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Case report

Isolated abducens nerve palsy in a patient with asymptomatic SARS-CoV-2 infection

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ABSTRACT

The neuro-ophthalmological complications of SARS-CoV-2 infection are emerging but the spectrum of presentations and pathophysiological mechanism underpinning the association remains to be fully determined. We describe the case of a 44-year-old female who presented with a 12-hour history of diplopia preceded by a mild headache and found to have an isolated right abducens nerve palsy. Initial vital signs were normal but she developed a fever and nasopharyngeal swab confirmed SARS-CoV-2 infection by RT-PCR. All other investigations returned normal including blood tests, chest X-ray, MRI brain and cerebrospinal fluid analysis. She remained systemically well, and there was complete resolution of the abducens palsy and diplopia at two week follow up. In the absence of an alternative underlying cause or risk factors identified, the aetiology was presumed to be microvascular and potentially related to the viral infection. We add to the evolving literature of neuro-ophthalmological associations of SARS-CoV-2, discuss possible causal mechanisms and suggest considering asymptomatic SARS-CoV-2 infection in cases of isolated abducens palsy without clear risk factors.

1. Background

Abducens nerve palsy is the most common isolated ocular motor palsy and has a wide range of potential aetiologies. In children, whilst most commonly associated with neoplasm, it has been associated with viral infections and following immunisations [1]. In older adults the most frequent cause is microvascular disease [2]. It is a rare presentation in younger adults, where the aetiology includes vasculopathies, neoplasia, multiple sclerosis and other inflammatory diseases, with viral aetiologies responsible for 1–10% of cases [3]. There are emerging cases of abducens nerve palsies related to SARS-CoV-2 infection – both isolated and in association with other ocular and central nervous system (CNS) manifestations - but the incidence and pathophysiological mechanisms behind these associations is yet to be fully established. We present a case of isolated abducens nerve palsy in an individual with otherwise asymptomatic SARS-CoV-2 infection.

2. Case

A 44-year-old right-handed female attended her local Emergency Department after she awoke with persistent diplopia. The preceding day, she had a mild right-sided headache and blurred vision, which had significantly improved at the time of presentation. There were no additional features of migraine or raised intracranial pressure. She denied recent history of fever, malaise, cough or anosmia. There was no antecedent history of trauma, rash, insect bites or foreign travel. Her past medical history included migraine with aura, without previously associated cranial nerve palsies. She had no known vascular risk factors.

On admission, the patient was afebrile with stable observations and no respiratory symptoms. Examination was notable for isolated, complete abduction failure of the right eye with associated horizontal diplopia which persisted on primary gaze and was exacerbated by distance fixation. All other extraocular movements were full, fundal and pupil examination was normal with no evidence of ptosis, proptosis, chemosis or fatigable weakness. The remainder of the neurological examination was normal.

Repeat routine observations on the neurology ward revealed a pyrexia of 39.5C with otherwise normal vital signs. The patient's

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admission nasopharyngeal swab subsequently confirmed SARS-CoV-2 infection by real-time reverse transcription polymerase chain reaction (RT-PCR). Routine blood tests including lymphocyte count, C-reactive protein and renal function were normal, as was the chest X-ray. HbA1c, cholesterol, plasma viscosity, thyroid stimulating hormone, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, angiotensin-converting enzyme and acetylcholine receptor antibodies later returned normal.

Magnetic resonance imaging (MRI) of the brain with gadolinium and dedicated venogram was normal. Lumbar puncture revealed a normal opening pressure and normal cerebrospinal fluid (CSF) constituents (WCC < 1 mm3, RBC < 1 mm3, protein 0.2 g/L, glucose 3.7 mmol/L), negative oligoclonal bands and a negative viral PCR for enterovirus, varicella zoster and herpes simplex type 1 and 2. CSF analysis for SARS-CoV-2 RNA was not available at our centre.

The patient's isolated pyrexia resolved; she remained systemically well and was discharged 48-hours post admission with a persisting ophthalmoparesis. No treatment was required other than paracetamol for the pyrexia. At two week follow up, there was complete resolution of the abducens nerve palsy and diplopia. She reported the double vision had resolved five days after discharge and she remained systemically well.

3. Discussion

SARS-CoV-2 is associated with a broadening range of neuro-ophthalmological complications [4]. These include conjunctivitis, retinal haemorrhage, headache and ocular pain, Miller Fisher syndrome and cranial nerve palsies; specifically of the facial, oculomotor and abducens nerves [4]. Previously reported cases have described abducens palsy in patients who have had typical preceding symptoms of SARS-CoV-2 infection, including malaise, fever, cough and hypoxia [5–8]. To our knowledge, we present the first case of abducens nerve palsy in association with otherwise asymptomatic SARS-CoV-2 infection.

