Neuralgic Amyotrophy Syndrome with Widespread Myokymia

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Introduction

We report a patient referred to us as possible motor neurone disease due to severe atrophy of his upper limbs and widespread 'fasciculations'. However, the onset was highly suggestive of Neuralgic Amyotrophy triggered by surgery,[1] along with florid myokymic discharges in the arms, chest wall and legs. We briefly discuss the variations of the classic presentation of neuralgic amyotrophy (or brachial neuritis)[2] and consider the differential diagnosis in this case.

Case Presentation

A 38-year-old man reported developing severe shoulder pain (graded 8/10), within 3 days after undergoing drainage of an abscess in the left axilla under generalized anesthesia, and 6 months prior to attending our service. The pain was first in his left, then his right shoulder, worse at night, and non-responsive to opioid analgesia. Soon after onset, he was unable to lift his arms above his head, and experienced numbness and paresthesiae in both arms. Over the next four weeks, the pain dissipated somewhat, but he developed profound weakness proximally and distally in both arms, such that he was unable to perform activities of daily living. He also noted that his muscles started 'jumping' in his arms, chest, and legs. On presentation to our service he was noted to have flail arms although he reported minor spontaneous improvement over the preceding 2 months in certain activities such as minimal improvement in shoulder abduction, elbow, and wrist flexion related activities.

He had not experienced spasms or cramps and had no cognitive or psychiatric symptoms. There was no history of any preceding illnesses, comorbidities, toxin exposure, or drug abuse. The patient mentioned chronic abdominal discomfort, for which he used antacids daily, and unintentional weight loss which started after the onset of pain and weakness, but without bulbar dysfunction.

The examination 6 months after onset was remarkable for excessive sweating of the forehead, but normal for cranial nerves and neck muscles. Widespread continuous myokymia was noted over the chest wall, abdomen, upper limbs, and thighs (see video). He had a resting tachycardia. There was marked, left more than right, atrophy of supra- and infraspinatus, pectoral muscles, thenar muscles, and first dorsal interossei (FDI) (Figure 1). The tone was reduced in the arms with absent deep tendon reflexes, except for the left triceps. Slight asymmetrical weakness (>left) was noted: strength of shoulder abduction was medical research council (MRC) grade 2/5; elbow extension and flexion 2/5; wrist extension 3/5, flexion 4/5; finger extension 1st-3rd digits 3/5, but 4-5th digits 1/5; finger flexors 4. The rectus abdominal muscles were weak. Apart from myokymia in the legs, the muscle bulk, tone, power and deep tendon reflexes were all normal. The sensory examination showed patchy hyperesthesia and decreased vibration sensibility in the first two

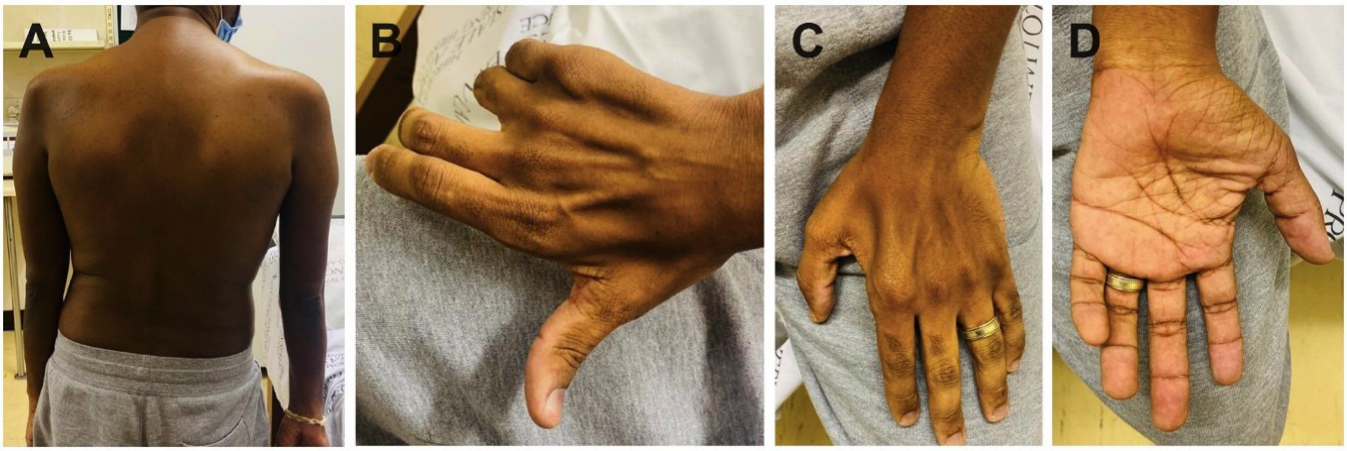

Figure 1. A. Significant wasting of the shoulder girdle including supraspinatus, infraspinatus, and deltoid muscles (> left), and mild scapular winging. B. Right hand: benediction posture with clawing of digits 4 and 5 due to weakness of the interossei and 3rd and 4th lumbricals. C, D. Left hand showing severe wasting of the first dorsal interosseus, but less atrophy of thenar and hypothenar muscles.

digits, and a glove and stocking loss to pinprick sensibility. The forced vital capacity (FVC) measured 3.4 liters sitting and supine (80% of expected).

