Multisystem Langerhans cell histiocytosis coexisting with metastasizing adenocarcinoma of the lung: A case report

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Abstract

Introduction. Langerhans cell histiocytosis (LCH) is an uncommon disease of unknown etiology characterized by uncontrolled proliferation and infiltration of various organs by Langerhans cells. Case report. We presented a 54-year-old man, heavy smoker, with dyspnea, cough, hemoptysis, headache and ataxia, who died shortly after admission to our hospital. On the autopsy, tumor was found in the posterior segment of the right upper pulmonary lobe as well as a right-sided occipitoparietal lesion which penetrated into the right ventricle resulting in internal and external hematocephalus. Histologically and immunohistohemically, the diagnosis of primary lung adenocarcinoma with brain metastasis was made (tumor cells showed positivity for CK7 and TTF-1 which confirmed the diagnosis). In the lung parenchyma around the tumor, as well as in brain tissue around the metastatic adenocarcinoma histiocytic lesions were found. Light microscopic examination of the other organs also showed histiocytic lesions involving the pituitary gland, hypothalamus, spleen and mediastinal lymph nodes. Immunohistochemical studies revealed CD68, S-100 and CD1a immunoreactivity within the histiocytes upon which the diagnosis of Langerhans’ cells histiocytosis was made. Conclusion. The multisystem form of LCH with extensive organ involvement was an incidental finding, while metastatic lung adenocarcinoma to the brain that led to hematocephalus was the cause of death.

Key words: histiocytosis, langerhans-cell; diagnosis; lung neoplasms; adenocarcinoma; immunohistochemistry.

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Introduction

Langerhans cell histiocytosis (LCH) includes diseases previously designated as histiocytosis X, eosinophilic granuloma, Letterer-Siwe disease, Hand-Schuller-Christian syndrome and Langerhans cell granulomatosis. This is an uncommon disease of unknown etiology characterized by uncontrolled proliferation and infiltration of various organs by Langerhans cells, often organized into granulomas. It occurs predominantly in children and young adults, but no age is an exemption. Practically any organ can be involved, but bone and skin are the sites of predilection. Patients are categorized as having single-system disease at a single or multiple sites, or as having multisystem disease. Single-system disease of LCH involves mainly bones or lungs and usually follows a benign course and can regress spontaneously. The clinical presentation of multisystem LCH, which carries a poor prognosis in a number of cases, is highly variable depending on the organs involved, mainly bones, skin, lungs, pituitary glands and less commonly liver, spleen, hematopoietic and central nervous system. The association of single-system disease with malignant neoplasm is not so rare (particularly in association with malignant lymphoma), but association of multisystem LCH with a malignant neoplasm is rare and, generally, has been the subject of isolated case reports. To our knowledge, this is the first case reporting on the association of multisystem LCH with metastasizing adenocarcinoma of the lung.

Case report

A 54-year-old man, heavy smoker (30 years/3 packs a day), was admitted to our hospital for further diagnostic approach to the radiologically detected change in the right lung. Four months before admission shortness of breath and cough with hemoptysis occurred, and a month before admission the patient was referred to the neurologist because of walking instability, loss of strength in the left half of the body, and morning headaches. Computerized tomography (CT) scan of the endocranium showed right-sided occipitoparietal lesion, which primarily exhibited characteristics of secondary infiltration, and CT scan of the thorax showed inhomogeneous, extensive infiltration predominantly localized in the upper lobe. On the fourth day after admission hemoptysis occurred, and bronchoscopic examination was performed, but histopathological findings did not clarify the etiology of the change. After two days a deterioration in general condition with intense headache developed, and despite all the applied therapeutic measures the patient passed away.

At autopsy, macroscopic examination of the lungs revealed an excavated tumor mass 1.8 cm in largest dimension in the posterior segment of the right upper lobe, which histopathologically corresponded to adenocarcinoma. In brain parenchyma, right-sided occipitoparietal necrotic, and hemorrhagic lesion 5.7 × 3.8 cm in largest diameter, which penetrated into the right ventricle resulting in internal and external hematocephalus, was observed. Histologically and immunohistochemically, the diagnosis of primary lung adenocarcinoma with brain metastasis was made (tumor cells showed positivity for CK7 and TTF-1 which confirmed the diagnosis) (Figures 1a and 1b).

Within the tumor, in the lung parenchyma around the tumor, as well as in the brain tissue around metastatic adenocarcinoma, histiocytic lesions were found (Figure 2a). Light microscopic examination of the other organs also showed histiocytic lesions involving the pituitary gland, spleen, hypothalamus, and mediastinal lymph nodes (Figures 2b and 2c).

Fig. 1 – a) Adenocarcinoma of the lung (HE, × 10); b) Metastatic adenocarcinoma in the brain parenchyma (HE, × 5).

Fig. 2 – a) Histiocytic lesion within the lung parenchyma around the tumor (HE, × 10); b) Histiocytic lesion in the mediastinal lymph node (HE, × 10); c) Histiocytic lesion in the hypothalamus (HE, × 20).
These histiocytic lesions were made of clusters and sheets of characteristically ovoid cells with abundant, lightly eosinophilic cytoplasm, grooved or contorted nuclei, fine chromatin, a thin nuclear membrane and inconspicuous nucleoli. Multinucleated giant cells were also present. Immunohistochemical studies revealed CD68 (histiocytic marker), cytoplasmic protein S-100 and glycoprotein CD1a (a marker of Langerhans’ cells) immunoreactivity within the histiocytes upon which the diagnosis of LCH was made (Figures 3a, 3b and 3c).

Discussion

Analysis of a large cohort of Mayo Clinic patients (314 patients between 1946 and 1996) with histologically proven LCH showed that 96 patients had LCH involving multiple systems, 114 had isolated osseous LCH, and remaining 104 had nonosseous single system LCH. Only 27 of 314 patients had coexisting neoplasms. Five patients had lung carcinoma (four adenocarcinoma and one small cell carcinoma), but all of them had pulmonary LCH without involvement of other organs with Langerhans’ cells. Four patients had multisystem LCH (mostly involving bones, skin, lymph nodes and pituitary gland) coexisting with breast adenocarcinoma, parathyroid adenoma, pancreatic cystadenoma and pontine mass.

A group of authors at the University of Minnesota reviewed their own charts as well as reported cases in the literature between 1960 and 1992. Of the 91 patients, 39 had LCH with malignant lymphoma (25 of these cases were Hodgkin disease), in 22 patients LCH was reported in association with leukemia, and in remaining 30 patients LCH was associated with a variety of solid tumors, including lung carcinoma in 12 patients (nine adenocarcinoma, two large cell carcinoma and one squamous cell carcinoma). In 11 cases of associated lung carcinomas and LCH, the diagnosis of LCH was confined pathologically to the lung. In one case reported by Hammar et al. LCH affected bone and lung and is the only reported case of lung adenocarcinoma coexisting with LCH which was not limited to the lung. According to these two studies, simultaneous association of LCH with lung carcinoma suggest that pulmonary LCH represents a reaction to the tumor.

Conclusion

LCH remains a rare, enigmatic disease which, in most cases, is detected relatively late in its course and which should be included in the differential diagnosis of patients with multisystem disease. In this case, the coexistence of multisystem LCH with extensive organ involvement and metastastic lung adenocarcinoma (that led to hematopoietic and death) represents a coincidental finding, because only in case of a single-system disease one can speak about the reactive nature of LCH.

References


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