

Cutaneous metastases of internal cancer

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ABSTRACT

Background Cutaneous metastases of internal malignant tumors are rare. Though, they sometimes reveal the first manifestation of a malignant tumor.

Methods The histopathologic files of two years in two German departments of dermatology (one in Thuringia, one in Saxonia) were investigated for histopathologic evidence of metastatic spread of internal cancer to the skin. Clinical and histologic data were collected. Outcome was evaluated.

Results We observed 11 cases of cutaneous spread of internal cancer. Primary tumors were breast, lung, and GIT cancer in 8 cases, and renal carcinoma, gallbladder carcinoma, and thyroid follicular carcinoma in one case each. Preferred sites were the head and neck region and the trunk, but one tumor was seen on the lower leg. The incidence of cutaneous metastasis due to internal cancer was estimated as 4/8,000-10,000 a year. The cutaneous spread is often a sign of poor prognosis since 3 of 11 patients died within the short mean follow-up of 7.5 months.

Conclusions Despite the fact that cutaneous metastasis of internal cancer is a rare event, one should be aware of it. It seems to be a sign of poor prognosis. A new and rapidly growing tumor on one of the above mentioned sites is suspicious for a cutaneous metastasis. A diagnostic biopsy is recommended in cases where a complete excision is not possible.

KEY WORDS

cutaneous
metastasis,
preferential
sites, biopsy,
histology

Introduction

Cutaneous metastases are quite common in patients with malignant melanoma of skin. Internal malignancies, however, rarely spread to the skin with the exception of breast carcinoma. The incidence of cutaneous metastases in internal malignancies has been reported between 0.7% and 10% (1-5). Any medical doctor dealing with patients should be aware of cutaneous spread

of internal malignancy.

We report on the occurrence of skin metastases in dermatological patients during a 2-year interval in two dermatological departments in Germany, the University-based Department of dermatology and dermatological allergology in Jena and the community-based Academic Teaching Hospital of Dresden-

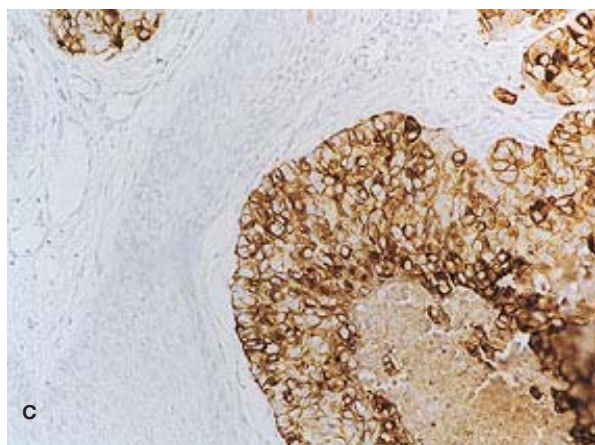
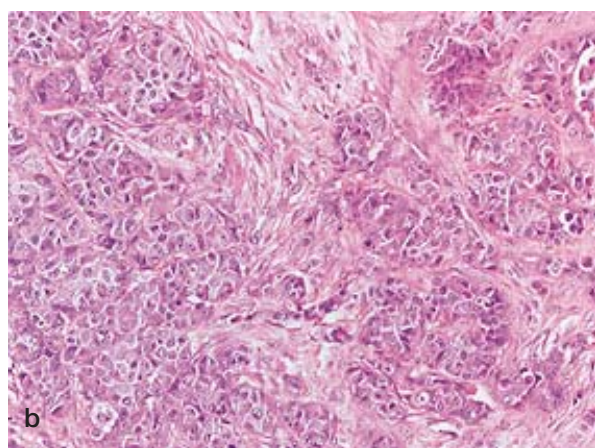
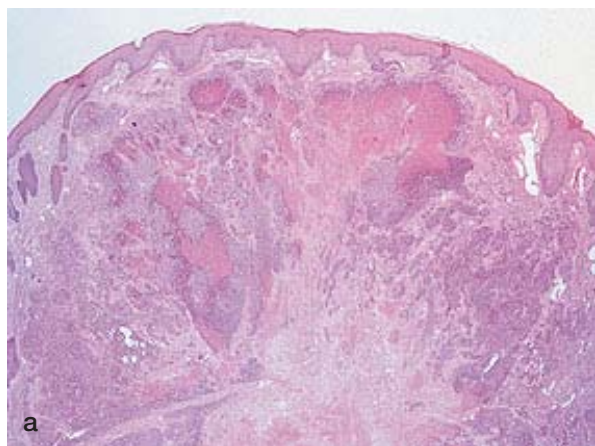


Figure 1. Skin metastasis on the forehead from small cell lung cancer (Case # 8). (a) Overview shows a dermal tumor composed of small cells with prominent nuclei, cellular and nuclear polymorphism and central necrosis (HE, x2). (b) Details (HE, x 20). (c) Positivity for cytokeratin 19 in tumor cells (Eurovision[®]; x 20).