Special investigations which had been performed 3 months after symptom onset by the first neurologist, included a normal MRI (with/without contrast) of the cervical cord and plexus, and acellular cerebrospinal fluid examination with normal chemistry. The creatine kinase was 3x the upper limit of normal, but the rest of the basic laboratory profile was normal, including erythrocyte sedimentation rate, electrolytes, urea, fasting glucose, and autoimmune antibody screen. The nerve conduction studies performed at 4 months are summarized in Table 1. Six months after onset, the anti-ganglioside antibody screen, serum protein electrophoresis, HIV- and hepatitis viral screen, and urine and blood porphyrin screens, were all negative. Repeat nerve conductions (not shown) showed reduced right ulnar compound motor amplitudes (CMAPs) with dispersion, borderline low median nerve CMAPs and normal tibial motor CMAPs, but with an absent tibial F-response. These were repeated at 8 months (Table 1) and showed similar results with mildly reduced sensory nerve amplitudes (SNAPs) in the arms but a normal sural SNAP. Electromyography (EMG) of the right deltoid, biceps, wrist extensors, FDI, quadriceps, and tibialis anterior revealed chronic neurogenic changes with fasciculations and large polyphasic motor unit action potentials with reduced recruitment, but only a small patch of fibrillation potentials in the FDI. Myokymic discharges were noted in the quadriceps. Facial muscle EMG was normal.

The onset was highly suggestive of brachial neuralgic amyotrophy. However, due to the widespread myokymia, small fiber sensory dysfunction in the legs (normal SNAPS), demyelinating features on electrophysiology (absent F-waves in the presence of CMAP >20% of the lower limit of normal), and severity of the phenotype, we started 1mg/kg prednisone 6 months after symptom onset.

After a month, the patient reported a similar trajectory of subclinical improvement to that experienced pre-prednisone. However, he had a new complaint of dyspnea and orthopnea, and recurrence of pain in the back and shoulders. The FVC was 1.9 liters (<50% of expected). The lung fields were clear on auscultation, the chest X-ray was normal, and a Covid19-PCR was negative. We administered 2g/kg of intravenous immunoglobulin (IVIG) over 3 days. Two weeks later, the patient felt the pain had improved, the orthopnea had resolved, and he was able to turn in bed independently. Objectively, the FVC had improved to 2.3 liters, and elbow extension had improved to normal strength (triceps jerk remained absent). Widespread myokymia remained visible. We elected to continue 0.5mg/kg prednisone. The patient has been referred for neurorehabilitation. At 8 months his modified Rankin remained at 3.

Discussion

We report an unusual presentation of a man with bibrachial neuralgic amyotrophy and generalized myokymia developing after surgery. After the initial severe shoulder pain subsided, he developed flail arms with severe atrophy and weakness around the shoulder girdle, distal weakness and atrophy especially prominent in the posterior interosseus branch of the radial nerve and ulnar nerve-innervated muscles, autonomic symptoms and milder sensory changes. An insidious second wave of pain and phrenic nerve dysfunction developed 7 months after the onset, with increasing truncal and respiratory muscle weakness, both of which responded partially to IVIG.

Post-operative inflammatory radiculoplexus neuropathy was described as a monophasic event separated from the 'site and time' (within 30 days) of surgery and characterized by severe pain at onset, in addition to weakness, and responsivity to immunotherapy.[3] Nerve conduction studies were characterized by variable sensorimotor axonal involvement, and nerve biopsies in the majority of their patients showed microvasculitis with epineural perivascular inflammatory cells and axonal degeneration.[3] These findings are similar to those found in the context of diabetes, viz. diabetic cervical radiculoplexus neuropathy,[4] although in diabetes the lumbosacral variant is more common.[5]

Neuralgic amyotrophy is thought to be more common than the estimated incidence of 1 per 100,000.[2] Motor symptoms predominate and atrophy is striking.[2] Although unilateral involvement occurs in most cases, ~29% have bilateral, albeit asymmetrical, plexopathy.[6] The condition was initially thought to be monophasic, but 25% may have a recurrence of painful attacks[6], which may involve the same or different regions.[2] The pathophysiological mechanism is postulated to be multifactorial such as the interactions between environmental and immune triggers (infections and/or surgery), genetic susceptibility, and biomechanical factors.[1]

Patients can also present with varied combinations of peripheral nerve involvement such as branches of the radial nerve, long thoracic nerve, and, rarely, phrenic nerve with diaphragmatic weakness and dyspnea, such as our case. Lower brachial plexus involvement with sympathetic symp-

Table 1: Clinical electrophysiology performed months after onset of symptoms.

