Case report

Miller Fisher syndrome and COVID-19: is there a link?

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SUMMARY

Beyond the typical respiratory symptoms and fever associated with severe acute respiratory syndrome, we may still have much to learn about other manifestations of the novel SARS-CoV-2 infection. A patient presented with Guillain-Barré syndrome in China with a concurrent SARS-CoV-2 infection. The following case report looks at a patient presenting with the rare Miller Fisher syndrome, a variant of Guillain-Barré while also testing positive for COVID-19.

BACKGROUND

COVID-19 is a novel virus and as such, we still have much to learn about its manifestations. There are well documented respiratory symptoms and fever associated with COVID-19 infection.[1 2]

Following the diagnosis of Guillain-Barré syndrome (GBS) in a patient in China presenting with COVID-19 symptoms,[3] perhaps consideration should be given to the possibility that COVID-19 may potentially cause neurological symptoms. The clinician should consider a thorough and complete systems examination as the possibility that neurological symptoms may be present in patients with COVID-19.

Zhao (2020) suggested in their article that GBS, associated with SARS-CoV-2, might follow the pattern of a parainfectious profile, instead of the typical postinfectious profile seen with the Zika virus epidemic.[4]

The following case study highlights the reason why clinicians should be cognisant to the possibility of COVID-19 presenting as neurological symptoms.

CASE PRESENTATION

A 63-year-old man, who has spent the month of February 2020 travelling around Cambodia, Thailand and Laos, presented to the emergency department on 7 April 2020 after waking with double vision and neurological changes to his mouth and fingertips in the form of paraesthesia. He admitted to feeling that he may have had a fever the night before but had no thermometer to confirm or refute this.

Initial findings

Initial investigations revealed that he was feverish at 38°C on arrival and thus, in line with departmental policy, was transferred to the isolating area of the department. Other observations were unremarkable and revealed oxygen saturations of 100% on room air, heart rate 93bpm and regular, a respiratory rate of 18 breaths per minute and blood pressure of 155/97 mm Hg. History suggested that he had no headache or pain of any kind and he denied any recent or current respiratory symptoms and, other than the numbness and diplopia that had brought him into the emergency department, he felt well otherwise. His medical history consisted of hypertension only for which he had been prescribed Lisinopril and Amlodipine with no known allergies. Social history was that of a retired operational manager who is a non-smoker, living independently with his wife. He now volunteers as an assistant harbour master.

On examination

The patients' cardiovascular and respiratory systems were unremarkable. Abdominal examination was also normal with no reported gastrointestinal disturbance or abnormal bladder function.

A gross neurological examination demonstrated that he was alert and orientated with a Glasgow Coma Score of 15. FAST (face, arms, speech test) was negative and recognition of stroke in the emergency room (ROSIER) score was zero indicating a stroke was unlikely. No abnormalities were found with speech and no swallowing difficulties were evident. The cerebellar examination demonstrated an ataxic gait which the patient attributed to the diplopia; all other cerebellar signs were normal.

A bilateral divergent squint was evident, but eye movements following the H test appeared normal. Other neurological findings were perioral paraesthesia, isolated to the right side only and some tingling in 1–4 finger tips bilaterally. Remaining sensation was normal throughout.

Along with these findings, there appeared to be a complete absence of all reflexes but normal downgoing plantars. Otherwise, peripheral examination of tone, power and sensation in all four limbs was normal.

Various blood investigations, a chest X-ray and CT and MRI scans of the brain were requested and carried out prior to admission (table 1).

DIFFERENTIAL DIAGNOSIS

The presenting symptoms pointed to a working diagnosis of a posterior circulation stroke. This type of stroke may affect the brain stem, occipital lobes and/or the cerebellum. These areas of the brain control balance, co-ordination and vision.

Due to the current Coronavirus pandemic, all patients with a fever above 38°C were suspected of having COVID-19 infection until proven otherwise.

