Primary neutrophil-rich, CD30-positive anaplastic large cell lymphoma of the stomach : case report and review of the literature

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Abstract

Primary T-cell lymphoma of the stomach is a rare disease, most gastric lymphomas being of B-cell type. Here we describe a unique case of primary neutrophil-rich CD30-positive anaplastic large cell lymphoma (ALCL) of the stomach that was treated and cured by combined chemotherapy. According to our literature review, only 7 cases of primary gastric ALCL have been previously reported, none of them being of the neutrophil-rich subtype. Although very peculiar in its histological presentation, which may simulate an inflammatory or carcinomatous process, the natural history as well as the clinical features of this unusual gastric lymphoma does not differ from the other reported cases of gastric ALCL. (Acta gastroenterol. belg., **2002**, 65, **237-240**).

Key words : anaplastic large cell lymphoma, CD30, gastric lymphoma, primary gastric.

Introduction

The stomach is the most common site of primary extranodal lymphoma in the adult population (1), where it is reported to be involved in one fourth of total cases. In contrast to the continuous decline to the incidence of gastric carcinoma, the frequency of primary gastric lymphomas has been increasing. Most of them are of B-cell type (2,3) and are considered to arise from the mucosa associated lymphoid tissue (MALT) of the stomach. In contrast only 6 to 7% are of T-cell lineage and they usually belong to the category of adult T-cell leukemia/lymphoma (ATLL), to that of peripheral T-cell lymphomas, large pleomorphic or immunoblastic subtype or to that of anaplastic large cell lymphoma (ALCL) (4). In this context, we report our experience with a patient who developed a primary ALCL of the stomach featuring numerous neutrophils. The clinical as well as the pathological findings in our case are compared to those previously described.

Case presentation

A previously healthy 45-year-old man from Angola, living in Belgium for four years was referred for evaluation of epigastric pain and weight loss. Four months ago, he underwent an esophagogastroduodenoscopy (EGD) revealing antral inflammation with *Helicobacter pylori* (Hp) infection found by pathology. Even though Hp was successfully eradicated, the patient kept complaining of abdominal pain and lost 15 kg.

He was a thin, lethargic middle-age man. His vitals were normal with low-grade fever of 38°C. The abdomen was soft and non-distended with tenderness in the epigastric area.

Laboratory data included hemoglobin 11.4 g/dl, hematocrite 37.8%, white blood cell count 3090/µL, platelet count 123,000/µL, erythrocyte sedimentation rate 72 mm/hr, C reactive protein 9 mg/dl and lactate dehydrogenase 640 IU/L. Electrolytes and renal function tests were within normal limits.

A second EGD was performed, which showed a large and ulcerated mass of 4.×.5 cm involving the whole fundus (Fig. 1). Microscopic examination of the biopsies revealed a tumoral process, made of large and clear lymphoid cells admixed with a large number of neutrophils (Fig. 2). By immunohistochemistry, the tumor cells were found to be positive for CD45, CD3 (Fig. 3), CD43, CD45RO, CD30 and granzyme B. These cells showed no immunoreactivity with antibodies directed against cytokeratin (CAM5-2, AE1/AE3), CD20, CD5, CD15 and with monoclonal antibody ALK-1 which recognize the anaplastic lymphoma kinase (ALK) resulting from the t(2,5) translocation that is usually associated with some ALCL variants. Therefore a diagnosis of primary gastric CD30-positive ALCL of the neutrophil-rich subtype was performed. No further Hp infection was demonstrated.

The rest of the workup included negative serologies for Human Immunodeficiency virus (HIV), Epstein-Barr virus (EBV), Cytomegalovirus (CMV) and Human T-cell leukemia virus (HTLV-I), normal chest x-ray and gallium bone scan, unremarkable ultrasonography and CT scan of the abdomen. An endoscopic ultrasonography of the stomach disclosed enlarged perigastric nodes. Since no other location of the tumor process could be evidenced, the disease was thought to be primarily gastric. Six cycles of a combined chemotherapy including cyclophosphamide, doxorubicin, vincristine, and prednisone were given successfully with a rapid clinical improvement and a complete cure, confirmed by both endoscopy and control biopsies, one and two year later.

