

Metastatic follicular dendritic cell sarcoma of the stomach : A case report and review of the literature

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Abstract

Follicular dendritic cell (FDC) sarcomas are rare tumours, typically seen in lymph nodes. However, in about one third of the reported cases, a FDC sarcoma presents as an extranodal mass. Involvement of the gastrointestinal tract is extremely rare, and only 3 cases have been described to date.

We report on a 40-year-old female patient with a follicular dendritic cell sarcoma located in the stomach and the presence of a metastasis in the liver at the time of diagnosis. Severe asthenia, nausea, back pain and loss of weight were the presenting symptoms. A CT scan of the abdomen and an upper gastrointestinal endoscopy revealed a tumour mass in the stomach.

The diagnosis of a FDC sarcoma was made on histological and immunohistochemical findings. We report the second case of a FDC sarcoma presenting in the stomach.

Due to its rarity, a FDC sarcoma seldom enters the differential diagnosis of spindle cells neoplasms of the gastrointestinal tract. Complete surgical resection is the treatment of choice for FDC sarcoma. (*Acta gastroenterol. belg.*, 2004, 67, 223-227).

Key words : follicular dendritic cell, follicular dendritic cell sarcoma, stomach cancer, liver metastasis.

Introduction

Follicular dendritic cell (FDC) sarcoma is a rare tumour arising from follicular dendritic cells in lymphoid tissue. Their main role is the presentation of antigen-antibody complexes to B-lymphocytes.

Today, approximately 65 cases have been reported with FDC sarcoma (1-11). This tumour affects mainly the lymph nodes, but it also involves extranodal sites in about one third of cases. The intra-abdominal organs, oral cavity and tonsils are the most involved extranodal sites (1). The gastro-intestinal hollow tract is a rare location, and only three cases are described today, one case involving the small intestine (4), one the colon (5) and one presenting as a submucosal tumour of the stomach (6). Therefore, FDC sarcoma is an entity rarely listed in the differential diagnosis of spindle cell neoplasms of the gastro-intestinal tract.

We report a case of a 40-year-old woman with a FDC sarcoma in the stomach and a metastasis in the liver at the time of diagnosis.

Case history

A 40-year-old female patient presented with severe asthenia, night sweating, nausea and back pain spread-



Fig. 1. — A Ct-scan of the abdomen showed a lobulated multinodular mass situated between the left liver lobe and the stomach with compression of the stomach and pancreas.

ing out to the abdomen. Over a period of 4 weeks, she lost 3 kilograms of weight. Clinical examination revealed a painful mass in the left upper abdomen. No other relevant findings were noted. Laboratory analysis showed a leukocytosis of 20600 cells per mm³ (normal 4000-10000 cells per mm³), elevated C-reactive protein (CRP) of 7 mg per dl (normal 0-0,5 mg/dl), a discrete microcytic anaemia, a slight hypoproteinemia and a highly raised alkaline phosphatase of 344 U/l (normal 30-120 U/l). Chest X-ray was normal. A CT-scan of the abdomen (Fig. 1) showed a lobulated multinodular mass situated between the left liver lobe and the stomach with compression on stomach and pancreas. No pathological retroperitoneal and mesenteric nodes were visible. A solitary nodule in the lobus quadratus of the left liver lobe was noted. Upper GI endoscopy revealed an exophytic cauliflower-like reddish mass (Fig. 2) from which several biopsies were taken.

Light microscopy showed a tumour consisting of ill-defined and loosely arranged epitheloid cells without signs of glandular differentiation. Because of lack of immunoreactivity for epithelial markers a diagnosis of

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Fig. 2. — Upper GI endoscopy revealed an exophytic cauliflower-like reddish mass in the stomach.

poorly differentiated sarcoma was made. Furthermore, because of faint and focal immunoreactivity for c-kit on the paraffin sections, a gastrointestinal stromal tumour (GIST) was taken into consideration too.

