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HORNER'S SYNDROME INDICATES BREAST CANCER PLEURAL METASTASES

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Summary

Horner's syndrome results from an interruption of the sympathetic nerve supply to the eye, and is characterized by the classic triad of miosis (ie, constricted pupil), partial ptosis, and loss of hemifacial sweating (i.e. anhidrosis). The most common factor producing the preganglionic Horner's syndrome is a malignant tumor. We report a case of Horner's syndrome in a young woman with a history of breast cancer. Radiographic methods revealed one-sided metastatic pleural effusion as cause of the sympathetic lesion. Metastatic breast disease usually affects lungs, bone, liver, adrenals and skin, and it is highly unusual for ocular involvement to be the first sign of its existence. This report presents a rare case of pleural metastatic breast cancer causing Horner's syndrome/Pancoast syndrome without lung involvement.

KEYWORDS: *Horner's syndrome, pleural effusion, breast cancer*

HORNEROV SINDROM PROUZROČEN PLEURALNIM METASTAZAMA KARCINOMA DOJKE

Sažetak

Hornerov sindrom nastaje zbog prekida simpatičke živčane opskrbe oka. Karakteriziran je klasičnom trijadom koju čine mioza (konstrikcija pupile), parcijalna ptoza i hemifacijalna anhidroza. Najčešći uzročnik preganglijskog Hornerovog sindroma su zloćudni tumori. Mi smo prikazali slučaj Hornerovog sindroma u mlade žene s karcinomom dojke. Radiografske pretrage su pokazale jednostrani pleuralni izljev kao uzrok simpatičke lezije. Metastaze karcinoma dojke obično zahvaćaju pluća, kosti, jetru, nadbubrežne žlijezde i kožu, te su krajnje neuobičajeni simptomi od strane oka kao prvi znak postojanja metastaza. U radu je prikazan rijedak slučaj pleuralnih metastaza karcinoma dojke bez zahvaćanja samih pluća koje su prouzročile Hornerov/Pancoastov sindrom.

KLJUČNE RIJEČI: *Hornerov sindrom, pleuralni izljev, karcinom dojke*

INTRODUCTION

Breast cancer is the second most common cause of cancer-related death in women. Aside from lymph nodes, to which one-third of breast cancers have metastasized to at presentation, breast cancer has a tendency to spread to the lungs, bone, liver, adrenals and skin. The thorax is a common site of metastasis, which may affect the lymph nodes, bone, lung, pleura, or heart and pericardium (1). Intrapulmonary metastasis may manifest as single or multiple pulmonary nodules, airspace pattern metastasis, lymphangitic metastasis, or endobronchial metastasis (2). Pleural metastasis usually manifests as pleural effusion, with or without a pleural mass (2). Currently, lung cancer is the most common metastatic tumor to the pleura in men and breast cancer in women. Together,

both malignancies account for approximately 50–65% of all malignant effusions (3). About 7 to 11% of patients with breast carcinoma develop a malignant pleural effusion during the course of the disease (4). For lung, breast and ovarian metastases, 92% of pleural effusions are ipsilateral to primary lesion (5). Besides the rare direct invasion through the chest wall, the pathogenesis of pleural involvement in breast carcinoma is through either lymphatic (internal mammary artery lymph node chain) or hematogenous spread. Horner's syndrome results from an interruption of the sympathetic nerve supply to the eye, and is characterized by the classic triad of miosis (i.e., constricted pupil), partial ptosis, and loss of hemifacial sweating (i.e., anhidrosis). Horner's syndrome can be congenital, acquired, or purely hereditary (autosomal dominant). The interruption of the sympathetic fibers may occur centrally (i.e., between the hypothalamus and the fibers' point of exit from the spinal cord [C8 to T2]) or peripherally (i.e., cervical sympathetic chain, superior cervical ganglion, along the carotid artery). Sympathetic innervation to the eye consists of a 3-neuron arc. Lesion at any location along this pathway between the hypothalamus and the orbit results in ipsilateral Horner's syndrome (6). The most frequent factors producing the preganglionic Horner's syndrome are malignant tumors (7). Common tumor-associated causes of acquired Horner's syndrome include Pancoast tumor, metastasis to cervical lymph nodes, and malignant pleural mesothelioma (8). It may be caused by extension of the tumor into the paravertebral sympathetic nerves and/or pressure on the sympathetic plexus. It is well known that preganglionic Horner's syndrome/Pancoast syndrome is most often caused by Pancoast tumor. This report presents a rare case of pleural metastatic breast cancer causing Horner's syndrome without Pancoast tumor as the first sign of tumor dissemination.

