



Neuralgic amyotrophy associated with COVID-19 infection: a case report and review of the literature

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Received: 31 January 2021 / Accepted: 16 March 2021 / Published online: 20 March 2021
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Introduction

Since the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) around the world, and the declaration of coronavirus disease 2019 (COVID-19) pandemic, it has become increasingly evident that several neurological manifestations are associated with this disease, involving both central and peripheral nervous systems [1].

Neuralgic amyotrophy is an uncommon clinical syndrome characterized by initial severe neuropathic pain and patchy weakness of the shoulder and arm muscles, usually involving the upper and middle trunks of the brachial plexus, followed by slow recovery. Neuralgic amyotrophy can be idiopathic or hereditary and is usually unilateral in 70% of cases [2].

Etiology and pathophysiology of neuralgic amyotrophy are still unclear; several precipitating factors had been reported including post-infectious, post-vaccination, post-operative, and post-traumatic, [3] with recent viral illness being the most common associated trigger [4].

To our knowledge, only 3 case reports have documented neuralgic amyotrophy in association with SARS-CoV-2 infection in the literature [5–7]. Herein, we present a case of severe, bilateral asymmetric neuralgic amyotrophy in a 32-year-old male, in association with laboratory-confirmed infection with

SARS-CoV-2. This represents the first case from the Middle East and North Africa (MENA) region, to the best of our knowledge, expanding the spectrum of neurological involvement in association with COVID-19 infection.

Case report

A 32-year-old right-handed male with no relevant past medical history developed fever, cough, and generalized body pain in November 2020. He tested positive for SARS-CoV-2 via a nasopharyngeal swab reverse transcription-polymerase chain reaction (RT-PCR). He was hospitalized in a specialized institution for COVID-19 and received oxygen, antibiotics, vitamins, and anticoagulants and was discharged after 7 days. During hospital stay, he experienced severe pain at the left shoulder, aggravated by touch and movement, for which he received acetaminophen with minimal relief. The pain involved the right shoulder one week later.

After discharge, the pain intensified and progressed to involve both forearms and hands. Two weeks from the onset, he started to develop progressive proximal weakness of both upper limbs, more on the left side, in addition to developing bilateral hand numbness, and an area of

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sensory loss over his left shoulder and radial forearm. He was initially evaluated by general physician and orthopedic surgeon and received pregabalin 300 mg/day, tramadol hydrochloride 50 mg twice daily, and local injection of steroids and lidocaine in both shoulders. He showed little improvement and was referred to our neurology outpatient clinic after 5 weeks of onset. He reported having severe pain ranging from 7 to 10 out of 10 on numerical rating scale (NRS), where 0 is no pain and 10 is the most severe pain.

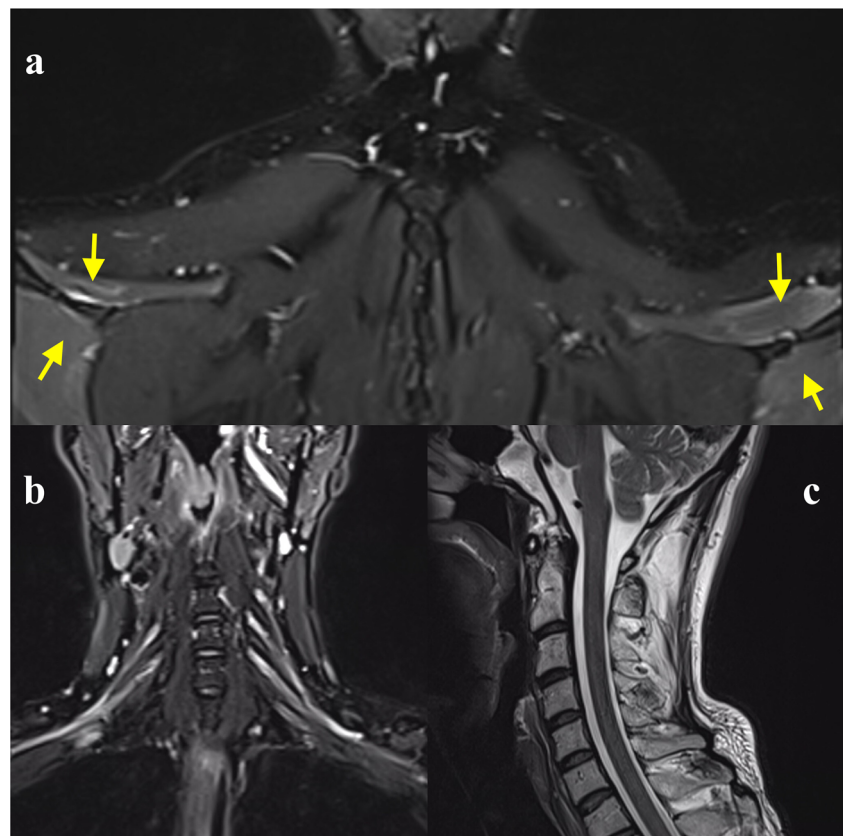
Findings of his systemic examination were normal. On neurological examination, he was alert, conscious, and oriented with normal speech and higher mental functions. Cranial nerve assessment was normal. Motor examination on the left side showed winging of scapula, weakness of shoulder abduction and flexion of Medical Research Council (MRC) grade 1/5, weakness of shoulder external rotation and elbow flexion of MRC grade 2/5, and weakness of flexion of the distal interphalangeal joints of the thumb and index finger “OK sign” of MRC grade 4/5. On the right side, he had weakness of shoulder abduction, shoulder flexion, and elbow flexion of MRC grade 4/5. Minimal atrophy was observed on both shoulders, more on the left side. Motor examination of both lower limbs was normal. Deep tendon reflexes were absent all over the

