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Case report

Angiocentric immunoproliferative lesion of the stomach

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Summary. We report here a rare case of angiocentric immunoproliferative lesion (AIL) of the stomach. The patient was a 61-year-old Japanese female whose medical history was unremarkable. Following a complaint of abdominal discomfort, a submucosal tumour of the stomach was found and gastrectomy was done. Histological examination of the tumour revealed multiple angiocentric or angiodestructive lesions with numerous lymphocytic infiltrates. These vascular lesions were histologically the same as those in benign lymphocytic vasculitis with granulomatosis (BLV) of the respiratory tract. AIL is a distinct entity, including BLV, lymphomatoid granulomatosis and angiocentric lymphoma with BLV representing a good prognosis group of AIL. A survey of the literature suggests that AIL is a spectrum of T-lymphocyte proliferative disorders. To our knowledge, this is the first case of AIL involving the stomach primarily.

Key words: Angiocentric immunoproliferative lesion – Benign lymphocytic vasculitis with granulomatosis – T-lymphocytes – Stomach – Immunohistochemistry

Introduction

Angiocentric immunoproliferative lesions (AIL) represent a spectrum of T-lymphocyte proliferative disorders, including benign lymphocytic vasculitis with granulomatosis (BLV), lymphomatoid granulomatosis or polymorphic reticulosis, and angiocentric lymphoma (Jaffe 1985). Usually, AIL affects the respiratory tract primarily and may extend to extrapulmonary organs, such as the skin and the central nervous system. Gastrointestinal involvement may occur (Rattinger et al. 1983). However, there are a few cases without pulmonary lesions (Chen 1977; Singh and Hellstrom 1978). To our knowledge, no case of AIL primarily involving the stomach has been reported. We present a rare case of gastric AIL without pulmonary.

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Case report

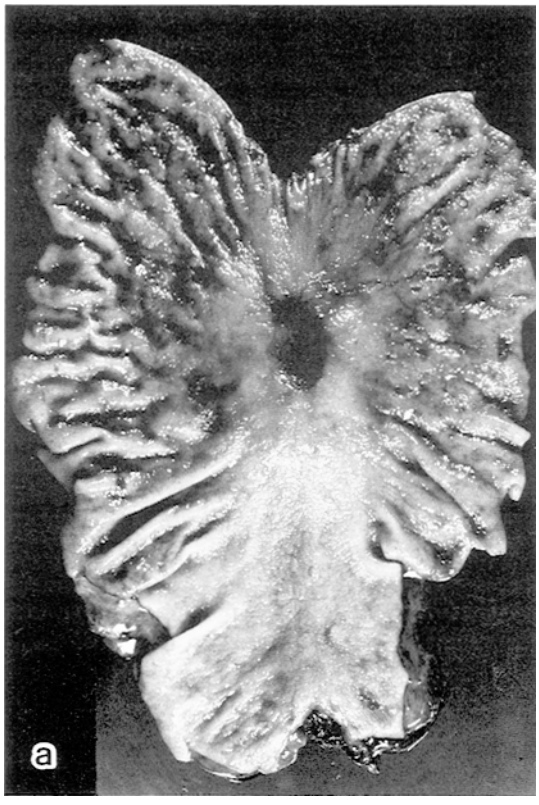
A 61-year-old Japanese female visited Prefectural Yoshida Hospital because of abdominal discomfort in August 1988. Her medical history included nothing remarkable. She had no disorder of the respiratory tract and showed no clinical features of Behçet's disease, including oral or genital aphthoid ulcers, skin lesions or ocular lesion. Radiological and endoscopic examinations of the upper gastrointestinal tract revealed a low but elevated mass with a central ulcer and surrounding by several erosions in the body of the stomach. As a submucosal tumour was suspected, gastrectomy was done in October 1988.

Routine laboratory and haematological examinations were within normal limits. Her chest X-ray films revealed no tumour shadow and no pulmonary infiltration. She is currently in good health and alive with no respiratory complaint.

The surgically resected stomach (Fig. 1a) showed a 10.1×7.4 cm slightly elevated lesion in the upper gastric body. Its margin was uncertain. A 1.5×2.9 cm open ulcer was found in the centre of the lesion with several surrounding small erosions. The ulceration involved the superficial muscle layer. However, the ulcer base was shallow and convergent folds were not clear. We suspected this lesion was an ulcerated type of gastric submucosal tumour or scirrhous type of carcinoma rather than a benign peptic ulcer.