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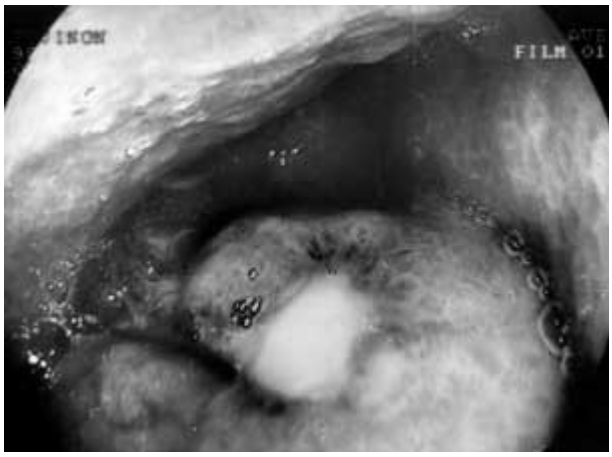

Fig. 1. — EGD showing a large ulcerated mass involving the fundus.

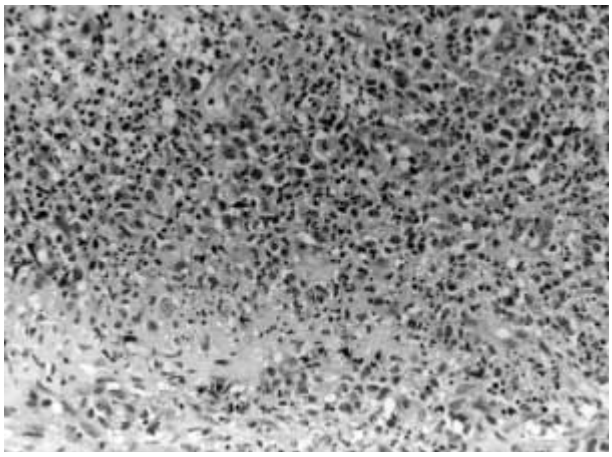

Fig. 2. — This photomicrograph illustrates the tumor process. The latter is composed of large and clear atypical cells admixed with numerous neutrophils.

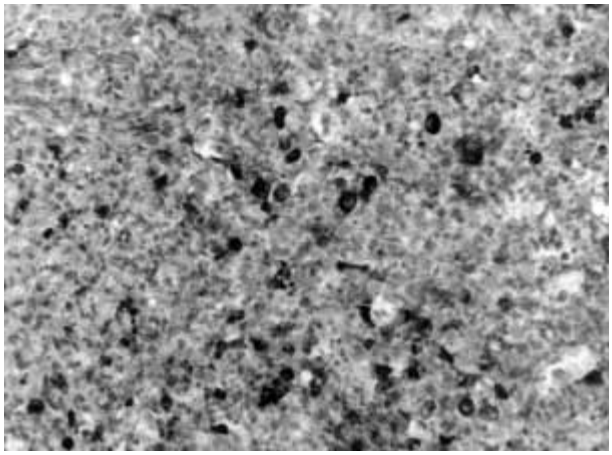

Fig. 3. — Immunohistochemistry with antibody against CD3. The tumor cells are strongly stained.

Discussion

A T-cell phenotype is found in 6 to 7% of primary gastric lymphomas (3,4,5). In this regard, it is worth noting that most cases of gastric T-cell lymphoma reported originate from East Asia, especially from Japan. An association between HTLV-I, which is endemic in the southwestern parts of Japan (6,7), and T-cell lymphomas has been described (3,8). Most of these cases belong to the category of adult T-cell leukemia/lymphoma (ATLL) subtype. In contrast, only two cases of HTLV-I positive gastric ALCL have been reported (9), thereby suggesting a poor relationship with this variant of T-cell lymphoma (10,11,12). EBV has been associated with primary gastrointestinal lymphoma, even those of T-cell phenotype (13). This is probably due to a higher incidence of EBV infection among patients originating from Far-East countries (4). In our patient, both HTLV-I and EBV serologies were, however, negative. Like in most cases of gastric marginal zone B-cell lymphoma of the MALT type, Hp has also been implicated in the pathogenesis of T-cell lymphoma of the stomach (14). Indeed, a high prevalence of Hp infection has been described in gastric lymphoma, regardless of the B or T phenotype of the neoplasm (15-17). It has been postulated that normal gastric mucosa does not contain lymphoid tissue and that the latter develops following chronic Hp stimulation, giving rise to chronic gastritis (16-20). T-cell activation by Hp in the gastric mucosa has already been mentioned in several reports (21,22). However, the transition from a chronic gastritis to a malignant lymphoma has not yet been fully explained. The presence of Hp-associated chronic gastritis may be essential to induce a gastric lymphoma, some other factors, such as gene abnormalities (23), may also play a role in malignant transformation (14). In our case, we can conceive that Hp infection may have possibly influenced the development of this lymphoma, through a sustained antigenic stimulus of T-cells. Although speculative, this hypothesis is supported by the absence in our patient of any other known risk factors for gastric lymphomas. Furthermore, since concomitant infection wasn't any more documented at time of diagnosis, one can imagine that malignant transformation took place during Hp infection and that its eradication couldn't stop the progression of the disease, in contrast to gastric marginal zone B-cell lymphoma. We admit that this hypothesis may appear rather speculative at first glance but it has the merit to be coherent and to stay in concordance with the knowledge about Hp infection and its implication in the pathogenesis of gastric neoplasm (24).

