lack of malabsorption, and localized nature of the lesion are typical for WTL (2-4), while the histologic finding of marked plasma cell infiltration around nodules of well-differentiated lymphocytic lymphoma is characteristic of MTL (2). A similar combination of features has been described in 5% of primary intestinal lymphomas in Iraq under the appropriate term "localized lymphoplasmacytic lymphoma" (11). So far, however, no such case has been described in this country. Other single cases with varying combinations of features of WTL and MTL (13-15) suggest that primary intestinal lymphoma comprises a spectrum with WTL and MTL at opposite ends and varying combinations in between.
IgG Lymphoplasmacytic Intestinal Lymphoma

The second unusual feature of this case is the nature and extent of the plasma cell infiltrate. In MTL it is found mainly in the mucosa, rarely extends into the submucosa, and never involves the muscularis propria and serosa (2). Since plasma cells represented approximately half of the volume of the entire mass, one may even speak of gross plasmacellular tumefaction. In the mesenteric lymph nodes they infiltrated the capsule and perinodal fat without mix-
Fig. 5
Mixed lymphocytic and plasmacytic infiltrate in the muscularis propria (HPS X625).

Fig. 6
Mesenteric lymph node with plasma cell infiltrate around residual cortical lymphoid follicle and in capsule and perinodal fat (HPS X250).

Fig. 7
Immunofluorescent findings of intestinal lymphomatous infiltrate. Band-like plasma cell infiltrate in center shows bright fluorescence with anti-IgG antiserum. Faint fluorescence is also seen within the lymphocytic infiltrates on either side. The same fluorescence was achieved with anti-kappa antiserum (X625).

Fig. 8
Ultrastructurally, lymphocytes (left) were characterized by fairly even round or oval nuclei, small nucleoli, and pale cytoplasm with few organelles. By contrast, plasma cells show a cartwheel nucleus, often with a large nucleolus, abundant granular endoplasmic reticulum, and a prominent Golgi apparatus (X6000).

...ing with other cell types. The immunofluorescent finding of a single class of immunoglobulins, IgG-kappa, in the cytoplasm of these plasma cells is further evidence of neoplasia, since a reactive inflammatory infiltrate should be composed of plasma cells that produce immunoglobulins with different heavy or light chains. Consequently, we conclude that the plasma cell proliferation in our case is neoplastic and an intrinsic part of the lymphoma. Since IgG-kappa was also identified within the lymphocytic component of the lymphoma, we suggest that
IgG Lymphoplasmacytic Intestinal Lymphoma

the two cellular proliferations are histogenetically related and represent two divergent populations of a single clone of B cells. Brouet, et al (16) reached the same conclusion in a case of immunoblastic sarcoma with plasma cell proliferation, since both cell types showed alpha chains. A similar relationship between plasma cell infiltrates and lymphoma has been suspected or demonstrated in other cases of alpha chain disease (17-19) by means of the immunoperoxidase technique (18).

The third unusual attribute of this patient concerns the type of immunoglobulin produced by the lymphoma cells. In most reported cases of MTL (5,17,18), alpha chains are produced, with protein demonstrated in the patients' sera only. Single cases of intestinal lymphoma with IgG and IgM paraproteinemia have been described (20,21,24), and five intestinal plasmacytomases producing IgG have been reported from England (22). While the significance of these different immunoglobulins remains to be determined, it has been speculated that the biological characteristics of IgA-producing or alpha chain-producing B cells differ from those producing IgG or IgM (21). The former tend to proliferate diffusely, whereas the latter tend to form localized masses. The only exceptions are the rare occurrence of alpha chain disease in localized intestinal lymphoma (14) and a case of IgG, gammopathy in diffuse gastrointestinal lymphoma (20). However, critical analysis of this latter case report suggests that it was not lymphoma but a diffuse gastrointestinal lymphoid polyposis (23). If so, our case is the first IgG intestinal lymphoplasmacytic lymphoma so far described in the literature.

References
