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CASE REPORT

Gullain-Barre' syndrome post-SARS-CoV-2 in Malta: a Case Report

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A 70-year-old lady presented three weeks after a mild SARS-CoV-2 infection with a nine-day history of worsening back pain, progressive lower limb weakness and paraesthesia, dysphagia, constipation and difficulty in completing full sentences. Outcome of her investigations were in keeping with a diagnosis of acute inflammatory demyelinating polyneuropathy. The patient made a rapid and full recovery after treatment with intravenous immunoglobulins (IVIG).

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INTRODUCTION

The SARS-CoV-2 virus was first identified as the cause of a new transmissible infectious disease in humans with respiratory complications in Wuhan, China at the end of 2019. The virus spread swiftly throughout China and within weeks emerged in several other countries around the world. On the 11thMarch 2020 the World Health Organization (WHO) declared SARS-CoV-2 a pandemic.[1]

SARS-CoV-2 is known to cause a wide range of symptoms. Most of the time these appear between 2 to 14 days post exposure to the virus. In the acute phase SARS-CoV-2 may cause fever, cough, shortness of breath, fatigue, myalgias, headache, sore throat, runny nose, nausea, vomiting and diarrhoea.[2] Neurological complications secondary to SARS-CoV-2 were also reported. These include hyposmia, ageusia, cerebrovascular accident, encephalitis, Guillain-Barre' Syndrome (GBS) and transverse myelitis.[2-6]

GBS is an acute type of polyradiculopathy which causes flaccid paralysis that commonly presents in a progressive symmetric weakness and areflexia. GBS usually occurs secondary to an immune system-activating event such as vaccination or infections including *Campylobacter jejuni*, cytomegalovirus, Zika virus and Epstein-Barr virus.[7] Other rarer causes of GBS include trauma, surgery, bone marrow transplantation, systemic lupus erythematosus (SLE), Hodgkin's lymphoma and sarcoidosis.[8,9] We report a case of GBS following shortly after infection with SARS-CoV-2 and its clinical outcome.

CASE

A 70-year-old woman presented to hospital with a nine-day history of back pain and a three-day history of progressive ascending paraesthesia which started bilaterally at the toes and progressed up to the groin. This paraesthesia was followed by progressive weakness in her lower limbs, causing unsteady gait, multiple falls and reduced mobility. Moreover, she also complained of progressive dysphagia, fatigability on completing full sentences and constipation. Three weeks prior to these symptoms the patient was diagnosed with SARS-CoV-2 via reverse transcription-polymerase chain reaction (RT-PCR) nasal swab test. At that time, she did not have fever, chills, rigors, cough, or shortness of breath. Her only SARS-CoV-2 related symptoms were a 2-day history of diarrhoea and runny nose.

On admission she was haemodynamically stable, afebrile, alert and oriented. She did not require oxygen supplementation within hospital, and her oxygen saturations on room air remained above 95% throughout her admission. No signs of meningism were noted. Her cranial nerve and upper limb examination were normal. On the other side her lower limb examination was not intact. Tone and muscle bulk were normal but she was noted to have diminished power (MRC) 4/5 across all lower limb muscle groups bilaterally. Reflexes were elicited but appeared diminished bilaterally. Plantars were down going bilaterally. Sensory testing revealed hyperaesthesia and allodynia in her lower limbs, with impaired vibration and proprioception. She was unable to stand independently.

Blood tests on admission revealed a raised white blood cell count of $17.4x10^9$/L and neutrophil count of $12.9x10^9$/L. Erythrocyte sedimentation rated and C-reactive protein were normal at 9mm 1st hour and 4mg/L respectively. An auto immune screen, thyroid function test and vitamin B_{12} were normal. Chest x-ray did not show consolidation or ground glass shadowing. Our two differential diagnoses were transverse myelitis and GBS post SARS-CoV-2 infection. Magnetic resonance imaging of the head and whole spine excluded intracerebral and spinal pathology.