Nerve		4 months	8 months	Reference Values
Right Median Motor[#]	DL, ms	3.9	4.2	<4.5
	CMAP, mV	5.3/4.5	3.8/2.9	>4.0
	CV, m/sec	60.2*	59.9*	>48
Left Median Motor[#]	DL, ms	3.45	3.4	<4.5
	CMAP, mV	4.6/3.5	1.1/1.1	>4.0
	CV, m/sec	62.9**	51.6**	>48
Right Ulnar Motor[#]	DL, ms	3.65	4.02	<3.6
	CMAP, mV	2.1/2.1	0.9/0.5	>6.0
	CV, m/sec	60.3**	43.3	>51
Left Ulnar Motor	DL, ms	3.1	2.8	<3.6
	CMAP, mV	3.1/2.5	2.4/2.1	>6.0
	CV, m/sec	55.7*	64.8*	>51
Right Tibial Motor[#]	DL, ms	ND	5.75	<6.0
	CMAP, mV	ND	21.2/19.4	>4.0
	CV, m/sec	ND	65.7*	>41
Left Tibial Motor	DL, ms	ND	4.55	<6.0
	CMAP, mV	ND	15.8/12.9	>4.0
	CV, m/sec	ND	56.9	>41
Left Peroneal Motor	DL, ms	ND	3.9	<5.9
	CMAP, mV	ND	5.3/5.2	>2.0
	CV, m/sec	ND	65.6	>41
Left Median Sensory	DL, ms	1.7	1.82	<2.2
	SNAP, µV	61	107[#]	>50
Right Ulnar Sensory	DL, ms	2.1	1.8	<2.1
	SNAP, µV	17.4	38.9[#]	>15
Left Ulnar Sensory	DL, ms	2.1	2.0	<2.1
	SNAP, µV	17.4	44.5	>15

DL- Distal Latency, ms- milliseconds, CV- Conduction Velocity, m/sec - meters/second-, CMAP- compound motor action potential, and the 2 values represent Distal/Proximal values. ND – Not done. The patient had a shortened examination at 6 months after symptoms (due to Covid19 lockdown); the results of the 3 nerves examined[#] (not shown) were similar to 8-month values. *absent F-waves in the presence of CMAP >20% of the lower limit of normal, **normal F-response. Right median and peroneal motor and sural sensory, not shown- all normal.

toms and lumbosacral plexopathy has also been described, even in the absence of diabetes.[2] Van Alfen and Van Engelen reported an "extended neuralgic amyotrophic syndrome" in which the phenotype extends beyond the classic upper trunk brachial plexopathy, also involving the lower trunk of the brachial plexus, individual nerves, and the lumbosacral plexus.[1] We postulate that our case has the features of this extended syndrome. However, widespread myokymia, as seen in our case, has not been reported in neuralgic amyotrophy.

Magnetic resonance imaging features of the plexus range from normal—to focal edema with T2 hyperintensity and contrast enhancement.[7] Nerve conduction studies may indicate an axonopathy with low CMAPs and normal

conduction velocities. SNAPs are usually normal. EMG may show fibrillation potentials and chronic neurogenic changes, although our patient showed very little evidence of active denervation in severely atrophic muscles. Generalized myokymia has been described in the setting of acute and chronic demyelinating polyradiculoneuropathy[8] and is thought to be due to motor axon hyperexcitability with ephaptic activation.[9] Although our patient did have some electrophysiological features of proximal conduction slowing with absent F-waves, myokymia has rarely been described in axonal disorders such as motor neuron disease.[9] It was important to exclude acute intermitted porphyria as this may present as a motor neuron disease mimic with rapidly developing severe atrophy.[10]

Corticosteroid therapy was used in a small open-label study, most frequently within 10 days of symptom onset, although the average was 30 days. Those receiving prednisone suffered more pain and greater disability compared to those not given prednisone. However , those receiving prednisone, appeared to have earlier recovery, although the degree of recovery was similar.[6] Anecdotal case reports also suggest that early treatment with IVIG followed by steroids may hasten recovery and improve outcomes.[11] Nevertheless, this is a disabling condition in most cases. Recovery of function is delayed and can take several years. Only 10% of patients report full recovery after 3 years and a further 10% remain with substantial morbidity currently.[6]

In conclusion, we describe a patient with a stuttering, extended neuralgic amyotrophy syndrome, which has resulted in flail arms, ongoing autonomic instability, and widespread myokymia after 8 months. It is uncertain whether earlier recognition and immune treatment may have altered the outcome in this case.

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