Metastatic involvement and perforation of the appendix in a patient with parotid gland tumor treated with paclitaxel
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Citation

Abstract
Salivary duct carcinoma is an uncommon malignant tumor, characterized by aggressive behavior and poor prognosis. It accounts for approximately 1–3% of all malignant salivary gland tumors (2), and it is found mainly in the parotid gland, followed by the other major salivary glands (2). Histologically, salivary duct carcinoma resembles ductal carcinoma of the breast (3). Immunohistochemically, the tumor cells are positive for keratin and epithelial membrane antigen. Stains for gross cystic disease fluid protein-15 (GCDFP-15) and androgen receptor are frequently positive, but only rare expression of estrogen and progesterone receptors has been described (3). Metastases are a common feature in the evolution of parotid gland cancer. Gastrointestinal metastases, however, and especially appendicular ones, are very rare. The intrinsic nature of malignant metastases in the appendix leads to a late presentation of appendicitis with a high incidence of perforation, associated with an increased mortality and morbidity (1). We describe the case of a patient presenting as an acute abdomen because of metastatic involvement with perforation of the vermiform appendix from a salivary duct carcinoma of the parotid gland treated with paclitaxel.

CASE PRESENTATION
This 69 year old male patient, receiving routine treatment for hyperlipidemia, presented with a nine month history of a mass in the right neck. The patient was afibrile and the mass was not tender. There was no weight loss. Computerised tomography (CT) of the head and neck revealed a mass in the right parotid gland measuring 27 x 22 x 20 mm with associated right cervical lymphadenopathy. A whole body CT scan showed no evidence of distant metastatic spread. Biopsy of the parotid mass revealed a mucoepidermal carcinoma. Right radical parotidectomy with radical neck dissection was performed. Pathological examination of the specimen showed two discrete firm masses measuring 14 mm and 12 mm in diameter, respectively. Of 54 lymph nodes examined, 52 were positive for cancer. The largest of these was 40 mm in diameter at level 2. Areas of cribriform and glandular growth were seen, with cords, nests, and single neoplastic cells adjacent to these areas. There were also areas of dense fibrosis. The tumor cells displayed apocrine features with abundant eosinophilic cytoplasm and pleomorphic nuclei (Fig. 1).

Figure 1
Figure 1: Salivary duct carcinoma.

The tumor resembles the solid and glandular pattern of a salivary duct carcinoma, (hematoxylin-eosin stain, x 200).

Immunohistochemical analysis showed that these cells were strongly positive for pankeratin, epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). Most of the tumor cells were positive for gross cystic disease fluid protein-15 (GCDFP-15) (Fig. 2) and negative for calponin (myoepithelial marker) and estrogen and progesterone...
receptors. The histological and immunohistochemical findings were compatible with salivary duct carcinoma (despite the absence of an intraductal component which is typically seen in salivary duct carcinoma).

**Figure 2**
Figure 2: GCDFP-15 stain

The cells of the primary tumor demonstrate intense positivity for GCDFP-15 stain (GCDFP-15 stain, x 200).

The extensive involvement of cervical lymph nodes suggested the possibility of distant metastatic spread and a PET-CT scan was performed. There was uptake in the right neck compatible with post-operative changes or residual disease, in the ribs, vertebrae (T1 and below), and in the pelvic bones with corresponding lytic lesions on the CT scan, and small nodules were seen in the middle and upper lobes of the right lung without FDG uptake. Because the patient was asymptomatic and no effective treatments for this condition are currently available, supportive care alone was provided. A subsequent PET-CT scan showed substantially increase in bony uptake in the ribs, vertebrae, pelvis, and femora, with underlying lytic lesions. Mediastinal, right axillary and retroperitoneal uptake was also noted. Weekly treatment with paclitaxel was then initiated. Three days after the third infusion of paclitaxel, the patient developed abdominal pain with associated diarrhea and vomiting. The total white cell count was 1,200/mm³ with 600/mm³ neutrophils and the platelet count of 92,000/mm³.

An abdominal x-ray showed small bowel distension but no fluid levels. A CT scan revealed small bowel obstruction with a closed perforation of the caecum and extraluminal gas between the caecum and sigmoid colon. An exploratory laparotomy was carried out. A perforated appendix, liver metastases, and peritoneal deposits were diagnosed. Appendectomy and peritoneal drainage were performed. On histological examination of the appendix, numerous metastatic deposits of large carcinomatous cells were observed (Fig. 3).

**Figure 3**
Figure 3: Metastasis of the carcinoma within the lamina propria of the appendix. (Hematoxylin-eosin stain, x 400)

These cells were similar in appearance to those of the primary tumor in the parotid gland. Immunohistochemical characteristics of the tumor were also identical to those of the parotid tumor, including positive staining for GCDFP-15 (Fig. 4).

**Figure 4**
Figure 4: Metastasis of the carcinoma within the lamina propria of the appendix

Tumor cells are positive for GCDFP-15. (GCDFP-15 stain, x 400).
During the post-operative period he experienced several septic events, and the patient expired over the following weeks.

**DISCUSSION**

Perforation of the bowel in patients with cancer are either a direct consequence of the cancer itself, with malignant perforation occurring at a site directly involved by tumor (1,2), or related to the death of rapidly dividing cells on the gastrointestinal mucosa because of treatment, or due to necrosis associated with neutropenia causing bacterial invasion of the bowel wall. These situations have been reported with bevacizumab, cytotoxic agents, and radiotherapy (4). In many instances the classical clinical picture of an acute surgical abdomen may be masked or distorted by the advanced nature of the malignant process, the high levels of analgesics, in particular opioids often required for pain control, and the concomitant administration of steroids. The differential diagnosis is a non-malignant cause for the perforation, such as an acute suppurative appendicitis. In the present case, the cause of the acute abdomen was most likely a combination of tumor infiltration, as indicated by the histological and immunohistochemical findings, and paclitaxel therapy. Most cases of appendiceal metastases with development of acute appendicitis have been related to breast cancer or cutaneous melanoma (3). Metastatic disease from a parotid cancer to the gastrointestinal tract is extremely rare (5). This is, to our knowledge, the first report of direct metastasis to the appendix from a parotid tumor, with subsequent perforation.

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**References**

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