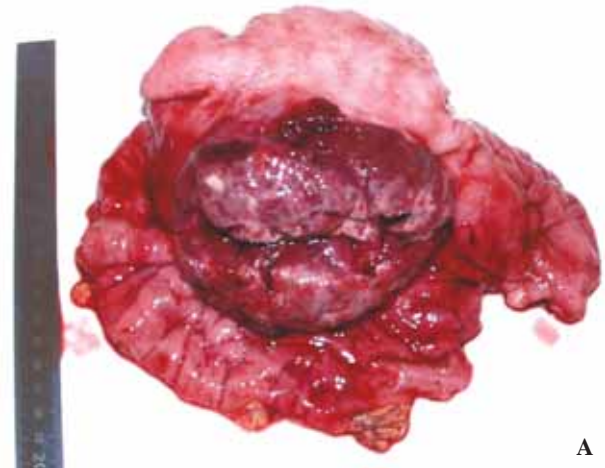
Since the tumour was considered resectable, the patient was referred for surgery. The surgeon found a tumoural mass, which was originating from the anterior wall of the stomach, with invasion of Couinaud segment III of the liver. The tumour was resected en bloc with a total gastrectomy, resection of segment III and lymphadenectomy of the left gastric artery, hepatic artery, portal vein and splenic artery. Peroperatively a palpable mass was detected in segment IV. Frozen sections of this nodule were inconclusive. Continuity was restored with a Roux en Y esophagojejunostomy.

Postoperative recovery was uneventful and the patient was discharged from the hospital after 19 days.

Pathological findings

Macroscopically, a reddish and spongy polypoid tumour with a diameter of 12 cm was located at the minor gastric curve (Fig. 3A). On cross-section, transmural growth was noted with infiltration of the resected liver segment III. Numerous lymph nodes along the minor curve were metastatically enlarged, some showing central cystic necrosis (Fig. 3B).

Microscopically, a different histology was seen at the tumour surface, at the invasive front or in the metastatically diseased lymph nodes. In the polypoid mass, low power view revealed a striking stream-like pattern of loosely arranged trabeculae alternating with blood-filled spaces. Tumour cells had poorly discernible cytoplasmic outlines and ovoid vesicular nuclei with one or more



A



B

Fig. 3. — (A) Gross view of the exophytic growing nodular tumour mass. (B) Cross-section of the gastric wall with transmural growth and invasion of adjacent liver parenchyma. A large metastatic lymph node in between shows central necrosis.

eosinophilic nucleoli. Focally, severe cytological atypia combined with atypical mitotic figures could be revealed (Fig. 4A). The mean mitotic rate was 3 (range 0-5) per 10 high power fields. Occasionally, multinucleated cells, resembling Warthin-Finkeldey giant cells were present. Tumour cells were intimately intermingled with small lymphocytes, the latter causing prominent perivascular cuffing (Fig. 4B). Near the invasive front, alveolar-like spaces were formed. Giant cells were more numerous here. In the largest metastatically involved lymph node, a spindle cell proliferation was seen, forming fascicles, storiform patterns and whorls.

The paraffin-processed biopsies from segment IV showed metastatic involvement of liver parenchyma with similar fascicular growth pattern. The lymph nodes around the gastric artery and portal vein were slightly enlarged due to reactive follicle hyperplasia. Hyaline-vascular changes, reminiscent of Castleman disease, could not be found.

