

# Skin and maxillary sinus involvement of colon cancer

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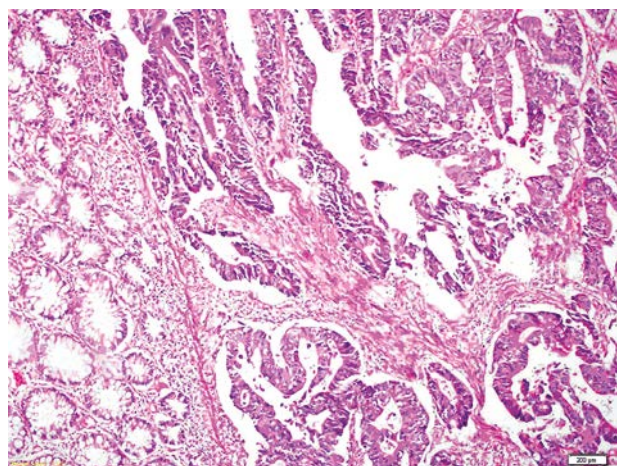
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Cutaneous and maxillary sinus metastases of malignancies are not frequent. The most common malignancies metastasizing to the skin in females are breast cancer (69%), colorectal cancer (9%), malignant melanoma (5%) and ovarian cancer (4%). However, lung cancer (24%) followed by colorectal cancer (19%), malignant melanoma (13%) and cancer of the oral cavity (12%) are the common sites in males [1, 2]. Herein, we present a colon cancer patient with maxillary sinus and skin involvement, which are rarely seen localizations of colon cancer metastasis.

A 62-year-old male patient underwent a surgical operation of right hemicolectomy and was diagnosed with stage III colon adenocarcinoma (pT3N1M0) in May, 2006. The pathology was compatible with moderately differentiated adenocarcinoma (Fig. 1) with clear surgical margins but with vascular and neural invasion. Computed tomography (CT) of the thorax and abdomen revealed no metastatic lesions and he received adjuvant oxaliplatin-5FU based chemotherapy for 12 cycles (Nordic-FLOX regimen; oxaliplatin 85 mg/m<sup>2</sup> day 1, 5FU 500 mg/m<sup>2</sup> and calcium folinate 60 mg/m<sup>2</sup> day 1 and 2 in each 14-day cycle). However, he locally relapsed in September 2011 and underwent surgery for the second time due to intestinal obstruction. Local recurrence at the anastomosis was observed and it was surgically resected with negative surgical margins. Postoperative CT scan revealed multiple lung metastases;



**Fig. 1.** Moderately differentiated colonic adenocarcinoma with hematoxylin-eosin staining (magnification 40×)

thus, a combination chemotherapy of CapeOX-bevacizumab (capecitabine: 2000 mg/m<sup>2</sup> for 14 days, oxaliplatin 130 mg/m<sup>2</sup> day 1 and bevacizumab 7.5 mg/kg day 1 in each 21-day cycle) was started in November, 2011. After three cycles, newly appearing skin metastases with nodular pattern were observed on lips, and the skin of the nape and face with a swelling on the maxillary region of the face (Fig. 2A, B). Serum CEA and CA19-9 level at that time were in normal ranges. Magnetic resonance imaging (MRI) of the maxillary sinus demonstrated a 36 mm × 46 mm × 43 mm-sized infiltrative mass on the anterior wall of the maxillary sinus with orbital invasion (Fig. 3A). The biopsy taken from one of the skin lesions was compatible with metastasis of adenocarcinoma of colon origin (Fig. 3B). Immunohistochemical staining was positive for CK20 (cytokeratin 20) and negative for CK7 (cytokeratin 7) (Fig. 4). Together with skin metastases, also CTscan revealed radiological progression in lung metastases. After then, a combination chemotherapy including irinotecan and capecitabine (irinotecan 180 mg/m<sup>2</sup> dl, capecitabine 1000 mg/m<sup>2</sup> 14 days in each 21-day cycle) was started as a second-line regimen. After two cycles, the skin and maxillary sinus metastases progressed and a cetuximab-irinotecan combination (cetuximab 400 mg/m<sup>2</sup> for initial dose and then 250 mg/m<sup>2</sup> each week, irinotecan 180 mg/m<sup>2</sup> dl every 2 weeks) was started as third-line therapy. He received the second cycle of this regimen last week and he is still alive after six months from the diagnosis of skin and maxillary sinus metastases.