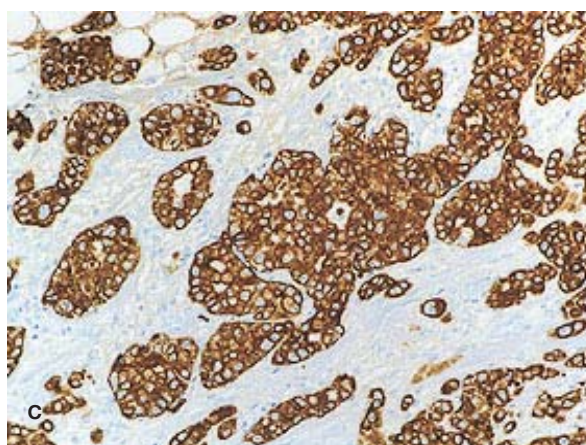
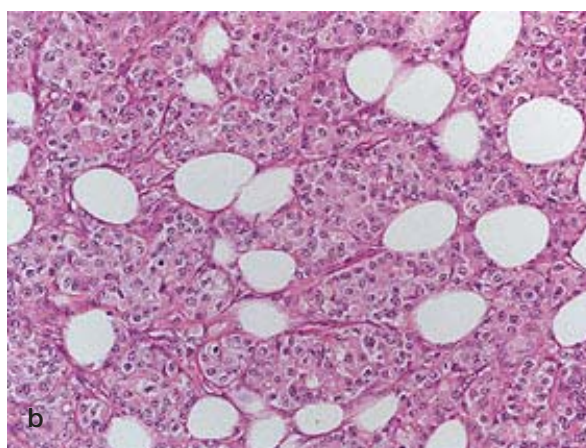
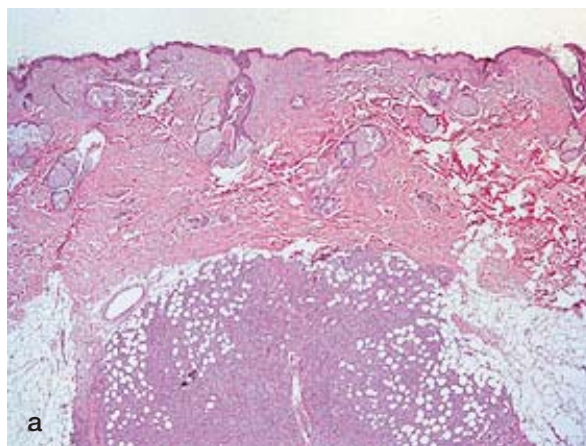


Figure 2. Subcutaneous metastasis on the capillitium from an adenocarcinoma of the gallbladder (case # 7). (a) Overview shows a densely packed glandular tumor infiltrating the subcutaneous fat tissue (HE, x 2). (b) Detail – with prominent cellular and nuclear atypia and polymorphism, numerous mitoses including some atypical (HE, x 20). (c) Tumor cells show strong reactivity for cytokeratin 7 (Eurovision[®]e, x 20).

Friedrichstadt. These departments together run about 100 beds, perform an extended consiliary ser-

vice for the whole Medical School and provide outpatient clinics as well.

Table 1. Data on the 11 patients with skin metastases from internal cancers.

| Patient | Age in years | Gender | Primary malignancy | Site of cutaneous metastasis | Other sites of metastasis |
|---------|-----------------|--------|---------------------------------|---|------------------------------|
| 1 | 51 | male | lung cancer | capillitium | suprarenal gland |
| 2 | 61 | female | breast cancer | lower leg | |
| 3 | 60 | female | stomach cancer | epigastrium | liver |
| 4 | 50 | female | colon cancer | epigastrium | liver |
| 5 | 79 | female | follicular thyroid gland cancer | capillitium | lungs, bone |
| 6 | 97 | female | breast cancer | presternal | |
| 7 | 67 | male | gall bladder cancer | capillitium, fossa supraclavicularis | |
| 8 | 55 | male | lung cancer | forehead | |
| 9 | 89 | female | breast cancer | upper thorax | |
| 10 | 66 | male | stomach cancer | pelvic region | |
| 11 | 74 | female | renal carcinoma | capillitium | lungs, bone, vulva |

Patients and methods

The histopathological files of a 2-year period (1999-2001 for Jena; 2001-2003 for Dresden-Friedrichstadt) provided the basis for collection of patients' data. The departments are of comparable size (about 60 inpatient beds) with a more extended outpatient clinic at the Department in Jena.