CASE REPORT

A 43-year-old woman was admitted to our hospital because of left palpebral ptosis. Her medical history was notable for grade II left breast infiltrating ductal carcinoma 14 months ago. 12/18 axillary lymph nodes were positive for tumor. Immunochemistry showed that the lesions were estrogen and progesterone receptor-positive with

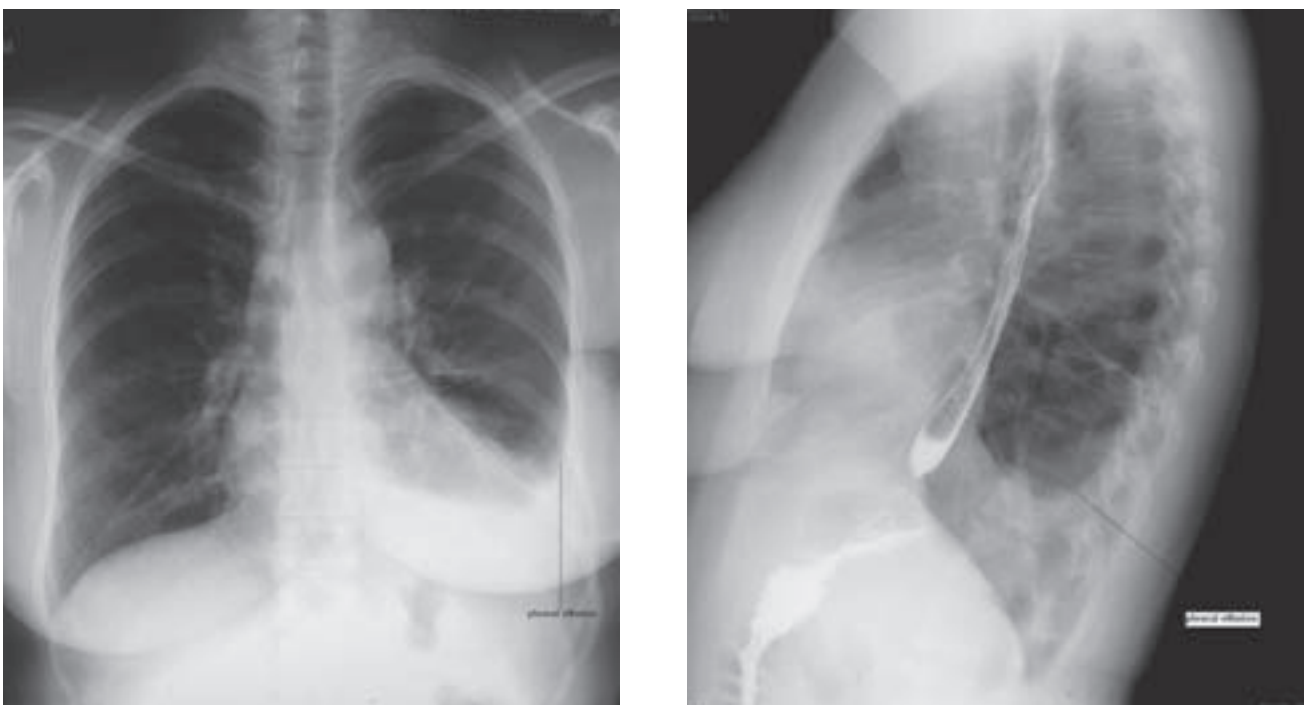

Figure 1. (a) posteroanterior view, (b) lateral view. With standard upright radiographs, pleural effusions are typically found originating below the lung, and create a meniscus that blunts the costophrenic angle and then tapers off superiorly.

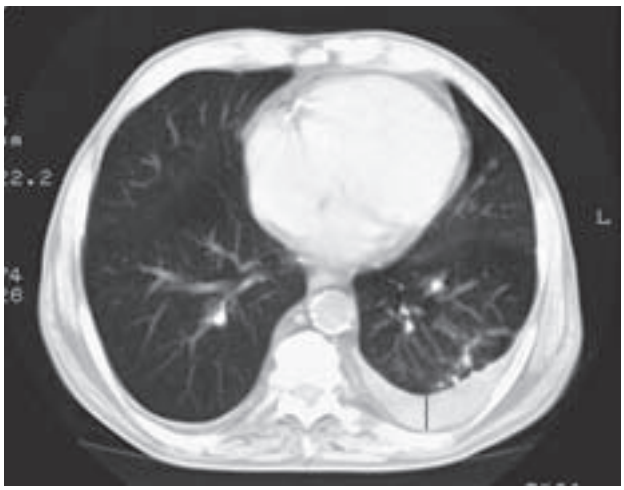

Figure 2. Axial section through thoracic outlet scans shows left dorsal pleural effusion with no pleural neither pulmonary mass.