Histological examination of the ulcer base revealed granulation tissue with dense infiltration of small lymphocytes. At the ulcer margin, several reactive lymph follicles were also identified. Sections from the elevated lesion show oedematous submucosal thickening with erosions. In the erosions, a few small and medium lymphocytes are present. Small and medium-sized lymphocytic infiltrates are scattered here and there in a patchy fashion, in the submucosal layer. They invade variably sized vessels and form vascular lesions of angiocentric or angiodestructive type. The vascular lesions are widely distributed in the submuocal and subserosal layers of the slightly elevated lesion. While the vascular lesions of submucosal layer are mainly distributed in the periphery of the elevated lesion, subserosal vascular lesions mainly exist near the central portion (Fig. 1b). Ulceration and the several small erosions are an inadequate explanation of the widespread distribution of the vascular lesions.

In what appear to be early stages, a few lymphocytic infiltrates are seen in the vascular wall (Fig. 2). Infiltrating lymphocytes gradually increase in number, but are relatively monotonous. Eosino-



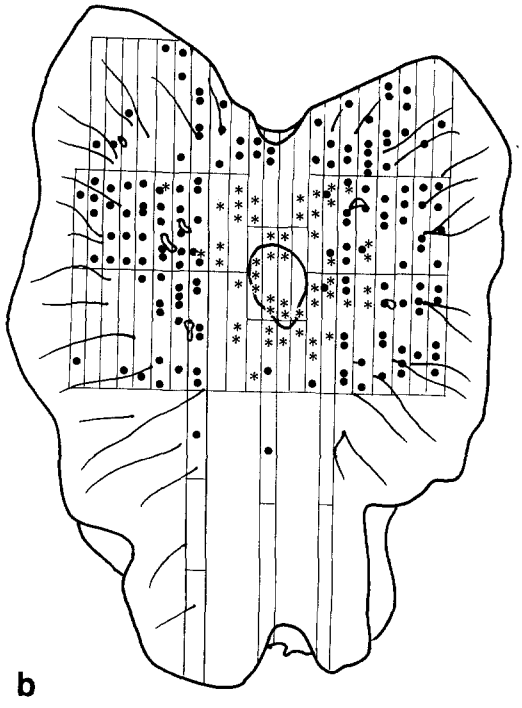
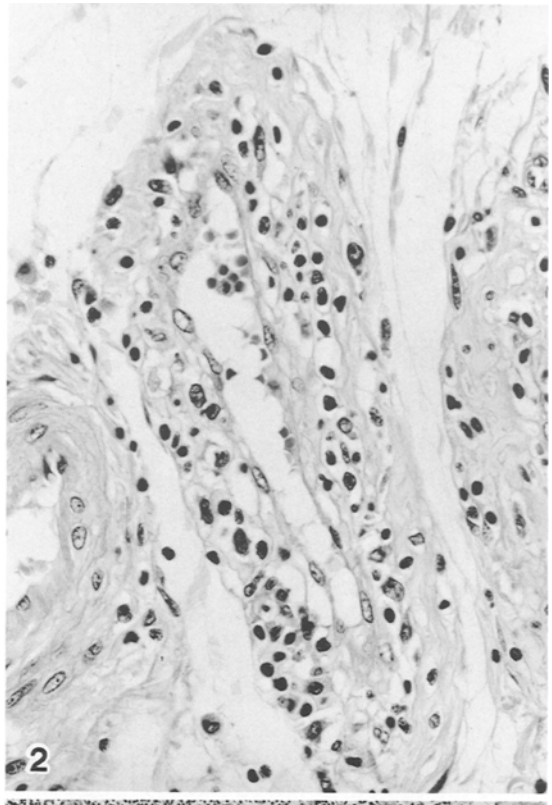


Fig. 1. **a** Photograph of the surgically resected stomach. A low but elevated lesion existed in the stomach. The lesion had central shallow ulcer and several small erosions with atrophic mucosa. **b** Schematic distribution of the angiocentric lesions: (●) showed lesions in the submucosal layer and (*) showed lesions in the subserosal layer