body, except for right triceps and brachioradialis reflexes. Sensory assessment showed reduced sensation over the right and left shoulders, and left forearm. Planter response was downgoing bilaterally.

Electrophysiological studies (nerve conduction tests and electromyography) were performed 5 weeks after initial presentation. It revealed sensory and motor axonal involvement, in the form of low amplitude of compound motor action potentials of musculocutaneous, axillary, and suprascapular nerves on both sides, and long thoracic and anterior interosseous nerve on the left side, with patchy denervation. The picture was compatible with bilateral neuralgic amyotrophy. A magnetic resonance imaging (MRI) showed hyperintense T2-weighted signal of supra- and infraspinatus muscles, indicating intramuscular edema, with normal cervical spine and both brachial plexuses, further confirming the diagnosis (Fig. 1).

An extensive blood workup showed normal complete blood count; renal and liver functions; serum electrolytes; creatine kinase; inflammatory markers (erythrocyte sedimentation rate, C-reactive protein); serum vitamins B1, B6, B12, and folate; protein electrophoresis; immunoglobulin assay; thyroid function; and antithyroid autoantibodies. There was no serological evidence of infection with hepatitis B, C, and E; herpes simplex virus (HSV);

Fig. 1 Magnetic resonance imaging (MRI) of cervical spine and both brachial plexuses in a 32-year-old male. **a** Coronal 3D T2-weighted images with fat suppression using sampling perfection with application-optimized contrasts by using flip angle evolution (SPACE) sequence, showing abnormal signal that involved the rotator cuff muscles bilaterally (arrows); **b** coronal 3D T2-weighted image through the brachial plexus showing no pathological changes; and **c** sagittal T2-weighted image of the cervical spine showing no myelopathy or compressing masses



human immunodeficiency virus (HIV); Lyme; syphilis; or toxoplasma. A panel for vasculitis and autoimmune antibodies yielded negative results. Cerebrospinal fluid (CSF) analysis showed normal protein and glucose levels, with no WBCs, negative culture and sensitivity, and gram stain for bacterial infection. Polymerase chain reaction screening for neurotropic viruses was negative in serum and CSF.

The patient was commenced on intravenous methylprednisolone 1000 mg per day for 5 days, but it was stopped due to dermatological side effects. He received a course of intravenous immunoglobulins (IVIg) in a dose of 25 g/day for 5 days. There was partial relief of pain with no improvement in muscle power. His motor and sensory examinations remained the same after 8 weeks of symptoms onset.

Discussion

Involvement of peripheral nervous system in patients with COVID-19 is on the rise. In an early study from China [8], it was estimated to affect 8.9% of patients; however, it is more likely underreported, requiring further electrophysiological studies to determine its true incidence and characteristics. This involvement may result from direct neuro-invasion or from an autoimmune, post-infectious mechanism [8]. Understanding the sequence and mechanism of events leading to neural damage in patients with COVID-19 might help in early diagnosis and treatment and highlights the need for prospective research on patterns of peripheral and central nervous system involvement in patients with COVID-19 [9].

Neuralgic amyotrophy is a rare form of peripheral neuropathy that has been rarely reported in association with COVID-19, to our knowledge. A PubMed search was performed using the following combinations of keywords: neuralgic amyotrophy, SARS-CoV-2, COVID-19, and brachial plexopathy. It revealed only 3 case reports in the literature [5–7], till the time of writing (Table 1). The report of Cacciavillani et al. includes a patient who developed pure sensory neuralgic amyotrophy, possibly related to infection with SARS-CoV-2, without any clinical or electrophysiological signs of motor nerve involvement. The report of Siepmann et al. reported a patient with sole median nerve involvement, as a rare clinical manifestation of neuralgic amyotrophy. A third report by Mitry et al. showed hyperintense T2-weighted signal of the supraspinatus, infraspinatus, teres minor, teres major, and trapezius muscles on MRI, with initial improvement on oral steroids. These different presentations of post-COVID-19 neuralgic amyotrophy highlight the possible variability of symptoms in patients with peripheral

nervous system involvement with SARS-CoV-2 infection, and the importance of detailed assessment of patients with COVID-19 for neurological deficits [9].