Patients with histopathologic evidence of cutaneous spread of internal cancer have been included. A rough calculation of the incidence of cutaneous metastases of internal malignancy was performed on the base of the average number of patients treated per year. Mean follow-up of patients was 7.5 months \pm 10.1 months.

Results

Patients

Eleven patients could be identified including four males (50-67 year old) and seven females (60-97 year old). Two patients asked for consultations by themselves, the other patients were referred to the dermatologist from the departments of internal medicine (1), surgery (4), or by physicians in own practise (GP – 1, surgeon – 1; dermatologist – 4). In nine cases the tumors were completely surgically removed, in two cases palliative radiotherapy was performed. Histopathology: in every case routine hematoxylin-eosin stains were available. Immunostains were performed when necessary by immunoperoxidase technique. Data are summarized in table 1.

Primary tumors were invasive ductal breast cancers (3 cases), lung cancers (2), signet cell carcinomas of the stomach (2), colon carcinoma (1), renal carcinoma (1), follicular thyroid carcinoma (1), and adenocarcinoma of the gallbladder (1). Figure 1 demonstrates the cutaneous metastasis of a small cell lung cancer to the forehead (case # 8). Figure 2 shows a skin metastasis on the capillitium from gallbladder adenocarcinoma (case # 7). The final outcome was death in 3 patients, progression in one, clinical and histologic remission in 5, and a stable disease in 2 patients. In the following we would like to present three case reports that may illustrate the difficulties in diagnosis of cutaneous metastasis from internal cancer.

Case reports

Case 1:

A 54-year old man came to the outpatient clinic with a nodule on the capillitium. There was an 18-month history of this growing tumor. One year before a small-cell lung cancer was found with metastases to the suprarenal gland. He was treated with several cycles of chemotherapy according to an established protocol.

On examination there was a 2 cm large, exophytic, painless parieto-occipital nodule with smooth surface and livid color (Fig.3). The tumor was surgically removed.

Histopathologic examination revealed a diffusely infiltrating tumor of the dermis and the subcutaneous fat. Two different cell populations could be identified: onion-like nests of cells with a cigar-like nucleus and



Figure 3. Skin metastasis from small cell lung cancer: clinical presentation as a firm, painless nodule (case #1).

trabecular cells in the deeper dermis with large basophilic nuclei. Numerous mitoses, some of them atypical, were found. In immunostains these cells showed a diffuse cytoplasmic reaction with a monoclonal antibody against neuron-specific enolase (NSE).

The diagnosis of a cutaneous metastasis of the lung cancer was established.

Therapy and course: the patient got further chemotherapy cycles. No other metastases occurred during a one year follow-up.

Case 2:

A 61-year old woman came to the department because of rapid development (within 6 weeks) of two nodules on her right lower leg. One year before a cervical squamous cell carcinoma was surgically treated. Four weeks before a relapse of the cancer was detected in the small pelvis. She had a clitoris metastasis as well. A palliative radiotherapy was started.

On examination we found two painless nodules of about 1.3 cm and 0.6 cm of a reddish color on the lower leg (Fig. 4), which were surgically removed.

Histopathology yielded similar findings in both lesions: a dermal tumor composed of densely packed solitary and tubular parts surrounded by a capsule-like connective tissue. There was no prominent cellular polymorphism but numerous mitoses, some of them atypical. Immunostainings with Cam 5.2 against glandular keratins and polyclonal antibodies against epithelial membrane antigen (EMA) were positive. S-100 was not detected.

The detection of metastases of a glandular tumor was surprising and could not be explained by her cervix carcinoma. After an indepth interview the patient remembered a breast cancer surgery in 1982. The cutaneous nodules could be identified as late metastases of the breast cancer 18 years after diagnosis of the primary tumor. The patient was treated with radiotherapy thereafter.



Figure 4. Skin metastasis from an invasive ductal breast cancer on the lower leg: erythematous, firm nodule (case # 2).