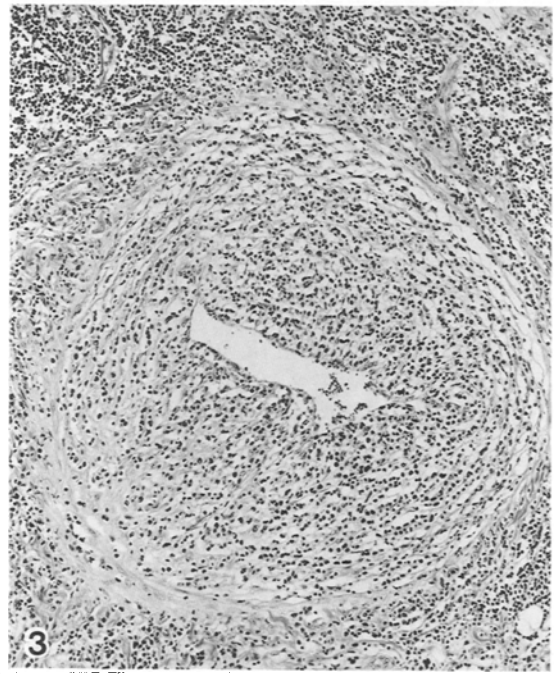


Fig. 2. Photomicrograph of the early vascular lesion. Lymphocytes with slight nuclear atypicality infiltrating the wall of a small artery. ×300

Fig. 3. Typical photomicrograph of the fully developed angiocentric lesion. Many lymphocytes diffusely infiltrate the affected vessel. The arterial wall shows complete wall destruction with marked narrowing. ×75

Table 1. Lymphocyte immunoreactivity in the several different portions of the stomach

	LCA	MT-1	UCHL-1	βF1	MB-1	L26
Lymphocytes						
in angiocentric lesions	+	+	+	+	−	−
in ulcer base	+	+	+	ND	−	−
in erosions	+	+	+	+	−	−
in lymph follicles	+	−	−	−	+	+

ND, Not done

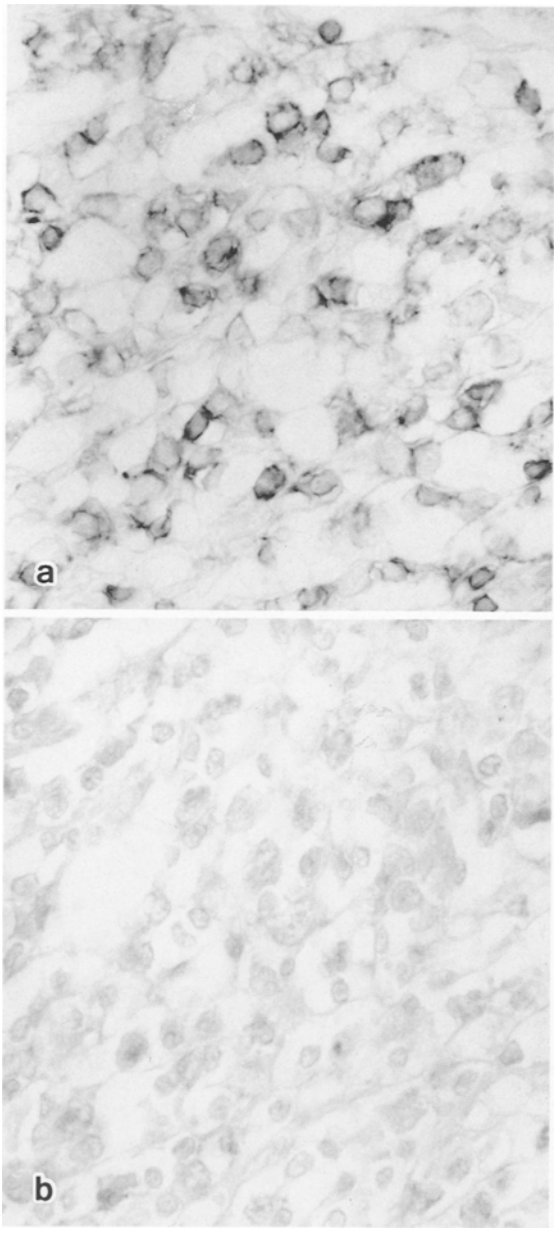


Fig. 4. Photomicrograph of immunohistochemical examinations, using (**a**) MT-1 and (**b**) L26. Nearly all of infiltrating lymphocytes showed MT-1 positive and L26-negative results and revealed a T-cell phenotype. × 520

phils or histiocytes are very few. The lumen of the affected vessel narrows more and more as lymphocytes increase. Fully developed vascular lesions typically show complete destruction of wall and pronounced narrowing due to lymphocyte infiltrations (Fig. 3). Plasma cells, histiocytes and eosinophils are also present. However, neutrophils, nuclear debris and fibrinoid necrosis are seldom observed.