Neuralgic amyotrophy is a distinct disorder that is more common in males, predominantly affecting the roots of the brachial plexus, and characterized by excruciating neuropathic pain followed by multifocal paresis and sensory loss in C5, C6, and less frequently in C7 distribution. It has two subtypes, hereditary neuralgic amyotrophy (HNA) and idiopathic neuralgic amyotrophy (INA), and is estimated to affect 2–3 cases/100,000 inhabitants/year. The involvement is mainly unilateral in 70% of cases, and bilateral or asymmetric in the other 30%. Diagnosis is confirmed by electrophysiological studies and sometimes with evidence of strain in the supra and infraspinatus muscles on MRI [10, 11].

The etiology of the disease is not well understood; however, an immune-mediated reaction, that is triggered by earlier or concomitant infection is believed to be the cause in 43% of cases [12]. Some features in our report are different from the other published cases. First, the bilaterality of pain and weakness, which is an uncommon feature of neuralgic amyotrophy in itself. Second, the very early onset of symptoms during the initial presentation of COVID-19, suggesting a probable direct viral neuroinvasion, rather than an autoimmune post-infectious response against SARS-CoV-2 [13]. Moreover, our report showed hyperintense T2-weighted signal of supra and infraspinatus muscles in MRI. This is explained by denervation of skeletal muscles in the distribution of the brachial plexus nerves, due to intramuscular edema [14]. MRI helps in ruling out other etiologies of painful shoulder weakness.

Treatment of neuralgic amyotrophy has not been validated, in the absence of randomized controlled trials (RCTs). A reasonable protocol for adults was found to be oral prednisone (1 mg/kg per day) for 1 week, followed by tapering of 10 mg per day during the second week [15]. Intravenous immunoglobulin (IVIg) has also been proposed as a treatment [16], in case of contraindication to steroids or the emergence of side effects, similar to our case.

Conclusion

Our case adds to the growing body of evidence of peripheral nervous system involvement in COVID-19 patients. Despite being a rare disease, neuralgic amyotrophy should be suspected and ruled out in COVID-19 patients, presenting with severe pain and weakness of the shoulder and arm muscles. This study highlights the importance of detailed assessment of patients with COVID-19 with neurological deficits, to avoid delay in diagnosis and allow for early management.

Table 1 Characteristics of patients with neuralgic amyotrophy associated with COVID-19 in the literature

Author	Age (years)/ gender	COVID-19 infection	Onset	Clinical picture	Neurological examination	Electrophysiological findings	MRI	Treatment	Outcome
Stepmann et al.	52/ M	Positive oropharyngeal swab	First 2 weeks	Severe pain during the first 2 weeks, progressive weakness after 4 weeks, presented after 6 weeks	Sensory motor; weakness of the right flexor digitorum profundus, flexor pollicis longus, abductor pollicis and opponens pollicis muscles, hypesthesia in the median nerve skin distribution.	NCS showed motor axonal neuropathy of the median nerve with partial conduction block in the upper arm. On EMG, slight decrease in motor unit recruitment in the abductor pollicis brevis and opponens pollicis muscles, no spontaneous activity.	Mild T2-signal increase of the ipsilateral C7–C8 roots	Oral prednisolone (1 mg/kg/day) for 7 days followed by tapering	Partial pain relief, no improvement in motor or sensory findings after 8 weeks of onset
Cacciavillani et al.	52/M	Positive nasopharyngeal swab	After 2 weeks	2 weeks, excruciating pain in the left wrist and upper limb in the distribution of the lateral antebrachial cutaneous nerve, followed by pure sensory affection. No weakness.	Pure sensory; hypoessthesia in the distribution of the lateral antebrachial cutaneous nerve, normal muscle strength, normal reflexes	potential amplitude of the lateral antebrachial cutaneous nerve. EMG, normal	Not done	Not mentioned	Hypoesthesia and dysesthesias persisted after 6 weeks of onset.
Mitry et al.	17/F	Negative nasopharyngeal swab. Positive serum IgG antibodies for SARS-CoV-2.	Few weeks	Left shoulder and hand pain, few weeks after probable COVID-19 infection. Dyspnea and joint pain after 3 months	Reported as normal.	Not mentioned	Increased T2-weighted signal of the supraspinatus, infraspinatus, teres minor, teres major, and trapezius muscles	Oral steroids	Initial improvement

Author contribution III, EAA, and SFA were involved with acquisition of data. III, RA, JYA, and SFA treated the patient. III, and SFA wrote the initial manuscript. All authors critically appraised and revised it. All authors read and approved the final manuscript.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval This case report was approved by the Institutional Ethics Committee.

Informed consent Written informed consent for publication of this case report was obtained from the patient.

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