Cutaneous metastases of malignancies are not frequent. Distant cutaneous metastasis occurs by vessel invasion and hematogenous spreading while lymphatic invasion and direct spreading are the most common ways for local cutaneous recurrence [3, 4]. The most common sites of skin metastases are the pelvic region, upper extremities, chest, head and neck region and rarely the glans penis in men [4]. The largest case series of skin metastases from colon cancer in the literature included 80 patients; in 77 cases they were located on the skin of the abdomen [5].

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in women [6]. The most common metastatic sites for colorectal cancer are liver and lung respectively [7]. Skin metastases due to colorectal cancer account for only 5% of metastatic skin

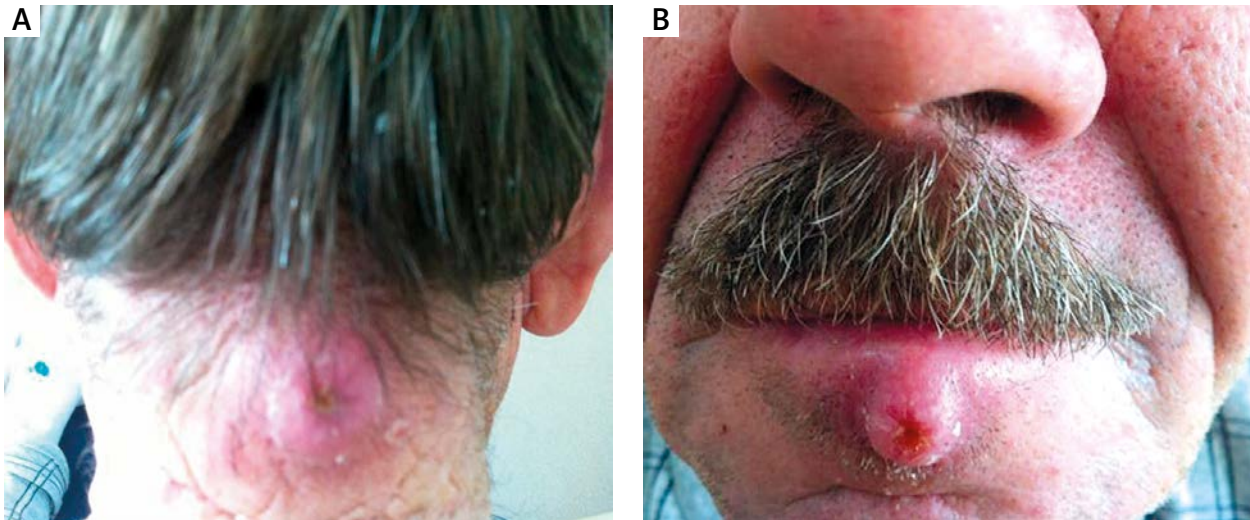


Fig. 2A, B. Photographs of the patient with involvement of the skin of lips and nape

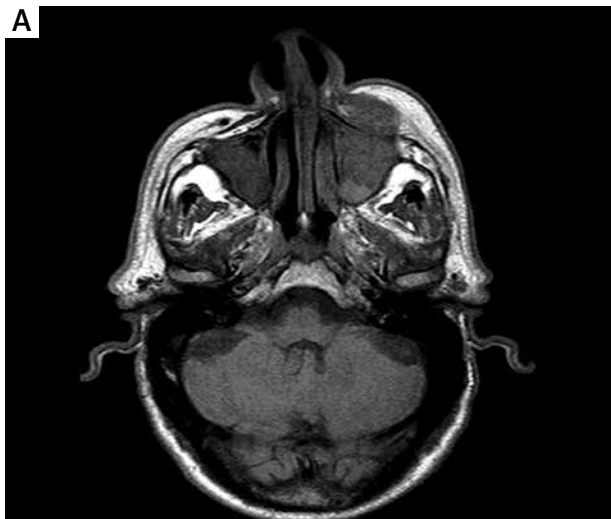


Fig. 3A. Involvement of maxillary sinus with adenocarcinoma in the magnetic resonance imaging

