CASE REPORT

Bilateral Neuralgic Amyotrophy Presenting with Left Vocal Cord and Phrenic Nerve Paralysis

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This article reports the difference between neuralgic amyotrophy and neuropathy caused by chemotherapy and radiation treatment which manifested with severe shoulder pain followed by marked weakness of bilateral upper arms and involvement of cranial nerves. A 62-year-old man presented with acute severe neuropathic pain at the left shoulder, bilateral shoulder weakness, hoarseness of voice from vocal cord palsy, and respiratory insufficiency from left diaphragm palsy, which all occurred sequentially over a 1-month period. The diagnosis of neuralgic amyotrophy was supported and differentiated from tumor-induced and radiation-induced neuropathy by clinical presentation, electrophysiologic and imaging studies. Unlike previous reports of the onset of neuralgic amyotrophy being associated with initiation of radiation treatment in cancer patients, this report demonstrates that neuralgic amyotrophy can occur at any point of the malignant disease process after radiation and chemotherapy. [*J Formos Med Assoc* 2007;106(8):680–684]

Key Words: nasopharyngeal cancer, neuralgic amyotrophy, phrenic nerve palsy, radiation-induced plexopathy, recurrent laryngeal nerve palsy

Neuralgic amyotrophy is an uncommon neurologic syndrome that was first described by Parsonage and Turner in 1948. The incidence has been estimated at approximately 1.64 in 100,000. It is common between the third and sixth decades of life and has a slight male preponderance. It is characterized by acute onset of neuropathic pain followed by sensory loss, weakness and atrophy of muscles with the involved nerves showing multifocal inflammation.[1,2] Despite its classical presentation in the brachial plexus, it has recently been recognized to affect all the peripheral nerves elsewhere, singly or in combination, producing diverse clinical syndromes.[3–7] Sanders et al[8] and Pierre et al[5] reported the association of neuralgic amyotrophy with cranial nerve involvement. Although the exact pathogenesis remains unknown, an immunologic factor has been postulated to play a role.[9] Most patients recover from pain and weakness slowly over months or years and can be treated symptomatically with steroid, analgesic and physical therapy.

Case Report

A 62-year-old man with a 5-year history of nasopharyngeal cancer awoke from sleep at night with a sudden sharp pain and numbness over the left shoulder girdle. The pain increased in intensity and spread to the lateral side of his arm and neck over the next 24 hours. Three hours after the onset of pain, he felt progressive weakness of his left shoulder girdle muscles that spread to the left

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upper limb, right shoulder girdle and right upper limb a day later. He noticed hoarseness 3 days later. Resting dyspnea and orthopnea ensued 4 weeks later. There was no preceding viral illness, recent vaccination, strenuous activities, surgery, trauma or family history of hereditary neuralgic amyotrophy. His nasopharyngeal cancer was diagnosed 5 years earlier at the age of 57 and he had received radiation treatment (totaling 70 Gy) combined with cisplatin chemotherapy at a dose of 20 mg/m^2/day and 5-fluorouracil 1000 mg/m^2/day for 5 days every 4 weeks for 2 cycles during radiation treatment and 4 cycles after radiation. Yearly follow-up did not show any recurrence of nasopharyngeal cancer.

On neurologic examination, severe weakness and atrophy (Medical Research Council [MRC] grade 0–1) in the supraspinatus and infraspinatus, moderate (MRC grade 2) weakness in the deltoid, and mild weakness (MRC grade 3) in the biceps brachii and brachioradialis of both upper limbs were noted. There was no weakness in the muscles of the lower limbs. Except for the absent deep tendon reflexes in bilateral biceps, the reflexes in all limbs were normal. Sensory examination revealed decreased sensation in the distribution of the left axillary nerve.

Laboratory workup including complete blood count, kidney, liver and thyroid functions, electrolytes, creatinine kinase, antinuclear antibody, rheumatoid factor, erythrocyte sedimentation rate, and cerebrospinal fluid were all normal (protein, 25 mg/dL; glucose, 75 mg/dL; red blood cell, 1/mm^3; white blood cell, 0/mm^3; negative Pandy test). Serology for cytomegalovirus and Epstein–Barr virus was negative.

Nerve conduction velocity (NCV) studies of the upper and lower limbs revealed mild sensorimotor type of polyneuropathy superimposed with decreased sensory nerve action potentials in bilateral lateral antebrachial cutaneous and radial nerves with decreased amplitudes of bilateral axillary and musculocutaneous nerves (Tables 1 and 2). Needle electromyography study of the affected muscles showed no myokymic discharges, but spontaneous activities like fibrillation potentials and positive sharp waves were noted in bilateral biceps and deltoid with polyphasic motor unit potentials in bilateral supraspinatus and infraspinatus, deltoid and biceps muscles. Cervical paraspinal muscles were normal.