A literature search revealed six previously reported cases of abducens palsy in symptomatic SARS-CoV-2 infection, summarised in Table 1 [5–8]. Of the cases described, 4 (67%) were female with ages ranging from 32 to 71 years. Common signs on presentation included fever in 3 (50%) and hypoxaemia in 4 (67%) cases. All but 2 (67%) patients reported at least partial recovery in symptoms days-weeks following the onset of the illness although extensive follow-up was limited. Proposed mechanisms include acute demyelinating inflammatory polyneuropathy secondary to a virus-mediated immune response, ischaemia or direct viral involvement of the CNS [4,7]. We discuss possible mechanisms behind the abducens palsy described in this case below.

3.1. Vascular and thrombotic

There is widespread evidence that SARS-CoV-2 is associated with vascular and thrombotic complications. Firstly, in cases of severe infection, uncontrolled immunothrombosis is thought to result in widespread microangiopathy [9]. Secondly, SARS-CoV-2 has been demonstrated to invade endothelial cells directly, via angiotensin converting enzyme (ACE)-2 receptors expressed on the cell surface. This results in loss of endothelial function and integrity and causes activation of the coagulation system [10]. Furthermore, ACE-2 has anti-thrombotic functions, but uptake of virus into cells is associated with a downregulation of its expression, contributing to a prothrombotic state [11]. In this case, the presence of a headache at the onset of diplopia was clinically suspicious for microvascular aetiology, as headache is commonly reported in ischaemic cranial nerve palsies [12].

3.2. Direct viral involvement of CNS

Whilst CSF testing for SARS-CoV-2 is not currently available in our centre, there are reports from other units globally with successful methods of detection [13–15]. These studies provide evidence of the neuro-invasive potential of the virus. One proposed mechanism of entry is via cellular ACE-2 receptors, which have been shown to be expressed in neurons, as well as endothelial and arterial smooth muscle cells in the brain [14]. Although there has been one reported case of SARS-CoV-2 detected in CSF but not in the nasal swab [15], reports of nasal swab-positive yet CSF-negative results in SARS-CoV-2 neurological disease suggest that SARS-CoV-2 presence in CSF may depend on the severity of systemic disease [14]. This, together with normal routine CSF constituents in our case, suggests it may be less likely to detect SARS-CoV-2 in the CSF of an otherwise asymptomatic patient. Wider availability of a validated CSF testing for SARS-CoV-2 PCR would enable this to be further explored.

3.3. Virus-Mediated immune response

Virus-mediated immune response is another proposed mechanism within the literature, with documented cases of Miller Fisher Syndrome in the context of SARS-CoV-2 infection [4]. However, this is usually a post-infectious phenomenon, therefore the timing of abducens palsy during the active stage of SARS-CoV-2 infection in this case would be atypical. Furthermore, the lack of other neurological signs, such as ataxia or areflexia, together with the normal CSF protein level would be unusual for a Guillain-Barre syndrome variant. However, anti-ganglioside antibodies were not

Table 1
Summary of reported cases of abducens nerve palsy in the context of Covid-19 infection [5–8]. Study details, symptoms, treatment and outcomes.

Study	Presentation	Neurological Signs	Treatment	Outcome
Dinkin *et al.* May 2020	36 M, fever, cough, myalgia 14 days pre-presentation	Left oculomotor palsy and bilateral abducens nerve palsies, presumed Miller Fisher Syndrome	Intravenous immunoglobulin, Hydroxychloroquine	Some improvement at day 3 post admission
Dinkin *et al.* May 2020	71 F, symptomatic hypoxaemia	Right sided abducens palsy	Hydroxychloroquine	Partial resolution at 2 weeks
E. Pascual-Goñi *et al.* June 2020	60 F, fever, hypoxaemia, hyposmia, nausea and cough	Right abducens nerve palsy	Hydroxychloroquine, Azithromycin	No improvement 1 month after admission
E. Pascual-Goñi *et al.* June 2020	35 F, vomiting and progressive encephalopathy, hypoxaemia	Bilateral abducens palsy, mild paraparesis, Wernicke's encephalopathy	Thiamine, Pyridoxine	Improvement at 1 month
Falcone *et al.* Aug 2020	32 M, acute hypoxaemic respiratory failure	Complete left abducens nerve palsy	Hydroxychloroquine	No improvement at 5 weeks
C. Gutiérrez-Ortiz *et al.* Aug 2020	39 M, fever, diarrhoea, generally unwell	Bilateral abducens nerve palsy	Nil specific	Full resolution at 2 weeks

tested in this case and a viral induced immune-mediated neuropathy cannot be excluded as a potential mechanism.

4. Conclusion

Whilst we acknowledge the occurrence of isolated abducens palsy and SARS-CoV-2 infection could be coincidental and unrelated, here we postulate a causative link due to the otherwise rare occurrence of abducens palsy in a young adults without risk factors. We add to the literature of emerging neuro-ophthalmological associations of SARS-CoV-2 infection. Further work is required to more confidently support causality and to elucidate the proposed mechanisms. Early follow-up suggests a full recovery is possible without specific treatment. As the pandemic continues across the globe, we suggest considering asymptomatic SARS-CoV-2 infection in patients presenting with ocular motor palsies without other risk factors.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2021.04.011.

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