Gastric metastases. An endoscopic series of ten cases

Métastases gastriques. Une série endoscopique de dix cas

N. Trouillet, B. Robert, S. Charfi, E. Bartoli, J.-P. Joly, D. Chatelain

Summary

We report a series of ten cases of the clinical, endoscopic and pathological features of gastric metastases. Patients were six women and four men between 54 and 88 years old, with gastric metastases from breast carcinoma (4), lung carcinoma (4) and melanoma (2). Patients underwent an upper gastrointestinal endoscopy for epigastralgia (2), hematemesis (2), dysphagia (1) and anemia (5). On endoscopy, tumors appeared as nodules with a central ulceration (5), an ulceration (4) or simulating linitis plastica (1). Metastases were located in the cardia (2), fundus (5) and antrum (3). Primary tumors had been diagnosed between one day and 20 years before upper endoscopy. Eight patients had multivisceral metastases. The microscopic features of the gastric metastases resembled a primary gastric cancer in eight cases. Thanks to clinical data, the pathologist confirmed the diagnosis of gastric metastases on immunohistochemistry. Nine patients died in the eight-month follow-up period. Gastric metastases are rare, occur at a late stage of the neoplastic disease, and have a poor prognosis. Diagnosis of gastric metastases is difficult because they simulate primary gastric cancer on endoscopy and on microscopic examination. A correct diagnosis is based on good communication between gastroenterologists and pathologists.

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Results

From 2001–2009, approximately 24,000 upper oesogastric endoscopies were performed in Amiens Hospital. Microscopic analysis of the gastric biopsies from these upper endoscopies diagnosed 261 malignant gastric tumors: 211 primary gastric adenocarcinomas, 21 primary lymphomas, nine gastrointestinal stromal tumors, six endocrine carcinomas, four cases of invasion of the gastric wall from pancreatic adenocarcinoma and ten gastric metastases.

Gastric metastases represented 3.8% of all malignant gastric tumors.

Gastric metastases were diagnosed in six women and four men ranging in age from 54 to 88 years old (Table 1).

Upper endoscopies were performed for epigastralgia (two cases), hematemesis (two cases), dysphagia (one case) and anemia (five cases) (Table 1).

The ten gastric tumors were metastases from breast carcinoma in four cases, metastases from lung carcinoma in four cases and metastases from cutaneous melanoma in two cases.

The primary tumor was known in all cases when upper endoscopy was performed. It had been diagnosed from one day to 20 years before gastric metastases were discovered (Table 1).

Some gastric metastases were bulging tumors with a central crateriform ulceration in five cases (Fig. 1), an ulceration in four cases, and an ulcerative and infiltrative lesion which resembled linitis plastica in one case (case no. 3). Tumors were unique in nine cases and bifocal in one case (case no. 10) (Table 1). They were located in the cardia in two cases, in the fundus in five cases and in the antrum in three cases (Table 1). Endoscopic ultrasound was not performed in any case.

CT-scan showed parietal tumors in five cases (cases no. 1,2,4,7,8) (Fig. 2). In the other five cases, gastric metastases were not detected on CT-scan (cases no. 3,5,6,9,10). CT-scan showed splenic (case no. 9), liver (cases no. 5,7,9), peritoneal (case no. 5) and adrenal metastases (case no. 10). MRI was not performed.

Clinical data were provided by the gastroenterologist in all cases; there was a past history of breast carcinoma, lung carcinoma or cutaneous melanoma.

A diagnosis of gastric metastasis was suggested by the endoscopist in two cases (cases no. 9,10). In eight cases, gastric biopsies were performed for bulging tumors or ulcers.

Figure 1 Ulcerative and bulging tumor of the fundus corresponding to a gastric metastasis of lobular breast carcinoma (case no. 1).

Figure 2 Contrast enhanced coronal CT-scan showing thickness of the gastric wall with increased enhancement corresponding to breast carcinoma metastasis (arrow) (case no. 2).