Laryngoscopy showed left vocal cord paralysis in the paramedian position (Figure 1). Cervical magnetic stimulation of the phrenic nerve showed

Table 1. Motor nerve study

Nerve	Stimulation site	Distance (cm)	Latency (ms)	Amplitude (mV)	Velocity (m/s)
Left median	Wrist	8	4.00	8.3	
	Elbow	17	7.20	8.1	53.1
Right median	Wrist	8	4.45	9.1	
	Elbow	19.5	8.10	9.1	53.4
Left ulnar	Wrist	8	2.85	10.5	
	Elbow	30.5	8.10	10.0	58.1
Right ulnar	Wrist	8	2.75	10.8	
	Elbow	28.5	8.00	10.6	54.3
Left radial	Elbow	15	4.45	7.5	
	Erb's point	29	8.85	1.0	65.9
Right radial	Elbow	16	4.70	7.5	
	Erb's point	30	9.20	1.5	66.7
Right axillary	Erb's point	20	5.55	0.4	
Left axillary	Erb's point	21	5.45	0.2	
Right musculocutaneous	Erb's point	33	6.55	0.5	
Left musculocutaneous	Erb's point	31.5	7.70	0.3	

Table 2. Sensory nerve study

Nerve	Recording site	Distance (cm)	Latency (ms)	Amplitude (mV)	Velocity (m/s)
Left medial ante-cut	Forearm	17	2.65	13.6	64.2
Right medial ante-cut	Forearm	14.5	2.15	15.1	67.4
Left lateral ante-cut	Forearm		NP		
Right lateral ante-cut	Forearm	12	1.80	3.6	66.7
Left median	Digit III	17.5	3.10	8.7	56.5
Right median	Digit III	18	3.15	9.7	57.1
Left ulnar	Digit V	15	2.75	8.1	54.5
Right ulnar	Digit V	15	2.75	7.8	54.5
Left radial	Thumb	13	2.40	1.6	54.2
Right radial	Thumb	13	2.20	4.2	59.1
Left sural	Lat malleolus	13	3.15	17.5	41.3

ante-cut = antebrachial cutaneous; NP = not performed.

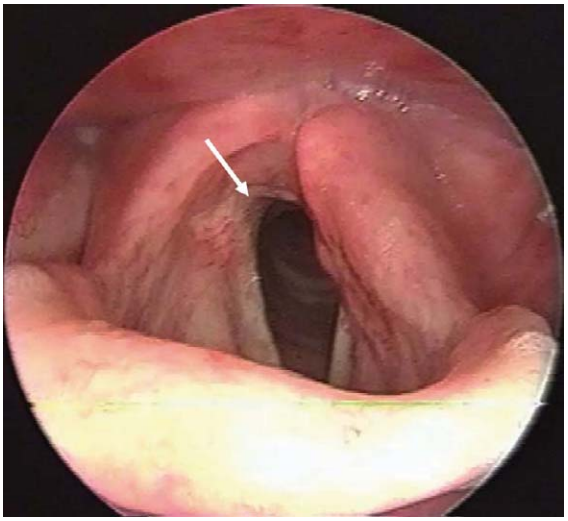

Figure 1. Laryngoscopy reveals the left vocal cord to be immobilized in the paramedian position.

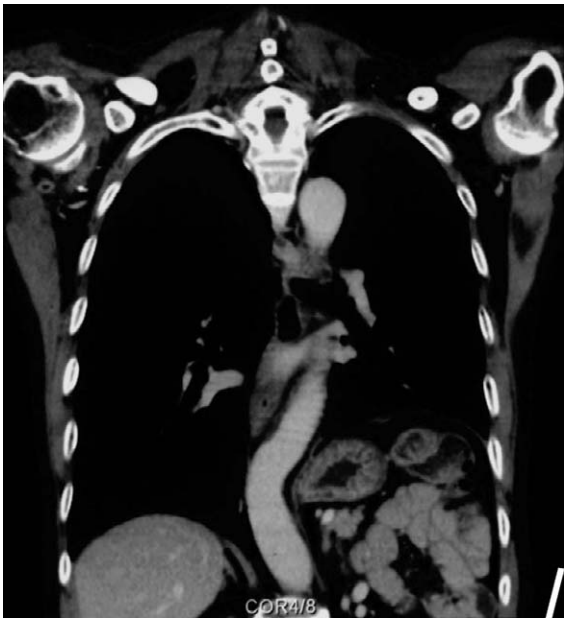

Figure 2. Computed tomography of the chest reveals elevation of the left diaphragm.

absent response from the left diaphragm. Elevation of the left hemidiaphragm was noted on chest radiography and computed tomography (Figure 2) taken at the onset of dyspnea and was confirmed by chest ultrasonography. Electrocardiography and laboratory tests ruled out cardiac and pulmonary causes of his dyspnea. Pulmonary function tests were normal.

Magnetic resonance imaging study showed normal brachial plexus without abnormal enhancement, but there was post-radiation change involving the upper cervical spine with circumferential disc bulging at C5–6 and C6–7 without any nerve compression and no tumor recurrence in the ear, nose and throat. Whole body bone scan (^{99m}Tc-methylene diphosphonate) and positron emission tomography scan (fluorine-18-fluoro-2-deoxyglucose) could not identify recurrent metastasis.

