Skin metastases of lung cancer

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SUMMARY

Skin metastases of lung cancer are rare. In over a 3-year period we found only 14 cases of skin metastases among 1,614 patients with lung cancer admitted to the University Clinic of Respiratory and Allergic Diseases in Golnik. The metastases are usually manifested on the skin of the chest. Skin metastases are symptoms of progressive disease, and usually a sign of a poor prognosis. The median survival time of lung cancer patients with skin metastases was 85 days from the time of detection of the skin lesion. Because skin metastases can be the first sign of the disease, the entire skin should be carefully inspected whenever malignant disease is suspected.

KEY WORDS

skin metastases, lung cancer, patients

Introduction

In Slovenia, lung cancer is the most common malignant disease in males, and the fourth most common among females. In the advanced stage of the disease metastases usually occur in the liver, but can also occur in the brain, bones, kidneys, and adrenal glands (1, 2). According to published studies, 2.8% to 8.7% of patients with lung cancer develop skin metastases (1–3), although some researchers estimate that the incidence reaches up to 24% (4, 5). Lung cancer is responsible for the majority of skin metastases in men and is second only to breast cancer in women (1). Skin lesions are usually found near the primary tumor, most commonly on the chest, head, neck, back, and abdomen, and rarely on the upper and lower extremities (1–4, 7, 8). Skin lesions are always a sign of a poorly differentiated and aggressive cancer, which in all probability has already spread to the other organs (2–4, 7). Prognosis in case of disseminated disease is poor (2–4, 7). In advanced stages, lung cancer can be treated with chemotherapy, radiotherapy, or a combination of both. These therapies are not successful in eliminating skin metastases, or in influencing long-term survival (2, 3).

Patients, material, and methods

Our retrospective study included patients that were histologically and/or cytologically diagnosed with lung cancer and admitted over a 3-year period to the University Clinic of Respiratory and Allergic Diseases in Golnik, Slovenia.

We assessed the incidence of skin metastases of lung cancer, the diagnostic procedure used for confirmation of metastasis, the histological type of lung cancer, and the locations of skin metastases. We were also interested in how often the skin lesion was the first sign of the disease and which diagnostic procedures were used to confirm the diagnosis. Other locations of metastases, therapy, and patient survival were also examined. We used descriptive statistical methods.

Results

From January 2005 to March 2008, 1,614 new cases of lung cancer were diagnosed at the University Clinic of Respiratory and Allergic Diseases in Golnik (nearly half of all of the cases diagnosed in Slovenia during that time period), of which 14 (8 male and 6 female) had skin metastases (0.9%). The median age of patients with skin metastases was 56 (47 to 89) at the time of lung cancer diagnosis.

In three cases, a skin lesion was the first sign of disease; in 11 patients, metastases were found during the physical examination of patients with an evident lung mass on a chest X-ray. In three cases, skin metastases occurred after chemotherapy and were evidently a sign of tumor progression.

In all 14 patients, metastases were found during physical examination. The most common site of skin metastasis was the chest (10 patients). Lesions also appeared on the abdomen, arm, hip, leg, and head (including neck). Metastases on each of these locations or additional locations were found in six patients. Most of the skin metastases were multiple, up to 2 cm in diameter, hard, mobile, sometimes painful nodules covered with a normal skin. In two cases they were not painful, and in one case the skin was eroded and covered with a crust.

The diagnosis of skin metastases was confirmed by fine needle aspiration biopsy in 11 cases, by surgery in one case, and the diagnostic procedure was not mentioned in the medical documentation in two cases.

Among 14 patients with skin metastases, adenocarcinoma was found in six cases, small-cell carcinoma in two, squamous cell carcinoma in three, poorly differentiated carcinoma in two cases, and large cell carcinoma in one instance.

Two patients had only skin metastases, whereas in the other 12 patients metastases were also found in the suprarenal glands (4 patients), liver (2), brain (2), bones (1), chest wall (1), intrathoracic lymph nodes (2), and supraclavicular nodes (1).

Ten patients were treated with chemotherapy, three of whom received additional radiotherapy because of brain, bone, or lymph node metastases. Four patients with poor performance status received only symptomatic treatment. Because of the skin lesions, none of our patients underwent radiotherapy. Eleven patients died during the study period. Their median survival time was 85 days (7 days to 322 days) from the time of detection of the skin metastases.

Figure 1. Skin metastasis on the thorax.

Discussion

Skin metastases of lung cancer are rare, but when present they can be easily seen during a physical examination and the correct diagnosis can be made quickly

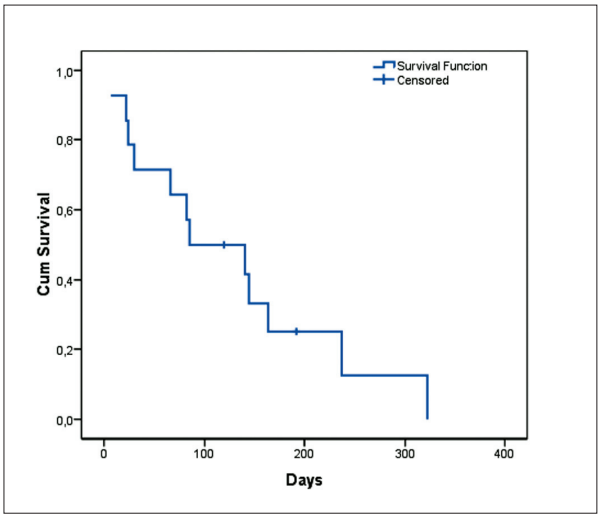

Figure 2. Kaplan-Meier curve of survival in patients with lung cancer and skin metastases.