Our review of the literature also showed that in cases where immunophenotyping was performed, 78% of primary gastric T-cell lymphomas were CD30 positive with expression by tumor cells varying from case to case (25). This antigen is expressed by the neoplastic cells of Hodgkin's disease, by those of non-Hodgkin lymphomas, as well as by some activated cells in nonneoplastic lymphoid tissues (26). It also characterizes

Table 1. — **Age, sex, symptoms and mode of presentation of CD30 positive primary gastric lymphomas (N/A : not available)**

Reference	Year	Age	Sex	Main Symptom	Weight loss	Gross
Moubayed (28)	1987	66	f	Epigastric pain	yes	Ulcer
Moubayed (28)	1987	18	m	GI bleeding	yes	Ulcerated mass
Chan (34)	1988	79	f	GI bleeding	N/A	GI bleeding
Yatabe (8)	1994	46	m	N/A	N/A	Polyps and Ulcer
Yatabe (8)	1994	59	m	Epigastric pain	no	Ulcer
Paulli (33)	1994	82	f	N/A	N/A	N/A
Takimoto (9)	1994	29	m	Epigastric pain	no	Ulcer
Our case	2001	45	m	Epigastric pain	yes	Ulcerated mass

Table 2. — **Immunohistochemistry, treatment and follow-up of CD30 positive primary gastric lymphomas**

Reference	Year	Immunohistochemistry	Treatment	Follow up survival
Moubayed (28)	1987	OKT11, OKT4	Chemotherapy	4 years
Moubayed (28)	1987	OKT11, OKT4	Chemotherapy	3 years
Chan (34)	1988	LCA, Ber-H2, EMA, CD12, CD2	Surgery	6 weeks
Yatabe (8)	1994	CD2,CD4,CD5,CD25,CD30, CD43,CD45RO	Surgery	10 months
Yatabe (8)	1994	CD2,CD3,CD4,CD5,CD25, CD30, CD43,CD45RO	Surgery	10 months
Paulli (33)	1994	CD3, MT1, UCHL1	none	45 days
Takimoto (9)	1994	MT1,CD15	Chemotherapy	4 years
Our case	2001	CD45, CD3, granzyme B, CD43, CD 45 RO and CD 30	Chemotherapy	24 months

ALCL, where its expression by tumor cells is diffuse (27). It is worth noting that in our patient, such CD30 expression was diffuse, allowing a diagnosis of ALCL to be made. In terms of clinical outcome, CD30 expression has been associated with a better prognosis in primary cutaneous T-cell lymphoma in comparison with those of nodal origin, but this relationship has not been clearly established for primary gastric T-cell lymphoma (28,29). Nevertheless, the prognosis of primary ALCL of the stomach might still be better than that of undifferentiated carcinoma, with which they are often confused (30,31).

Hitherto, only eight cases of primary CD30-positive ALCL of the stomach, including ours, (8,9,10,28,32-34) have been described in the literature (tables 1 & 2). None of them seemed to be of the neutrophil-rich variant. The disease is more common in the older age (mean : 53.5 + 22.8 years, range : 64 years), with a slight predominance of males (F/M ratio : 3/5). Symptoms and endoscopic findings are misleading since one half of the patients were complaining of epigastric pain and one half of them had an ulcer seen on EGD. Regional lymph nodes were almost always involved (7 patients). Chemotherapy appears to be the mainstay of treatment since patients (50%) who were treated with this therapeutic modality had a better survival (mean : 3 years and 3 months) than those treated by surgery alone (mean : 7 months and 5 days). Thus, although rare in occurrence, the recognition of this unusual condition in the stomach has a significant clinical implication.

Conclusion

This case report shows how it is crucial for the pathologist to remain vigilant while seeing a tumoral process admixed with numerous neutrophils, since the diagnosis of ALCL should be suspected and confirmed by immunohistochemistry.

Our case seems to be unique since no other case of primary CD30-positive T-cell lymphoma of the stomach featuring numerous neutrophils could be found in our literature review. The natural history as well as the clinical features in our patient were, however, very similar to those described in the other cases of gastric CD30-positive ALCL and confirm that early diagnosis is important to achieve better survival with a chemotherapy regimen adapted for aggressive lymphomas.

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