The patient was treated conservatively, with steroid, analgesic and physical therapy for weakness, and β-agonist and steroid for dyspnea. His pain disappeared after 1 week and his dyspnea and hoarseness of voice resolved slowly over 2 months. However, weakness of bilateral upper

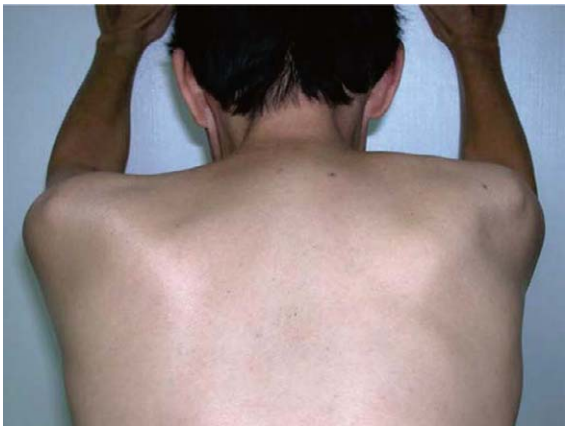

Figure 3. Atrophic shoulder.

shoulders persisted (Figure 3) as manifested by MRC grade 2 in the supraspinatus and infraspinatus, and MRC grade 3 in the deltoid, biceps brachii and brachioradialis. Follow-up NCV study did not show any significant change.

Discussion

Neuralgic amyotrophy has been reported to present with sudden onset of neuropathic pain, usually at night,[10] in bilateral shoulder and arm areas followed within hours and weeks by paresis or paralysis of muscle groups innervated by the affected nerves, nerve roots or plexi.[11,12] There are articles reporting the link between neuralgic amyotrophy with recurrent laryngeal nerve palsy;[7,8] neuralgic amyotrophy should be suspected in unexplained acute neuropathic pain in the shoulders and upper limbs or unexplained diaphragmatic palsy with respiratory insufficiency. Recently, advanced imaging studies, such as magnetic resonance neurography, have contributed significantly to the evaluation of brachial plexopathy.[13]

Nerves can be damaged by radiotherapy depending on the total or fractional dose of radiation as well as the premorbid state of the irradiated nerve.[14] Radiation-induced neuropathy presents in three distinct clinical syndromes: classic delayed injury from fibrosis,[15] transient or reversible ischemic injury,[16] and acute ischemic injury.[17] It usually results from radiation to the neck or axillary regions, as commonly seen in breast cancer and lymphoma patients.[18] Unlike the clinical manifestations of neuralgic amyotrophy, delayed radiation-induced neuropathy has slow progressive onset of sensory loss and paresthesia, mild or no pain, muscle weakness and atrophy, and long duration (months or years) of muscle weakness and disability.[18] Neuralgic amyotrophy has been reported to occur within days to 2 months after initiation of radiation in patients with Hodgkin's disease.[19] Gorkhaly and Lo described a case of radiation-induced brachial plexopathy in nasopharyngeal cancer.[20]

Chemotherapy is known to significantly increase the incidence of neuropathy by a magnitude of two folds or more. Concomitant chemotherapy with radiation treatment has become the treatment of choice for advanced head and neck cancers. Cisplatin, paclitaxel, suramin and vincristine commonly cause neuropathy.[21,22] Barbieux et al reported a case of neurotoxicity induced by 5-fluorouracil.[23] Cisplatin-induced peripheral neuropathy is characterized mainly by sensory deficit, with occasional motor disturbance and decreased deep tendon reflexes. Though the symptoms of neuropathy may begin 3–8 weeks after the last dose of cisplatin, they commonly occur during the chemotherapy cycles. Chemotherapy-induced neuropathy can also present subclinically with abnormalities in study reports but no clinical features.[24,25]

In cancer patients with radiation treatment, distinguishing neuropathy induced by cancer, radiation and neuralgic amyotrophy is important for choosing treatment modalities.[19,26] History and clinical presentation are the most useful. Though it is a challenge to distinguish between neuralgic amyotrophy and radiation-induced neuropathy by imaging, tumor mass can be found by advanced imaging alone.[27] Myokymic changes can be found on electromyography in radiation-induced neuropathy.

The clinical picture and evidence reported here with this nasopharyngeal cancer patient 5 years after radiation and chemotherapy clearly favor neuralgic amyotrophy rather than delayed onset radiation-induced brachial plexopathy or cancer

recurrence. It is noteworthy that the onset of neuralgic amyotrophy might not have a temporal relationship to radiation treatment in cancer patients treated with both radiation and chemotherapy. Although the exact mechanism of delayed neuralgic amyotrophy in this case remains unknown, nerves damaged subclinically by radiation and/or chemotherapy are predisposed to develop neuralgic amyotrophy at any time after the treatments.

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