Cerebrospinal fluid (CSF) showed albuminocytological dissociation with a raised protein level of 1068mg/l (Normal range: 150-450mg/l) but no leukocytes. Paired oligoclonal bands in CSF and serum were detected, indicating a systemic immune reaction. Anti-ganglioside profile including anti-MAG, GM1, GM2, GD1a, GD1b and GQ1, was negative.

On day four post admission, the patient complained of bilateral paraesthesia at the tips of her fingers and experienced worsening of the power in her lower limbs (MRC 3/5 in most of the muscle groups), absent ankle reflexes and increased breathlessness. Nerve conduction studies (NCS) identified a severe, generalized, patchy, sensory more than motor, mixed demyelinating, and axonal peripheral neuropathy, consistent with a diagnosis of GBS.

Baseline lung function test revealed a reduced forced expiratory volume (FEV_1) of 1.17 and forced vital capacity (FVC) of 1.47 with a FEV_1/FVC ratio of 0.80. She was treated with 2g/kg of IVIG over two days. Pregabalin 50mg twice daily was prescribed to relieve the neuropathic pain.

After IVIG was administered the progression of her symptoms stopped, and the patient manifested steady signs of recovery. Her shortness of breath, and dysphagia improved after four days. Three weeks post treatment the patient was able to walk independently with a Zimmer frame and was discharged home. A repeat lung function test after four weeks showed an increase in FEV_1 from 1.17 at baseline to 1.56. Two months after the IVIG treatment a follow up nerve condition study showed that the multifocal polyneuropathy had resolved.

DISCUSSION

GBS post SARS-CoV-2 infection was reported in several cases around the world.[3] The mean latency of GBS post SARS-CoV-2 infection was 12.1 days, with most of the patients experiencing their first neurological signs between 7 to 28 days.[10] Although numerous cases of GBS were reported post SARS-CoV-2 infection, it is a rare complication. In fact, Toscano et al. studied 1000-1200 patients between 28th February and 21st March 2020, and found out that only five patients had GBS post SARS-CoV-2 infection. Three of these patients had respiratory failure.[11] It is well known that GBS can cause respiratory muscle weakness and 10 to 30 percent might require ventilatory support.[12] It is important to remember that SARS-CoV-2 can cause GBS since patients which are sedated on ventilatory support might be missed.

In our case report we found that the patient's findings were in keeping with acute inflammatory demyelinating polyneuropathy (AIDP). Abu-Rumeileh et al pointed out that AIDP was reported in 46 patients out of 74 cases, making it the most common GBS variant post SARS-CoV-2 infection.[13] AIDP is an autoimmune reaction directed towards epitopes which are found on the schwann cell surface membrane or myelin.[14] It is known that a small number of patients who have AIDP can develop severe secondary axonal degeneration.[15]

Other subtypes of GBS post SARS-CoV-2 infection include Miller Fisher Syndrome (MFS), which causes ataxia, areflexia and ophthalmoplegia, Acute Motor Axonal Neuropathy (AMAN) which is characterised by sparing of sensory nerves and most of the time it is preceded by *Campylobacter jejuni* infection, and Acute Motor and Sensory Axonal Neuropathy (AMSAN) which is similar to AMAN but effects the

sensory nerves as well.[15] A literature review showed that only seven AMSAN type of GBS and only three AMAN type of GBS were noted out of 74 cases and that 70% of the patients had good recovery with IVIG.[13] They also mentioned that other post-infectious GBS and post-SARS-CoV-2 GBS share most features, raising the question whether they share the same immune-mediated mechanisms.[13]

CONCLUSION

Our case report demonstrated that mild SARS-CoV-2 infection may also cause GBS, in this case our patient had AIDP subtype. GBS may be missed when it disguises itself as a myelopathy. GBS may also be missed in those patients which are sedated in ITU and in those who have SARS-CoV-2 infection which develop respiratory failure secondary to GBS rather than SARS-CoV-2.

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