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LETTER TO THE EDITOR

Bilateral phrenic nerve paralysis as a manifestation of paraneoplastic syndrome

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To the Editor

To a growing list of causes of phrenic nerve paralysis, we report a case of a 58-year-old lady, non-smoker, non-alcoholic, who was referred to the American University of Beirut Medical Center for the management of a locally advanced inflammatory right breast cancer. Her physical examination revealed a 10 cm tumor in the right breast associated with inflammatory skin changes all over the right chest wall. She also had right axillary lymphadenopathy that induced severe pain and difficulty in moving the right arm. Neurologic examination revealed normal cranial nerve function and adequate muscle tone and power in all extremities. The remaining physical examination was unremarkable. Biopsy of the breast lesion revealed poorly differentiated adenocarcinoma with negative hormonal receptors and over-expression of Her-2/Neu. Metastatic work up including positron emission tomography (PET) scan and computerized tomography (CT) scan showed that the tumor was confined to the right breast and axilla. She was started on systemic neo-adjuvant chemotherapy and received four cycles of Docetaxel and Trastuzumab with good clinical response. She then received one cycle of FAC (5-fluorouracil, doxorubicin and cyclophosphamide) chemotherapy with poor tolerance, followed by two cycles of Vinorelbine and Trastuzumab.

Before finishing her chemotherapy, she started complaining of cough and shortness of breath. A few weeks later she presented with acute onset dyspnea, more in the supine position, that improves in the standing position. On inspiration, the patient's abdomen moved inward rather than outward. Her chest wall however, moved normally outward. Her respiratory failure required mechanical ventilation which later showed good clinical response; however she could not be entirely weaned off the respirator. A chest radiograph was done and revealed consistently elevated hemidiaphragm on both sides. A chest CT scan was negative for any mediastinal involvement. Electromyography (EMG) and nerve conduction studies showed that phrenic nerve stimulation evoked no responses from either hemidiaphragm. Needle electromyography of the right diaphragm showed a reduction in the number of firing motor unit potentials. The clinical and laboratory findings were suggestive of weakness of both leaves of the diaphragm and so she was diagnosed with paraneoplastic bilateral phrenic nerve paralysis with secondary respiratory failure. Later on, she underwent tracheostomy and was put on mechanical ventilation at home using a portable ventilator.

After finishing neo-adjuvant chemotherapy, the patient underwent preoperative evaluation that showed good radiologic response of tumor with no metastasis. A follow-up EMG showed progression of the phrenic nerve disease. She then underwent a right modified radical mastectomy and axillary dissection with no postoperative complications. The pathology report showed no gross tumor with persistence of microscopic foci of residual ductal carcinoma *in situ* and metastatic adenocarcinoma (2 mm) to one of 15 axillary lymph nodes. She was then put on adjuvant chemotherapy with Vinorelbine and Trastuzumab for seven cycles and received radiation

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therapy. EMG was then repeated three months after the surgery but showed no improvement.

By that time the patient's respiratory condition had improved; she used the ventilator only at night, ambulated with ease and had spontaneous voluntary breathing. She continued chemotherapy and re-evaluation by neurography (11 months after surgery) showed absent phrenic motor responses bilaterally. Her neoplastic disease progressed despite multiple cycles of chemotherapy. On her last admission the patient experienced several episodes of desaturation and she passed away after bleeding through the tracheostomy tube.

Although numerous cases of unilateral diaphragmatic paralysis have been reported, bilateral paralysis is rare [1]. Bilateral diaphragmatic weakness is a rare condition and is usually associated with generalized neuromuscular diseases such as amyotrophic lateral sclerosis, multiple sclerosis, poliomyelitis, spinal muscular atrophy, myasthenia gravis, and muscular dystrophies [2]. Bilateral diaphragmatic paralysis was previously reported in association with mediastinal radiotherapy for the treatment of Hodgkin's lymphoma [3]. The association of malignancy with bilateral phrenic nerve paralysis was reported in only four cases in the English medical literature [4–7]. To our knowledge, the paraneoplastic phenomenon of bilateral phrenic nerve paralysis was only reported once previously in breast cancer [7].

In our patient there was no evidence in the clinical history or in the neurological and neurophysiological examinations of generalized neuromuscular diseases (such as motor neuron disease and myasthenia gravis) or of other conditions leading to phrenic nerve damage. Both the clinical picture and the investigational findings in our patient were consistent with bilateral diaphragmatic weakness. Idiopathic diaphragmatic paralysis was unlikely because it is usually unilateral. In addition, the patient improved and was partially weaned off the respirator during the course of chemotherapy. We suggest heightened suspicion for phrenic nerve paralysis as a potential paraneoplastic manifestation of breast cancer. Although the conditions could have fortuitously coexisted, bilateral phrenic nerve paralysis may represent a unique paraneoplastic syndrome secondary to breast cancer. This condition is potentially reversible as evident in our case.

References

[1] Piehler JM, Pairolero PC, Gracey DR, Bernatz PE. Unexplained diaphragmatic paralysis: A harbinger of malignant disease? J Thorac Cardiovasc Surg 1982;84:861–4.

[2] Brander PE, Jarvinen V, Lohela P, Salmi T. Bilateral diaphragmatic weakness: A late complication of radiotherapy. Thorax 1997;52:829–31.

[3] De Vito EL, Quadrelli SA, Montiel GC, Roncoroni AJ. Bilateral diaphragmatic paralysis after mediastinal radiotherapy. Respiration 1996;63:187–90.

[4] Adams RD, Richardson EP. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 42-1970. N Engl J Med 1970;283:806–14.

[5] Thomas NE, Passamonte PM, Sunderrajan EV, Andelin JB, Ansbacher LE. Bilateral diaphragmatic paralysis as a possible paraneoplastic syndrome from renal cell carcinoma. Am Rev Respir Dis 1984;129:507–9.

[6] Rijnders B, Decramer M. Reversibility of paraneoplastic bilateral diaphragmatic paralysis after nephrectomy for renal cell carcinoma. Ann Oncol 2000;11:221–5.

[7] Chroneou A, Katsaounou P, Gangadi M, Pampukos S, Kougianos K, Zias N, et al. An unusual cause of dyspnea in a patient with relapsing breast cancer. Lung 2006;184:245–8.