Case 3:

A 60-year old woman with a severe cholestasis and a history of a subtotal stomach resection 6 months ago, was treated in the Internal medicine department. She developed

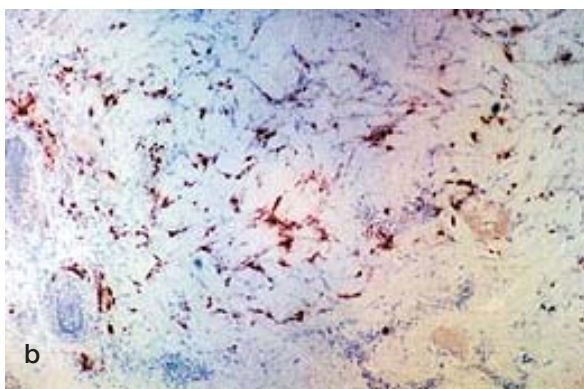
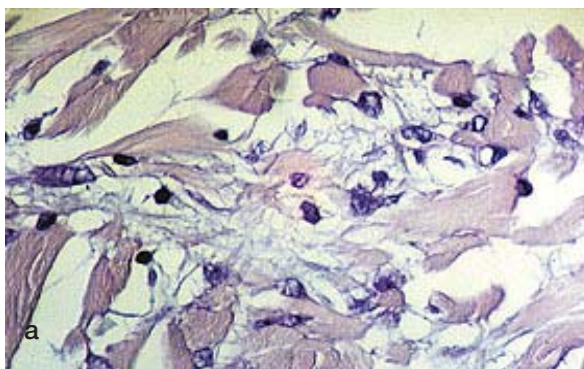


Figure 5. Skin metastasis from a signet-ring carcinoma of the stomach (case # 3): (a) Interstitial tumor cells between collagen bundles (HE, x 40); (b) diffuse dermal and subcutaneous infiltration with Cam 5.2-positive tumor cells (immunoperoxidase).

an 1 cm large soft nodule in the epigastric skin. A metastasis was suspected and the painless tumor was removed.

Histopathologic examination showed a marked mucin-deposition in the dermis. There were large polymorphous cells with half-moon-like nuclei in between the collagen bundles (Fig. 5a). The cells were reactive for glandular keratins (Cam 5.2; Fig 5b) and carcino-embryonal antigen (CEA).

The diagnosis of a metastasis of the signet-ring carcinoma of the stomach was made. The patient died some weeks later.

Discussion

The occurrence of cutaneous spread of internal malignancies is quite rare despite the fact that our skin is one of the largest organs of the human body (1-3). Based on our records, the incidence is about 4 in 8,000 to 10,000 patients of a dermatology department.

Cutaneous metastases can occur either by lymphatic or hematogenic spread. Skin implant metastasis has been observed after percutaneous radio-frequency therapy of a liver metastasis of a colorectal carcinoma (6). Most common sites of cutaneous metastases are the neck and head region and the trunk. The epigastric area seems to be particular prone for cutaneous spread of metastases. Periumbilical metastasis is also known as Sister Mary Joseph's nodule (7). On the other site, metastases on the limbs are even rarer (8,9). In our files we found a single case of metastatic spread to the lower leg from breast cancer. The most common primary malignancies in males are lung cancer and colon cancer. In females breast cancer is the most common with a cutaneous spread (10,11). The present series shows 8/11 patients with lung, breast or GIT cancer.

There is a very low percentage of renal, thyroid gland, ovarian carcinoma, and bladder cancer with cutaneous filiae (4,12-15). We saw three patients with secondaries from renal, thyroid and gallbladder carcinoma.

Extremely rare are cutaneous metastases in carcinoids or chordoma (16,17).

The most common clinical presentation of cutaneous spread of internal cancer is the developments of nodules, usually firm and painless. However, there are exceptions to this rule as shown in patient #3, who developed a soft nodule. Other clinical presentations include neoplastic alopecia, carcinoma erysipelatoides, erythema annulare-like, herpetiform or zosteriform, target-like, pyodermatic, and morphea-like lesions (18-23).

The confirmation of a cutaneous metastasis is not always simple. In case #1 there was a nodule on the typical site of lung cancer spread to the skin – the head. The histopathologic examination, however, did not show cells of the typical oat-cell carcinoma. The positivity for NSE, on the other hand, could eventually confirm the diagnosis. In case #2 a cutaneous metastasis was detected that could not be derived from the suspected primary cancer, a squamous cell cervical cancer. The glandular tumor phenotype led to a breast cancer removed 18 years before that has never caused a metastatic spread during this long period of time. The site of metastasis – the lower leg – is quite unusual.

Though cutaneous metastasis by themselves rarely cause any severe medical problems they may be a sign of unknown internal malignancy, reactivation of malignant disease or a preterminal event (3,24). In many cases, spread to the skin is a sign of systematic spread of disease (3,25,26). In the present series 50% of patients had evidence of secondaries at other internal sites. High-resolution and color Doppler sonography can be helpful in the evaluation of skin metastasis (27). Hypoechoic, irregular nodules with high vascularity are highly suspicious of metastasis. In any case they deserve a histopathologic examination that should be accomplished by immunostaining in case of discrepancies to the presumed primary cancer. Fine needle aspiration cytology may be used as a minimal invasive diagnostic tool (28), but complete excision is still the method of choice to ensure the best quality of histopathologic examination.

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