The changes differ from well-known vasculitides, such as necrotizing or hypersensitive vasculitis. Several affected vessels show complete obstruction and, on rare occasion, re-canalization. However, they do not show appearances resembling thromboangitis.

Infiltrating cells in all portions of the ulcer base, affected vessels and erosions are morphologically the same. They are mainly composed of mature-appearing lymphocytes which show slight or no nuclear atypicality. There are scarcely any mitotic figures.

We examined the infiltrating lymphocytes on the paraffin sections using several rabbit antibodies (Dakopatts Glostrup, Denmark) including anti-human IgA, IgM, IgG, IgD, κ, λ, and lysozyme. The results are non-specific and show no monoclonal staining pattern. Histiocytes showed positive results with anti-lysozyme. We also used several mouse monoclonal antibodies as lymphocyte markers, including MT-1 (Bio-science Emmenbücke, Switzerland), MB-1 (Bio-science), leukocyte common antigen (Dakopatts), UCHL-1 (Dakopatts), L26 (Dakopatts), and β F 1 (T-cell Science Cambridge, USA). Table 1 summarizes the results of lymphocyte markers. It shows that infiltrating lymphocytes nearly all show the T-cell phenotype (Fig. 4).

Discussion

In this case, ulceration was an unadequate explanation for the widely distributed vascular lesions. We reviewed 56 resected specimens of benign gastric or duodenal ulcers and observed several vascular lesions, including endothelial swelling, intramural fibrosis, vascular occlusion, perivascular infiltration of lymphocytes and necrosis, due to direct involvement by ulceration. While we rarely observed slight or focal infiltration of lymphocytes in vessels and we never identified the typically fully developed vascular lesions seen in this case. From histological appearances the vascular lesions of this case can be grouped into vasculitis. However, there is nothing worthy of notice about the patient's medical history or physical signs. Routine laboratory examinations and heamatological studies were within normal limits. We decided that this case differs from the well-known groups of vasculitis, such as polyarteritis nodosa, hypersensitive vasculitis, giant-cell arteritis, thromboangitis and so on. The histological picture of the vascular lesion corresponds well with that of BLV.

BLV was proposed by Saldana et al. (1977) as a differential diagnosis from lymphomatoid granulomatosis (LYG; Liebow et al. 1972). In BLV, dense benign-appearing infiltrates of mature lymphocytes, plasma cells, and histiocytes are present in the vessels. BLV and LYG have been usually described as diseases primarily involving the respiratory tract. It is well known that LYG have extrapulmonary manifestations (Liebow et al. 1972) and extrapulmonary involvement was also reported in BLV (Weiss et al. 1984). While gastrointestinal involvement has been noted (Rattinger et al. 1982), cases without pulmonary lesion are very rare (Chen 1977; Singh and Hellstrom 1978). A case involving stomach primarily has not been reported.

It is unclear whether BLV and LYG are indeed separate entities (Fauci et al. 1982). LYG has a poor prognosis (Fauci et al. 1982; Katzenstein et al. 1979; Liebow et al. 1972) and often develops into malignant lymphoma. Some authors have suggested that LYG and polymorphic reticulosis are histologically the same (DeRemme et al. 1978; Stamenkovic et al. 1981). Jaffe (1985) suggested that AIL is a distinct clinicopathological entity, including BLV, LYG or polymorphic reticulosis, and angiocentric lymphoma. BLV corresponds to a good prognosis group of AIL with little or no atypicality of infiltrating lymphocytes. We conclude that this case is within the good prognosis group of AIL.

There have been several reports that LYG or polymorphic reticulosis is a peripheral T-cell disorder (Chott et al. 1988; Nichols et al. 1982; Petras et al. 1981). Recently, some cases of LYG and polymorphic reticulosis were demonstrated, using DNA analysis, to be clonal T-cell disorders (Gaulard et al. 1988). AIL is thus a spectrum of post-thymic T-cell proliferations and often develops in extranodal organs; infiltrating lymphocytes nearly all showed a T-cell phenotype in this case. However, clonal proliferation was not demonstrable (we could not obtain the unfixed material).

We cannot prove that this case is a malignant lymphoma. However, even in those cases of AIL with little or no atypicality of small lymphocytes, progression to malignant lymphoma sometimes occurs (Lipford et al. 1986). Moreover, in cases of malignant lymphoma of the gastrointestinal tract, neoplastic lymphocytes may infiltrate into vessels and are associated with eosinophils and plasma cells (Lewin et al. 1978), resembling a vasculitis. We will watch the course of this case with special attention to the possibility of progression to malignant lymphoma.

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