overexpression of HER-2/neu. The patient underwent conservative treatment – segmental mastectomy, postoperative first-line chemotherapy (CMF protocol), radiation therapy (External Beam Radiation) and hormone therapy (tamoxifen). At admission, she denied associated symptoms. On physical examination, the patient had ptosis, myosis, anhydrosis and enophthalmos on the left side, suggesting Horner's syndrome and no definitive other neurologic abnormalities. We performed MRI scan of the head and neck. There was no obvious metastatic process of CNS or cervical lymph nodes. A standard upright chest radiograph showed a moderate-sized left pleural effusion (Figure 1a, 1b). A subsequent thoracic CT scan confirmed the pleural effusion on the left hemithorax and pleural thickening with no significant chest or pleural mass (Figure 2). Thoracentesis yielded adenocarcinoma cells in pleural fluid. Ultrasonographical examination of the abdomen revealed multiple liver metastases. In the next few weeks, the patient started to complain of dull ache in the shoulder, lancinating pains in the elbow and pain and dysesthesia in the ulnar aspect of the hand, weakness in the left hand, as well as shortness of breath and back pain. These symptoms, clinical examination, electromyography evaluation, and repeated chest radiograph revealed a lesion of the low brachial plexus, as well as enlargement of the pleural effusion. Treatment was initiated with second-line chemotherapy (paclitaxel) and immunotherapy (trastuzumab). With completion of the chemotherapy cycle, liver metastases were reduced but the pleural effusion and Horner's syndrome were unchanged in their intensity at the initiation of therapy. Immunotherapy was continued for a short time further until the patient refused any suggested conventional therapy, and died after a period of approximately 6 months.

DISCUSSION

This report presents a rare case of pleural metastatic breast cancer causing Horner's syndrome without upper lobe pulmonar tumor as the first sign of tumor dissemination. According to the literature, the major cause of Horner's syndrome is neoplasia, with malignant lesions being twice as frequent as benign tumors (7). Metastatic breast disease usually affects lungs, bone, liver, adrenals and skin, and it is highly unusual for ocular involvement to be the first sign of its existence (9). Nevertheless, among malignant tumors, breast cancer is the primary tumor most frequently metastasizing to the ocular structures. A wide spectrum of ophthalmic manifestations could be found, including cranial nerve involvement, brain involvement with papilledema, Horner's syndrome, and choroidal and orbital tumors (10). With corresponding diagnostic techniques, we excluded CNS/orbital metastasis in our patient. The most common tumor manifestations that could be etiologically related to acquired Horner's syndrome include Pancoast tumor, metastasis to cervical lymph nodes, and malignant pleural mesothelioma (8). Cancers of the top of the lung (the portion closest to the collar bone) may grow into the nerves that supply the arm, making the arm painful, numb, and weak—this combination of symptoms is called Pancoast syndrome. Pancoast syndrome and Horner's syndrome may coexist (11). Our patient showed no clinical or radiological signs (MRI, CT, standard upright chest radiograph) of Pancoast tumor/apical tumor or metastasis to cervical lymph nodes. There are some references of Horner's syndrome due to malignant pleural mesothelioma with radiological findings of pleural effusion, pleural thickening and/or nodular pleural lesions. It is caused by local invasion of the chest wall and surrounding structures (8). There is also a rare possibility of Horner's syndrome present-

ing due to breast surgery if paravertebral block is an alternative to general anaesthesia (12).We should point out that our patient underwent general anesthesia. Nevertheless, our patient presented pain and dysesthesia in her left arm, the well-known symptoms that correspond to brachial plexopathy. We had to distinguish radiation plexopathy from cancer plexopathy in the patient with a known history of cancer and radiation. Clinical presentation involving lower brachial plexus and electromyography findings of segmental slowing was suggestive of cancer plexopathy. However, the presence of Horner's syndrome was indicative of neoplastic brachial plexopathy, rather than radiation-induced plexopathy (13). It should be noted that the brachial plexus morbidity could also result from surgical trauma or perioperative stretching of the nerve plexus.

We found no radiological signs of apical lung tumor. Plausible explanations of Horner's syndrome/Pancoast syndrome without thoracic apical tumor in breast cancer metastatic pleural disease is an extended thickening of the parietal pleura and malignant pleural effusion with involvement of the thoracic sympathetic trunk and lower brachial plexus. In general, the treatment for Horner's syndrome depends upon the cause. In many cases, no effective treatment is known. Treatment in acquired cases is directed toward eradicating the disease that produces the syndrome. Recognizing the presence of the syndrome and expedient referral to appropriate specialists are tantamount to early diagnosis. After a cycle of chemotherapy our patient refused further suggested conventional therapy and died after 6 months approximately. In most of the studies the mean or median survival of treated breast cancer patients after the onset of pleural effusion ranges from 6 to 15 months, indicating a poor prognosis (14,15). Metastatic breast disease usually affects lung, liver, bone, and it is highly unusual for such ocular involvement to be the first sign of systemic metastasis from a primary neoplasm. Horner's syndrome in patients with a history of breast cancer could be indicative of metastatic pleural dissemination.

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