Figure 3 Gastric metastasis of lobular breast carcinoma simulating primitive signet-cell ring gastric carcinoma on the microscopic examination (case no. 3) (HES × 10).
## Table 1: Patients in our series with a diagnosis of gastric metastases.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Sex/Age (years)</th>
<th>Primitive tumor/diagnostic time</th>
<th>Clinical manifestations</th>
<th>Endoscopic features</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F 77</td>
<td>Breast/15 months</td>
<td>Epigastralgia</td>
<td>Fundus, unique</td>
<td>Ulceration</td>
<td>DOD 8 months</td>
</tr>
<tr>
<td>2</td>
<td>F 70</td>
<td>Breast/14 years</td>
<td>Anemia</td>
<td>Fundus, unique</td>
<td>UB</td>
<td>Lost of follow-up</td>
</tr>
<tr>
<td>3</td>
<td>F 88</td>
<td>Breast/20 years</td>
<td>Hematemesis</td>
<td>Antrum, unique</td>
<td>UI (simulating linitis plastica)</td>
<td>DOD 1 month</td>
</tr>
<tr>
<td>4</td>
<td>F 58</td>
<td>Breast/2 years</td>
<td>Dysphagia</td>
<td>Cardia, unique</td>
<td>UB</td>
<td>DOD 4 months</td>
</tr>
<tr>
<td>5</td>
<td>M 65</td>
<td>Lung/concomitant</td>
<td>Anemia</td>
<td>Antrum, unique</td>
<td>Ulceration</td>
<td>DOD 2 months</td>
</tr>
<tr>
<td>6</td>
<td>M 69</td>
<td>Lung/1 month</td>
<td>Anemia</td>
<td>Fundus, unique</td>
<td>UB &quot;volcanoid&quot;</td>
<td>DOD 2 months</td>
</tr>
<tr>
<td>7</td>
<td>M 74</td>
<td>Lung/1 month</td>
<td>Epigastralgia</td>
<td>Cardia, unique</td>
<td>UB &quot;volcanoid&quot;</td>
<td>DOD 2 months</td>
</tr>
<tr>
<td>8</td>
<td>M 54</td>
<td>Lung/5 months</td>
<td>Anemia</td>
<td>Antrum, unique</td>
<td>Ulceration</td>
<td>DOD 1 month</td>
</tr>
<tr>
<td>9</td>
<td>F 64</td>
<td>Melanoma/5 years</td>
<td>Hematemesis</td>
<td>Fundus, unique</td>
<td>UB &quot;volcanoid&quot;</td>
<td>DOD 2 months</td>
</tr>
<tr>
<td>10</td>
<td>F 78</td>
<td>Melanoma/10 months</td>
<td>Anemia</td>
<td>Fundus, 2 lesions</td>
<td>UB &quot;volcanoid&quot;</td>
<td>DOD 3 months</td>
</tr>
</tbody>
</table>

and lobules (Fig. 3). Tumor cells showed nuclear staining eosinophilic cytoplasm, isolated or organized in ribbons features of lobular carcinoma with round cells with an the diagnosis of gastric metastases.

Histohistochemistry was performed in all cases based on clinical data provided by the endoscopist, allowing confirmation of the diagnosis of gastric metastases. Metastases of breast carcinoma had the microscopic features of lobular carcinoma with round cells with an eosinophilic cytoplasm, isolated or organized in ribbons and lobules (Fig. 3). Tumor cells showed nuclear staining with the estrogen receptor antibody in all cases and in one case with the progesterone receptor antibody. Lung metastases were composed of round or cylindrical cells with a compact architecture in three cases and a tubular and cribriform architecture in one case. In all cases, tumor cells showed nuclear staining with thyroid transcription factor-1 (TTF1) (Fig. 4). They were not stained with endocrine markers. Melanoma metastases included large clear cells, some containing a dark melanic pigment with an enlarged nucleus with prominent nucleolus, and a compact architecture. Tumor cells stained with the HMB-45 antibody in both cases and with S-100 protein in one case.

Local treatment was performed in two cases, with an adrenalin injection in one patient (case no. 10) and plasma argon electrocoagulation in another (case no. 6). The stenosed cardial tumor was treated by an esophageal endoprothesis (case no. 4). Proton pump inhibitors were given to all patients. Three patients were already being treated with chemotherapy (cases no. 4, 9, 10). Hormonotherapy was given to two patients (cases no. 1, 2).

Eight patients had other metastases: bone (cases no. 1, 2, 3, 8), brain (case no. 5), liver (cases no. 5, 7, 9), peritoneal (case no. 5), cutaneous (case no. 10), lymph node (cases no. 9, 10), lung (cases no. 9, 10), splenic (case no. 9) and adrenal metastases (case no. 10).

There was no follow-up in one patient. The nine other patients died between one and eight months after the diagnosis of gastric metastases (Table 1).

Microscopic analysis showed adenocarcinoma, most often poorly differentiated in eight cases (except in the two cases of melanoma) suggesting gastric adenocarcinoma. Immunohistochemistry was performed in all cases based on clinical data provided by the endoscopist, allowing confirmation of the diagnosis of gastric metastases.

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Discussion

Gastric metastases (excluding parietal infiltration of the stomach by nearby tumors, such as esophageal, liver or pancreatic carcinomas) represent 3.8% of all gastric tumors diagnosed endoscopically in our series. However, the frequency of gastric metastases is probably underdiagnosed. Autopsy series show that gastric metastases are identified in 1 to 5% of patients who have died from cancer [2—4]. Taal et al. diagnosed gastric metastases by upper endoscopy in 0.3% of patients treated for breast carcinoma [5]; however, autopsy series show that gastric metastases are found in 7 to 18% of patients who have died from breast carcinoma [6—9].