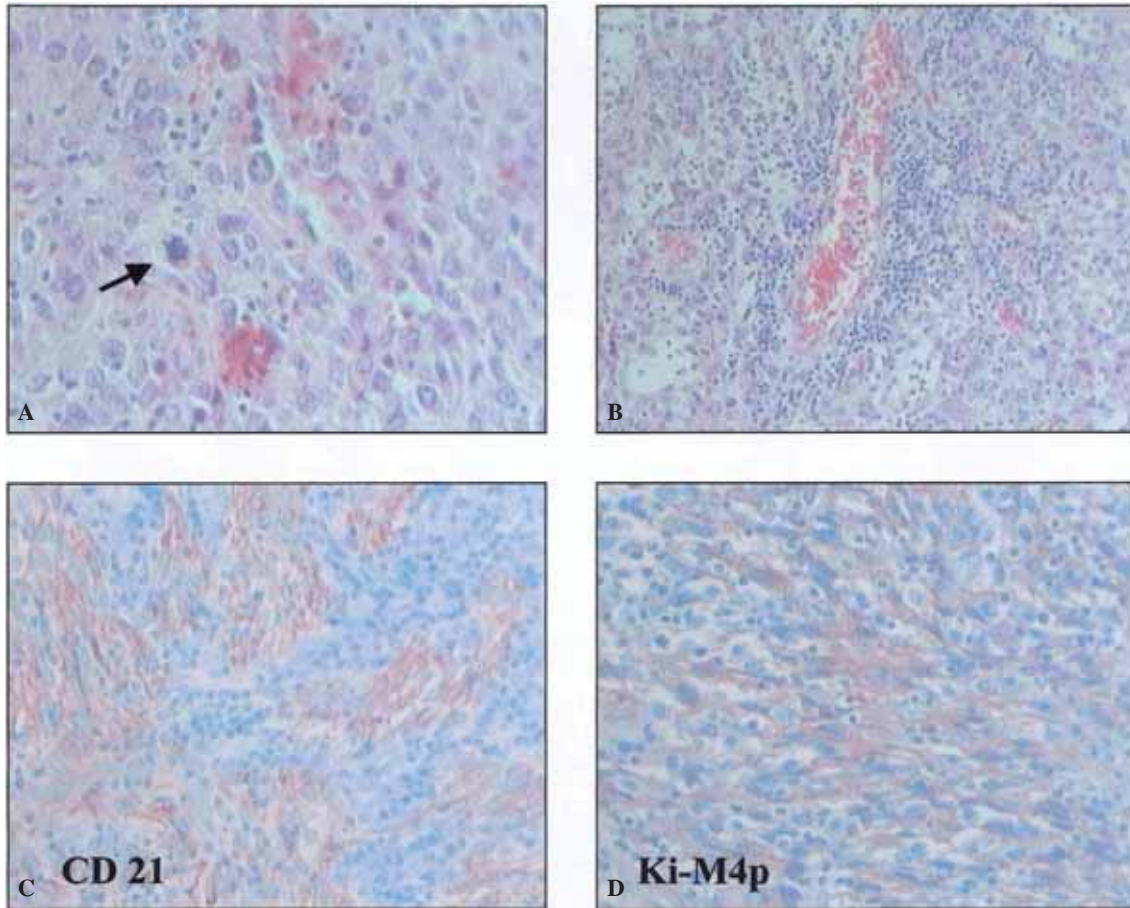


Fig. 4. — (A) High-power view showing marked cytologic atypia with large vesicular nuclei, thick nuclear membrane, coarse chromatin and an abnormal mitotic figure (arrow). (B) Prominent perivascular cuffing by lymphocytes. Metastatic focus with oval and spindle tumour cells, showing positive staining with CD 21 (C) and Ki-M4p (D).

Immunohistochemistry was performed on formalin-fixed paraffin-embedded material from the aforementioned different tumour areas, using the Nexes Autostainer (Ventana). Unless otherwise specified all antibodies were purchased from DAKO Cytomation. Epithelial differentiation was searched for using antibodies against broad spectrum cytokeratins (AE1-AE3, 1/300, Biogenex), EMA (MFGM/5/11, 1/500, SeraLab) and CEA polyclonal (1/4000). The diagnostic workout for a sarcoma with muscular differentiation required a panel consisting of SMA (AB 128M, 1/40, Biogenex), MSA (AB 090M, 1/40), myoglobin (MG1, 1/100, Biogenex), desmin (D33, 1/100) and vimentin (V9, 1/200). For the diagnosis of angiosarcoma the vascular markers CD 31 (JC/70A, ready-to-use, Neomarkers), CD 34 (QBEND10, ready-to-use, Immunotech) and FVIII (1/200) were used. The possibility of a haematologic malignancy was investigated with the markers myeloperoxidase (1/3000) and LCA (MS-413-R7, ready-to-use, Neomarkers) as well as with the dendritic cell markers CD1a (O10, ready-to-use, Immunotech), CD 21 (1F8, 1/10), CD 35 (Ber-MAC-DRC, 1/25) and Ki-M4p (a generous gift from Professor R. Parwaresch,

