Skin Metastases from Primary Lung Cancer. Report of Three Cases and a Brief Review

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Abstract. Skin metastasis from lung cancer is an unusual event carrying an ominous prognosis. Three cases with non-small cell lung cancer (NSCLC) with skin involvement and rapidly fatal clinical course due to extensive CNS metastasis are reported. The eventual association of skin metastases and a phenotype with "CNS-predilection" or an aggressive phase of NSCLC are discussed.

Lung cancer is a common neoplasm, in most cases fatal, affecting men and women usually after the age of fifty. Only early stage operable disease can be cured, while the remainder of patients develop distant metastases and die. Most common sites of metastasis include the bones, liver, adrenal gland and brain, while the skin is rarely affected and is an indicator of bad prognosis. We report here three cases with non-small cell lung cancer (NSCLC) and skin metastases, their clinical course and outcome.

Case Presentation

Case 1. A 60-year-old man was diagnosed by bronchoscopy biopsy with a stage IIIa poorly-differentiated lung adenocarcinoma. The patient received three courses of chemotherapy with docetaxel and gemcitabine with no response, followed by three courses of carboplatin and vinorelbine with neither detectable response nor evidence of progression. The tumour was thereafter irradiated with 40 Gy. All therapy was completed in approximately five months from the initial diagnosis.

A month after discontinuation of therapy, the patient presented with multiple nodules in the skin of the abdominal and chest wall, the inner side of the right thigh and the neck. Skin lesions were nodular, measuring 1-1.5 cm arising from the subcutaneous tissue. Fine needle aspiration biopsy showed adenocarcinoma and surgical excision biopsy confirmed the cytological diagnosis. The morphological findings of the skin lesion were compatible with the primary lung tumour. A restaging work-up was then performed that revealed bone and brain metastases; the latter, multiple and extensively involving the brain, were associated with severe CNS symptoms, predominantly those of increased intracranial pressure. The symptoms regressed partially with corticosteroid administration; the patient denied total cranial radiotherapy and died four months later from septic shock, probably secondary to an opportunistic infection, without evidence of dissemination other than bone and skin.

Case 2. A 69-year-old woman presented with a right middle lobe lung mass. Radiological findings and sputum cytology were consistent with a stage IIb primary lung adenocarcinoma. Given a history of bilateral breast cancer, treated with bilateral mastectomy 15 years before, 6 IV, CMF courses and 5 years of tamoxifen as adjuvant therapy, a full work-up to exclude metastasis from breast cancer was performed. However, no evidence of recurrent breast cancer could be documented and the lung tumour was considered as primary adenocarcinoma of the lung. The patient received six cycles of docetaxel 100 mg/m² monotherapy with a major partial response.

Six months after completion of chemotherapy, while maintaining disease remission, the patient developed skin metastases in the chest wall and the proximal arms. FNA and excisional biopsy of two skin lesions showed adenocarcinoma consistent with lung rather than breast cancer metastasis (pathological evaluation). Two months later she was hospitalized for status epilepticus. A CT scan revealed multiple metastatic foci in the brain and the patient received total cranial irradiation, 30 Gy, without significant improvement. The patient died a month after completion of radiotherapy and 3 months from the diagnosis of skin metastasis.

Case 3. A 79-year-old man presented with nodular lesions on the skin of the neck and over the left scapula. FNA findings from the lesions were compatible with a possible...
adenocarcinoma and after a full clinical and radiological evaluation the patient was diagnosed with primary lung cancer in the left upper lobe. Sputum cytology showed squamous cell carcinoma while a second fine needle aspiration was consistent with the sputum cytology, revealing infiltration from squamous cell carcinoma. As the patient was not a candidate for systemic chemotherapy because of advanced age and poor performance status, only a surgical removal of the neck nodule was offered in order to decrease "emotional distress" and relieve local pain; also, standard supportive care was provided. Two months later the patient was found to have bone and peritoneal metastases, as well as intramuscular nodular lesions in the pelvic region; moreover, a CT scan revealed extensive metastatic disease in the brain, that was treated only with corticosteroids and supportive care. The patient died 4 months after lung cancer diagnosis first presented with skin metastasis.