In our study and others, gastric metastases most often develop from breast carcinoma (usually lobular breast carcinoma), lung adenocarcinoma (in particular, large cell carcinoma and small cell endocrine carcinoma) and cutaneous melanoma [1—4,6—11]. There are rare cases of gastric metastases from germ cell testicular tumors, colonic adenocarcinoma, ovarian or endometrial carcinoma... [2—4,12,13].

The clinical signs of gastric metastases are often non-specific. They may be asymptomatic or cause various digestive symptoms, such as epigastralgia, nausea, or vomiting. These clinical signs are often initially considered to be side effects of chemotherapies to treat the primary tumor [4,13].

Gastric metastases can bleed and cause hæmatemesis, melena or anemia [4,13]. There are very rare cases of gastric perforation [5,14] or pyloric stenosis [15].

Imaging features of gastric metastases are unspecific. These tumors are often missed on CT-scan, endoscopic ultrasound and MRI [5]. In some cases, they show a thickened gastric wall or intraparietal tumor nodules, as in four cases of our series [5]. These imaging techniques particularly show other peritoneal, lymph node, liver or splenic metastases.

On upper endoscopy, gastric metastases are more frequently isolated than multiple [5,13]. In most cases, they are located in the cardia or the fundus [5,13], as in our study. These metastases present as ulcerative or bulging tumors. In typical cases, there are volcanoid or crateriform features with a sub-mucosal tumor that is ombilicated, depressed and ulcerated on the top [5,13], as in half of the cases in our series. However, this endoscopic feature is non-specific. Although gastric metastases from melanoma are sometimes black or brown, this stain was not found in the two cases in our series [13].

Gastric metastases are diagnosed from a few days to a few years after discovering the primary tumor [5]. They are rarely discovered before the primary tumor. In two cases in our series, gastric metastases from breast carcinoma were found 14 and 20 years after the diagnosis of the primary tumor. In the literature, one case of gastric metastases was discovered 30 years after diagnosis of the primary tumor [16].

Diagnosis of gastric metastasis may be difficult for the gastroenterologist and the pathologist if clinical data and the past history of the patient is lacking. Gastric metastases can simulate primary gastric carcinoma on upper endoscopy and on microscopic analysis. Gastric metastases from breast carcinoma have the same endoscopic, imaging and micro-
Gastric metastases. An endoscopic series of ten cases

The gastric wall is thickened and rigid due to a sub-mucosal tumor. Like in linitis plastica, superficial gastric biopsies are not sufficient for a microscopic diagnosis in 10 to 30% of cases [5].

Without clinical data the diagnosis of gastric metastasis is difficult for the pathologist. Gastric metastasis can simulate the microscopic features of primary gastric carcinoma, in particular gastric metastasis of lobular breast carcinoma [5,17—19]. Gastric metastasis from melanoma without intra-cytoplasmic melanic pigment can simulate poorly differentiated gastric carcinoma. Although immunohistochemistry is very useful for the pathologist to confirm the diagnosis of gastric metastasis, it is not systematically performed. The pathologist can only be prompted to perform immunohistochemical stains based on clinical data. Breast carcinoma is positive for estrogen receptor (in 70% of the cases), for progesterone receptor (in 30% of cases) and gross cystic disease fluid protein (GCDFP-15) (in 80% of cases) [20]. TTF1 stains lung adenocarcinoma tumor cells in 70 to 90% of cases, small cell lung carcinoma in 90% of cases and of large cell carcinomas in 25% of cases [21]. Melanoma is positive for HMB-45, S-100 protein or melan-A.

There is no consensus for the treatment of gastric metastases. Bleeding metastases can be treated by local injections of alcohol or vasoconstrictors or by electrocoagulation. Surgical resection is limited to emergencies, such as gastric perforation or massive hematemesis [5,22]. Some groups perform partial or total gastrectomy in cases of gastric metastases from melanoma [23,24]. When these metastases are isolated, surgical resection may increase patient survival [23,24]. Chemotherapy and hormone therapy of gastric metastases from breast carcinoma can be effective, in particular in patients who have not yet been treated or have only received a few lines of chemotherapy [5].

Gastric metastases have a poor prognosis. Patients often have metastases in other organs [5], as in our study. Patient survival is often less than 12 months [5,22].

In conclusion, gastric metastases are a rare but probably underdiagnosed entity, which has non-specific gastric symptoms. It is often difficult for the gastroenterologist to differentiate metastases from a primary gastric carcinoma on upper endoscopy and for the pathologist on microscopic examination. Immunohistochemical stains are very useful for confirming the diagnosis of gastric metastasis. However, immunohistochemistry will only be performed if the gastroenterologist provides pertinent clinical data to the pathologist. Treatment of gastric metastasis is often symptomatic. Prognosis is poor and patient survival rarely exceeds 12 months.

Conflict of interest

No conflict of interest.

References