Institute of Haematopathology Kiel, Germany). Metastatic melanoma was checked by S100 (1/1600) and HMB45 (HMB45, 1/100, Enzo Diagnostics). The epitheloid cells, giant cells and spindle shaped cells showed only strong reactivity for vimentin and CD 21 (Fig. 4C) and moderate reactivity for CD35 and Ki-M4p (Figure 4D). Ki-67 labelling (MB67, 1/100, Neomarkers) ranged from 5 to 15 %. The larger quantity of material allowed proper analysis of a repeated C-kit staining (1/50), the signal of which subsequently could be interpreted as background signal. In situ hybridisation could not detect EBV viral RNA (Inform EBER kit, Ventana).

Finally, based on histological and immunohistochemical findings, the diagnosis of a FDC sarcoma was made.

One month after surgery, it was decided to treat the 3.5 cm large metastatic lesion in segment IV with radiofrequency (RF) ablation. A control CT-scan after 4 weeks showed a hypodense nodule in segment IV after ablation, but also 2 new lesions in segment V, suspicious for new metastasis. Ct scan of the thorax showed no evidence of lung metastases. A second RF ablation of the liver lesions was performed 6 weeks later.

The patient is actually 5 months after diagnosis still alive.

Discussion

The existence of a follicular dendritic cell sarcoma (FDC sarcoma) was first demonstrated by Monda *et al.* in 1986. These authors described four patients with malignant tumours involving cervical lymph nodes.

Follicular dendritic cell sarcomas affect young or middle-aged adults. There is no gender predilection. The most common clinical presentation is a solitary, slow-growing and painless cervical lymphadenopathy (1). Other lymph nodes can be involved, including axillary, supraclavicular, and mediastinal nodes. The intraabdominal organs (pancreas, peripancreatic tissues, liver, spleen, intra-abdominal soft-tissues), tonsils and oral cavity are the most involved extranodal sites. Abdominal pain and weight loss are presenting symptoms.

We report a case of a FDC sarcoma located in the stomach with a metastatic lesion in the liver. Today, only three cases of a gastrointestinal location are described.

The pathological diagnosis of a FDC sarcoma is challenging and may require a combination of morphologic, immunophenotypic and ultrastructural analyses. FDC tumours have been mostly described as well-circumscribed nodular masses of pink or white colour and solid consistency. The size appears to be largely dependent on the tumour location, and ranges from 1 to 20 cm. The tumour is composed of oval to spindle cells with pale to eosinophilic cytoplasm, and ill-defined cell outlines resulting in a syncytial appearance. Tumour cells grow in whorls, fascicles, sheets or a storiform pattern. Two other characteristic features are the intimately admixture of tumour cells and small lymphocytes and the presence of perivascular cuffs of mature lymphocytes. Most tumours show some degree of mitotic activity (2).

Although FDC sarcoma has characteristic histological findings, confirmation with immunohistochemical studies is essential for a definite diagnosis. In mucosal sites and soft tissues, sarcomatoid carcinomas and various sarcomas are by far more common than FDC sarcoma. If the possibility of FDC sarcoma is not considered, this diagnosis will not be made because specific FDC markers are not routinely used in the immunohistochemical evaluation of poorly differentiated neoplasms. The immunophenotype of FDC tumours closely parallels that of nonneoplastic FDC.