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Table 1 Initial investigations and results

Investigations	Results
ECG	Normal sinus rhythm
Urea and electrolytes	Normal
Liver function test	Alanine Aminotransferase elevated 41 (IU/L)
C reactive protein	Elevated 13 (mg/L)
Coagulation	Normal
Full blood count	White Cell Count reduced 2.4 (10^9/L) Neutropaenia 1.2 (10^9/L) Lymphopaenia 0.5 (10^9/L)
Glucose	Normal
Thyroid function test	Normal
Chest X-ray	No evidence of consolidation or collapse. Linear left basal atelectasis. COVID-19 cannot be excluded
CT brain	Normal
MRI brain	Normal

The patient was admitted for further ward-based investigations (table 3) and a neurological assessment and was also swabbed for COVID-19.

With both CT and MRI scans being reported as normal with no evidence of a stroke, further examinations were carried out by the neurological team.

Impression

Presentation in keeping with Miller Fisher syndrome—a variant of Guillain-Barré syndrome

The assessment carried out by the neurological team demonstrated largely complex ophthalmoplegia, ataxia and areflexia (table 2). This triad of symptoms are found in Miller Fisher syndrome.

Review

Subsequent COVID-19 swab results proved positive to SARS-CoV-2.

Table 2 Neurological team assessment and findings

Assessment	PEARL
Complex ophthalmoplegia	Left eye—failure of adduction, elevation and restricted depression Right eye—failure of adduction, restricted elevation and depression Mild ptosis left eye >right eye not defatigable
Visual field	Full to confrontation
Face	No facial weakness Tingling right side both lips and upper gum. Normal pin prick Tongue and neck strong
Tone	Normal tone in all limbs
Power	Normal power in all limbs
Reflexes	Biceps—absent Triceps—absent Supinator—(R) present with reinforcement Knees—absent Ankles—just present without reinforcement
Plantars	Down
Sensation	Tingling 1–4 finger tips. Normal pin prick
Proprioception	Normal
Vibration	Normal
Finger nose/heel shin	Normal. No ataxia
Gait	Ataxic
Rombergs	Negative

Table 3 Ward investigations and results

Human immunodeficient virus screen	Negative
Serum total protein	Normal
Vitamin B12	Normal
CSF	Elevated protein level 0.54 (g/L) CSF glucose normal White Cell Count 1×10^6/L Red Blood Cell 16×10^6/L Mononuclear cells. 100% Gram stain. No organisms seen Culture. No bacterial growth
Blood cultures	Negative

CSF, cerebrospinal fluid.

TREATMENT

The diagnosis and prognosis was explained to the patient. He was advised to return if symptoms progressed or he became non-ambulant or experienced breathing or swallowing difficulties where he may need to be readmitted and may receive intravenous immunoglobulin (IVIG).

Prior to discharge 2 days later, as there had been no deterioration in the patients' condition, no pharmacological intervention was required.

OUTCOME AND FOLLOW-UP

The patient was advised that a full recovery is likely although this may take weeks or months.

The week prior to developing symptoms, the patient had visited his mother who was receiving end of life care. During this time he had contact with two sisters, the younger of whom has since developed COVID-19 symptoms.

The patient has used an eye patch since discharge to counter the dizziness on walking and has improved the divergent squint by using eye exercises.

While the patient was aware that he may have had a fever the night before, there was no delay in presenting to the emergency department the following morning when he became aware of the more concerning diplopia and ataxic gait. Likewise, there was no delay in the care provided. He was seen by a clinician within 15 min of arrival in the emergency department and all emergency department investigations were carried out and results available within 4 hours.

DISCUSSION

Miller Fisher syndrome

Miller Fisher syndrome is rare with an annual incidence of 0.1 per 100 000 population in the UK.[5] It is thought to be an autoimmune-acquired disease affecting the nerves and considered to be a variant of GBS. Like GBS, symptoms may be preceded by a viral illness. As with GBS, treatment includes IVIG and plasmapheresis. They likewise have similar prognoses and the majority of cases resolve within 6 months. Rarely, it may progress resulting in permanent neurological deficit.

Although respiratory symptoms and fever are the recognised distinctive features of patients presenting with COVID-19, over 100 publications have demonstrated neurological findings affecting the central and peripheral nervous system and muscular system of patients testing positive for COVID-19.[6]

American neurologists are reporting subtle symptoms like fatigue, encephalopathy and ataxia in their patients with COVID-19.[7] Anecdotally, a loss of smell and taste was also widely reported

Patient's perspective

Events contributing to attendance to Poole A&E on Tuesday 7 April 2020

On Monday, 6th April, I went to bed at approximately 21:00 with a raised temperature.