Discussion

We described three cases with NSCLC and skin metastases. Adenocarcinoma was the histological type in two of them, while the third patient had a squamous cell lung carcinoma. A full pathological assessment of the primary tumour was not feasible in all patients, in contrast with the skin lesions, where a complete biopsy was performed in all cases. All three patients had similar nodules located on the thorax, neck and proximal sites of the extremities, which were associated with aggressively progressive disease, two of them in the viscera and all of them in the CNS. Although some characteristics of the disease differed considerably, metastatic fatal dissemination, soon after the diagnosis of skin involvement, led us to further examination of these patients.

A literature review on skin metastases from primary lung cancer yielded a very limited number of publications. Breast cancer is the solid tumor that most commonly metastasizes to the skin (1); however, lung cancer also spreads to the skin in up to 7% of patients, ranging from 1.5% to 12% of patients (2, 3) in different reports, while malignant melanomas, renal cancer and tumours of the mouth, pharynx, colon, ovaries and stomach involve the skin less frequently (4). Average survival following diagnosis for all types of tumors is 7.5 months (5).

Skin areas usually affected by lung cancer metastasis are the chest wall, neck, abdominal wall, scalp, dorsum and face (6-8) but the scrotum, lip, nose, perianal region (9) and fingers (10) have also been reported. In a large retrospective study of patients with lung cancer and skin metastases (9), adenocarcinoma was found to be the predominant cell type of cutaneous spread, but other investigators support that the skin is equally affected by all histological types (7). A case of basaloid carcinoma presenting with cutaneous metastasis has also been reported (11). Nodular lesions can be either solitary or in clusters, usually painless, 0.5 to 5 cm in size, but lesions measuring 15 cm, or more are also encountered. They may appear as inflammatory or ulcerating, but also as erythematous papules. The skin is reported to be the first site of metastasis in about 25% of lung cancer cases (7). The presence of skin metastases indicates an ominous prognosis. If other extracutaneous metastases exist, median survival does not exceed three months (12); however, if the skin is the only site of metastatic disease, survival can reach 10 months (7). Response to chemotherapy is poor, possibly because of poor blood supply to the skin (8).

The surgical removal of a solitary skin lesion, without any signs of metastatic disease elsewhere, should always be considered. It has been proven that surgery for solitary brain (13) or adrenal (14) metastasis improves survival; this may also be the case with skin metastasis although, given its rarity, is difficult to demonstrate.

The clinical manifestations and course of our three patients with NSCLC were, in general, quite similar to those reported in the literature. All had subcutaneous nodules extending to the epidermis and all progressed to visceral sites and died within 3-4 months from skin metastasis diagnosis.

In the case with co-existent breast cancer, the recurrence of the "old" primary was excluded by the following: standard pathological criteria, tumour markers, the presence of one parenchymal lesion with nodal involvement and intrabranchial expression of cancer; the long interval between breast cancer and "relapse" was also taken into account. However, a recurrence of breast cancer cannot definitely be rejected.

Of particular interest is the presence of extensive CNS involvement in all three patients; although this is a rather early event in lung cancer, the multifocality is not the rule. The presence of extensive CNS disease might therefore suggest either a particular with "CNS-predilection" phenotype or a rapidly progressive phase of the disease associated with skin involvement. To our knowledge, such an association has not been reported so far.

In conclusion, whether cutaneous spread is associated with a particular biological behaviour of NSCLC or simply heralds widespread dissemination of cancer cannot be answered. This case report study may contribute to the understanding of NSCLC cancer natural history, emphasising the unfavourable prognosis of skin involvement in this malignancy and the need for appropriate treatment decision in such cases.

References


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