Immunoreactivity with antibodies directed against CD21 and CD35 has been reported in approximately 95% of the cases. Other specific markers such as Ki-M4p and Ki-FDC1p can be used. Vimentin and R4/23 are also consistently positive in most of the FDC tumours investigated. FDC tumours show variable expression of S-100 protein, EMA (epithelial membrane antigen), CD68, muscle-specific actin (MSA), desmoplakin, CD45RB. They are negative for CD1a, CD20,

cytokeratin, desmin, CD31, CD34, c-kit or HMB-45. Ultrastructural examination shows complex interdigitating cytoplasmic processes joined by desmosomes (1).

The differential diagnosis of FDC sarcoma is large. The major differential diagnoses are ectopic meningioma or thymoma, malignant fibrous histiocytoma, inflammatory pseudotumor, malignant peripheral nerve sheath tumour, angiosarcoma, lymphoepithelioma-like carcinoma, malignant melanoma and interdigitating reticulum cell sarcoma (2). For extranodal locations a distinction from better known mesenchymal sarcomas, such as the gastro-intestinal stromal tumours (GIST) must be considered.

In our case, we also made the initial diagnosis of GIST on histological examination of the gastroscopy biopsy specimens. GIST tumours have features that mimic FDC sarcomas, namely fascicular arrangement of spindle cells admixed with epithelioid or myoid areas. A histological feature that is helpful to distinct GIST from FDC sarcoma is the lack of a lymphocytic component. However, immunohistochemical confirmation is essential for the definitive diagnosis. C-kit (CD 117) immunoreactivity has been accepted as a highly sensitive marker of GIST. In our case, comparison of c-kit immunoreactivity on the biopsied material versus tumour bulk forced us retrospectively to refrain from diagnosing a GIST. Moreover, the tumour lacked CD 34 immunoreactivity, which is frequently seen in GIST.

The majority of the reported cases of FDC sarcomas have no known etiologic or predisposing factors. Hyaline-vascular Castleman's disease is the only predisposing factor identified for FDC sarcoma in a minority of cases. Epstein-Barr virus has been demonstrated in selected cases, but does not appear to play a significant role in the usual form of FDC sarcoma (2).

The natural history of FDC sarcoma is variable and often difficult to predict. They should be considered as a sarcoma of at least intermediate grade malignancy, rather than as lymphoma.

In the study of Perez *et al.* (1) 36% developed local recurrences and 28% metastatic disease. Metastatic lesions are primarily described in lymph nodes, lung, liver and peritoneum. At the time of last follow-up, there was a mortality rate of 14%. Approximately the same figures are described in the study of Chan *et al.* in 1997 (2). Both studies (1,2) show that intraabdominal locations are associated with particularly aggressive course. A high mitotic count (> 5 mitoses per 10HPF), coagulative necrosis, nuclear pleomorphism and significant cellular atypia are correlated with an aggressive clinical behaviour (2).

Complete surgical resection is the treatment of choice for FDC sarcomas. Usually, this can be easily done in tumours involving cervical or axillary lymph nodes. Intraabdominal or mediastinal tumours are more difficult to resect because of their large size or involvement of adjacent structures. The role of adjuvant therapy, such as chemotherapy and/or radiotherapy, remains unclear

because of the retrospective nature of published studies and the small series.

Conclusion

We report the second case of a FDC sarcoma presenting in the stomach. At diagnosis a metastatic lesion in the liver was present.

FDC sarcomas are rare tumours, typically seen in lymph nodes. One third of cases were localised in extranodal sites. In recent years, this malignant proliferation became widely recognised as a distinct entity, showing characteristic histopathologic, immunophenotypic and ultrastructural features. However, one should think of this entity, especially when no immunoreactivity is detected for epithelial and mesenchymal markers. The diagnosis can be made reliably using CD21, CD 35 and Ki-M4p antibodies.

Due to its rarity, a FDC sarcoma seldom enters the differential diagnosis of spindle cells neoplasms of the gastrointestinal tract. Complete surgical resection is the treatment of choice for FDC sarcoma.

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