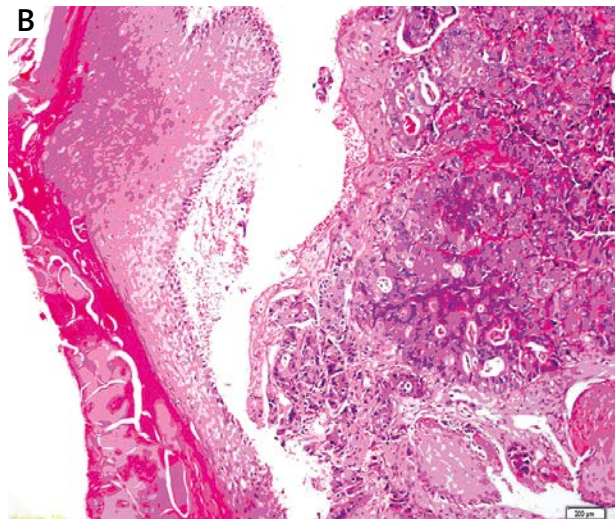


Fig. 3B. Image of adenocarcinoma focus under the normal squamous epithelium of the skin with hematoxylin-eosin staining ( $\times 40$  magnification)

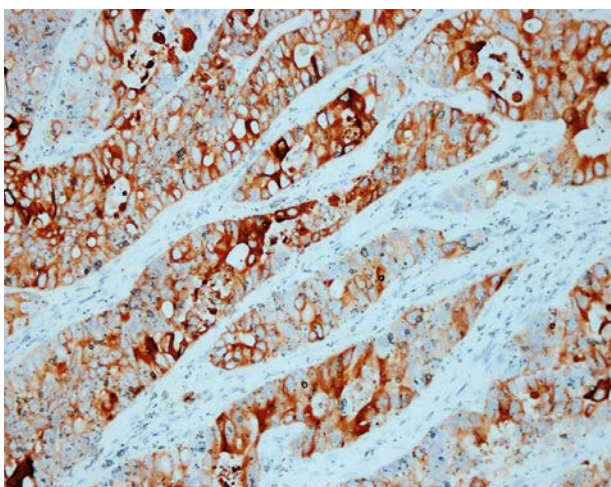


Fig. 4. Immunohistochemically positive staining with CK20 as seen in brown color (magnification 40 $\times$ )

cancers [8], and usually are located on the skin of the abdomen followed by extremities, glans penis in men and head-neck region [9–12]. The presentation of skin metastases can be nodular, ulcerative, or as small tumor deposits [13]. Lookingbill *et al.* reviewed 4020 patients with metastatic cancer, of whom 413 had colorectal carcinoma, and only 18 (4.4%) patients were determined to have cutaneous metastases; of those only one patient had metastatic facial involvement [14]. Cutaneous metastases usually occur approximately 3 years after diagnosis and median overall survival time from the diagnosis of skin metastasis is reported as 18–20 months [4]. The survival of a patient with colon cancer with scalp metastasis was reported as only a few months in a recent paper [8].

Malignancies of the paranasal sinuses are also extremely rare; they account for around 3–5% of all head-and-neck cancers and less than 1% of all malignancies [15, 16]. Maxillary sinus is the most common reported involvement site

of paranasal sinus malignancies. Ten to 20% of all sinonasal malignancies are in adenocarcinoma histology [17]. Many of these originate from salivary glands; however, some of them have similar histologic features as colonic adenocarcinoma and thus are named as "intestinal type adenocarcinoma". The distinction between the metastasis of colonic adenocarcinoma and primary adenocarcinoma of paranasal sinuses is generally performed by using immunohistochemical features of the tumor. CK20-positive/CK7-negative immunoprofile is considered specific for colorectal tumors. The prognosis of metastatic tumors of paranasal sinuses is also reported to be poor [18]. Because of its rarity, only a few cases with poor prognosis are reported in the literature [19–21].

In this case, the patient had skin metastases in the head and neck region and in the pelvic region, which were previously reported as rare localizations of skin metastases in the literature. Additionally he had maxillary sinus involvement at the same time as skin metastases. Our patient developed nodular skin and maxillary sinus metastases 5 years after the diagnosis of colon cancer. The patient did not respond to the first two lines of chemotherapy and progressed rapidly in five months. He is still being treated with third line chemotherapy. In conclusion, skin and maxillary sinus involvement in patients with colorectal cancer rarely occurs and predicts poor prognosis, as was the case in our patient.

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