with a simple needle aspiration biopsy. Compared to the literature, where the incidence of skin metastases of lung cancer was reported to be between 2.8% and 24%, our study found an incidence of only 0.9% (1–5). The reason for the low incidence is difficult to explain. We assume that this is just another number in a very a diverse range of incidences mentioned by other authors. It is also worth noting that skin metastases are probably often overlooked because physical examination is not thorough enough.

Patients with lung cancer present with different leading symptoms or signs. The majority have respiratory symptoms (cough, hemoptysis, and dyspnea). Some patients present with symptoms related to disease progression (general fatigue, chest pain, or pain due to bone lesions). Only a minority of patients have dermal signs as a first sign of the disease (3). According to the literature, skin metastases were the first sign of disease in 7 to 19% of patients with lung cancer (1, 4, 6). In our study, the incidence of skin metastases as the first sign of lung cancer was much lower, only 0.2%.

Tumors spread to the regional skin, in all probability through the lymphatics, and subsequently were further disseminated through the blood stream (7). Our study confirmed that skin lesions are most commonly found on the chest; all other locations were present in 29% of the patients.

Metastases of lung cancer are macroscopically undistinguishable from metastases of other cancers. Usually they present as a fast growing, solitary nodule or multiple nodules with a diameter of 5 mm to 10 cm (Fig. 1). They are firm, mobile, and covered with normal skin. Sometimes exudative or ulcerated lesions and nodules covered with pigmented skin are found. Authors generally agree that the lesions are not tender (1–4, 6, 9, 10); however, surprisingly, some of our patients complained about painful nodules.

When a suspicious skin lesion is found in a lung cancer patient it is very likely to be a metastasis, but fine needle aspiration biopsy or histological examination of the lesion are the gold standards for diagnosing skin metastases (2, 7). Some researchers also propose immuno-histological and immuno-histochemical appraisals (9, 10). Our clinic usually confirms suspicious skin lesions by fine needle aspiration biopsy.

Terashima and Hidaka et al. confirmed that large-cell carcinoma has the greatest tendency to spread into the skin (10.3%), with adenocarcinoma in 3.1 to 3.4%, microcellular carcinoma in 1.7 to 2.0%, and epidermoid carcinoma occurring in 0.4 to 1.5% of cases. Nevertheless, adenocarcinoma is the most common lung carcinoma, and its skin metastases are consequently the most frequent.

Kimble et al. used radiotherapy and chemotherapy (a combination of capsulation and VP-16, adriamycin, and vincristine), or a combination of both. They concluded that neither therapy cures skin metastases (2). Hidaka et al. used a combination of cisplatin, cyclophosphamide, adriamycin, interferon-â mitomycin, vindesine, etoposide, and carboplatin, also without significant success. Two patients underwent radiotherapy for the skin lesions, resulting in their temporary reduction (3). Both studies concluded that chemotherapy has less effect on skin metastases than on the primary tumor, probably because of poorer blood supply to the skin in comparison to the lung (2, 3). Our clinic also used chemotherapy with different chemotherapeutics in the treatment of advanced lung cancer: in small cell carcinoma, Cisplatin + Vepesid or Endoxan + Farmorubicin + Oncovin; in non-small cell carcinoma, Gentamycin + Cisplatin. We did not observe any significant therapeutic influence on the skin metastases. Chemotherapy in advanced lung cancer is essentially palliative. Its most important effect is symptom relief and an improvement in quality of life. Surgical removal is indicated only when tissue is needed for histological examination, when metastasis causes pain due to local invasion, or when metastasis causes a significant functional or cosmetic inconvenience (9). Palliative chemotherapy is used in the case of disease progression (6). Palliative radiotherapy might be useful for bleeding or painful skin metastases (2).

Despite the combination of radio- and chemotherapy, patients with lung cancer that has spread to the skin have a poor prognosis. For patients with clinical stage IV disease (distant metastases), the 5-year survival rate was 2%, with a median survival of 6 months (11). The median survival time of a patient with lung cancer and skin metastases is 3 to 4 months (1 to 19 months). Survival time longer than 10 months is rarely observed (1–4). Our 12 patients that died had a median survival time of less than 3 months (85 days) from the time skin lesions were found. The other two patients were still alive at time of data analysis, with follow-up at 4 and 6 months.

Conclusions

Skin metastases of lung cancer are rare. They are a sign of an aggressive, malignant tumor. In differential diagnosis of a newly developed skin lesion, metastasis of lung cancer must be considered, especially if the lesion is firm, slowly growing, and the patient has a history of smoking. It is important to stress that all surgically removed skin lesions should be histologically examined.

A careful physical examination, including skin inspection and palpation, is important for correct and rapid diagnosis of lung cancer, as well as for staging and treatment planning.

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