I took 2×500 mg Paracetamol.

On Tuesday, 7th April, I awoke with the feeling of a severe migraine.

I had blurred vision, tingling sensation in the fingertips of both hands and lips.

In an attempt to dislodge this sensation, I took a further 2× Paracetamol and returned to bed.

At approximately 10:00, I attempted to stand up and found that I had a serious loss of balance.

My wife insisted that I try and obtain assistance and following a telephone call to the GP Surgery, she then called 999 and was advised to take me to A&E Poole.

By this time, I had realised that if I covered either eye, I could focus with the uncovered eye.

My left eye was definitely stronger, but my balance was compromised if I tried to walk using my right eye.

My thoughts were that I may have had a mild stroke affecting my eye coordination.

At Poole General, I was checked in and due to my reporting a high temperature, was taken to Isolation in A&E.

The staff were very attentive and reacted fast to my needs

The previous Thursday, 2nd April, I had driven to Milton Keynes to visit my mother who was at 'End of Life' in a care home. The only direct contact was with my two sisters. My younger sister has since suffered Covid 19 symptoms. My Mum passed away on Saturday, 4th April, after which I returned home to Dorset.

On Thursday, 9th April, I was discharged from Poole General and advised to return if certain conditions arose, relating to breathing and swallowing.

On Friday, 10th April, I received a call confirming the presence of Covid-19.

Over the weekend, my temperature was extremely high and I went to bed with severe symptoms. I had no appetite or a desire to drink. My taste was ok, but I did not like anything, all too sweet or too salty. I took 2× Paracetamol every 5–6 hours.

On Monday, 13th and Tuesday, 14th, my breathing was laboured and I considered a return to A&E. I was extremely tired and would become exhausted just by moving around.

My eyes continued to not coordinate, and I wore an eyepatch if attempting to walk or focus on anything.

Every day I tried to read. Using an E-reader and an eyepatch, I would read chapters alternatively with my right and left eye until I became tired, usually about an hour at a time.

Occasionally, I would use the eyepatch to stand up and move. Using my left eye, I could maintain balance, but using my right eye, I had no real coordination and had to sit down.

By Wednesday, 15th, I was taking Paracetamol every 12 hours but feeling extremely ill by 18:00. I still had no appetite but was drinking extremely weak lemon juice and a spoon of honey.

Each afternoon, I exercised my eyes by looking at an object with both eyes and trying to bring the two images in line with each other.

By Thursday, 16th, I was managing to bring the two images together for short periods. This control disappeared if I changed focus, and I still needed an eyepatch to balance enough to walk.

Continued

Patient's perspective Continued

Over the weekend, Friday 17th–Sunday 19th, my eyesight improved and I could walk without an eyepatch.

The numbness in my fingers gradually subsided over the weekend as well. But my left hand took until Monday, 20th, to return to normal.

From Monday, 20th April, my eyesight has improved daily. I am still unstable when walking and suffer extreme fatigue. I am getting headaches in the evening which I attribute to maintaining focus throughout the day. On Thursday, 23rd, I attempted some strenuous lifting in the garden and suffered an extreme headache causing me to take 2× Paracetamol and immediate rest.

My appetite is returning for small portions, preferably fruit and vegetables.

I still feel generally weak, but every day is improvement.

I would like to extend my thanks to the staff at Poole General, who were efficient and extremely attentive to my strange condition.

Learning points

- Consider multisystem examination on all patients presenting with novel viruses.
- Neurological symptoms are a growing feature of COVID-19.
- Expect the unexpected.

in the media but this has not been upheld scientifically although increasing cases are being acknowledged. Gutiérrez-Ortiz documents two patients presenting with areflexia, oculomotor palsy and ataxia who also reported anosmia and ageusia and both tested positive for COVID-19. They were subsequently diagnosed with Miller Fisher syndrome and multiple cranial neuropathy.[8]

In conclusion, as diversity of symptoms and presentations continue to emerge with COVID-19, it is important to assess all systems and be mindful of all unanticipated findings.

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Lessons learned

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