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Case Report

Internal Medicine Section

A Rare Case of Adenovirus-induced Transverse Myelitis: A Clinical Insight into Diagnosis and Treatment

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ABSTRACT

Adenovirus (Ad), a common virus, can cause a variety of symptoms such as respiratory issues, fever, and occasionally neurological problems. Transverse Myelitis (TM) is defined as a neurological disorder marked by inflammation of a section of the spinal cord which further damages the myelin sheath surrounding the nerve fibers. This can result in a variety of symptoms, including general weakness, sensory changes, pain and difficulties with bowel and bladder control. Ad causing TM is a topic of great significance in the field of medicine as it involves a rare yet serious condition. Hereby the case report of a 64-year-old female who presented to the Emergency Room with fever and bilateral lower limb weakness and was diagnosed with TM, with the Cerebrospinal Fluid (CSF) report Polymerase Chain Reaction (PCR) showing Ad. The patient was treated with plasmapheresis, antivirals, steroids and physiotherapy. The present case emphasises that timely diagnosis and identification of the underlying cause of TM are essential to prevent respiratory paralysis and other complications. It is also important to exclude other autoimmune conditions, as well as, bacterial and fungal infections, in every patient.

Keywords: Cerebrospinal fluid, Lower limb weakness, Methyl prednisolone, Plasmapheresis

CASE REPORT

A 64-year-old female patient presented to the Emergency Room with complaints of fever and vomiting for 15 days, along with a history of cough for five days. She had bilateral progressive lower limb weakness and sharp, non radiating, pins and needles type of pain in bilateral lower limbs, along with decreased urinary output for one day. She was diabetic, hypertensive, asthmatic, and on medications, with a past history of left lower limb poliomyelitis. She had no previous history of vaccination.

On physical examination, she was conscious, oriented to time, place, and person, and was haemodynamically stable. On neurological examination, the patient had normal higher mental function. The tone was flaccid in bilateral lower limbs but normal in upper limbs. Power was 0/5 in bilateral lower limbs (no flickering movements) and 5/5 in bilateral upper limbs, with diminished reflexes of both knees and ankles. The plantar reflexes on both lower limbs showed an extensor response. She had no sensory deficit. There were no complaints of band-like sensations, and cerebellar signs were absent. No neck rigidity or involuntary movements were seen, suggesting that the patient did not have meningitis. The differential diagnosis was Guillain-Barré Syndrome (GBS), Acute TM (ATM), diabetic neuropathy and spinal cord compression, with the signs and symptoms mainly suggestive of ATM.

Laboratory investigations revealed mild elevation of C-reactive Protein (CRP), procalcitonin and Erythrocyte Sedimentation Rate [Table/Fig-1] [1]. CSF reports showed an elevated total cell count with increased protein and normal glucose levels. CSF culture and sensitivity indicated no growth. CSF Cartridge-based Nucleic Acid Amplification Test (CBNAAT) results were negative [Table/Fig-2]. Special blood investigations were conducted, including testing for Neuromyelitis Optica (NMO) Myelin Oligodendrocyte Glycoprotein (MOG) antibody titres antinuclear antibody by immunofluorescent assay and antinuclear antibody blot, all of which were negative. CSF TRUPCR® (viral panel) revealed the presence of human Ad [Table/Fig-3].

Radiological investigations were also performed. A chest X-ray showed no parenchymal changes. Magnetic Resonance Imaging (MRI) of the brain was normal. However, MRI of the cervicodorsal spine (plain with contrast) displayed a mildly swollen spinal cord from the D1-D4 vertebral level with T2 hyperintense signal involving the central portion, but no obvious intramedullary abnormal enhancement, suggestive of Transverse Myelitis (TM) [Table/Fig-4]. Additionally, there was focal hyperintensity on T1 and T2 imaging, indicative of a haemangioma.

Extensive work-up was carried out to rule out common infections such as Human Immunodeficiency Virus (HIV), tuberculosis and syphilis as causes of TM. Postvaccine TM was also excluded based on vaccination history. Serum antinuclear antibody tests were conducted to investigate systemic autoimmune conditions causing TM. Furthermore, NMO MOG antibody titres of serum and MRI

Investigations	Laboratory value	Normal value [1]
Haemoglobin (g/dL)	10	12-16
White blood cells (/microlitre)	9500	4500-11000
Platelet count (/microlitre)	185000	150000-400000
Serum sodium (mmol/L)	137	136-145
Serum potassium (mmol/L)	3.6	3.5-5
C-reactive protein (mg/L)	20	≤0.8
Procalcitonin (ng/mL)	1.25	≤0.10
Erythrocyte sedimentation rate (mm/hour)	30	0-20
Human Immunodeficiency Virus (HIV) test	Negative	-
Venereal disease research laboratory test	Negative	-

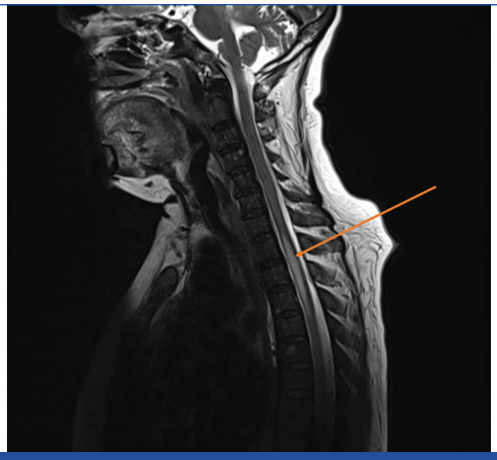
[Table/Fig-1]: Laboratory investigations [1].

Parameters	Result
Total cell count	20
Lymphocytes (cells/microlitre)	18
Glucose (mg/dL)	54
Protein (mg/dL)	64.2
Adenosine deaminase	3.3
Culture and sensitivity	No growth
Cartridge-based nucleic acid amplification test	Negative

[Table/Fig-2]: Cerebrospinal Fluid (CSF) reports.

Investigations	Results
Blood tests	
Blood test: Neuromyelitis Optica (NMO) Myelin Oligodendrocyte Glycoprotein (MOG) antibody titres	Negative
Blood test: Antinuclear antibody by immunofluorescent assay	Negative
Blood test: Antinuclear antibody blot	Negative
CSF test: CSF TRUPCR® (viral panel)	
Herpes Simplex Virus (HSV)	Not detected
Cytomegalovirus (CMV)	Not detected
Human Adenovirus (Ad)	Detected

[Table/Fig-3]: Special investigations.



[Table/Fig-4]: MRI of cervicodorsal spine of the patient showing mildly swollen spinal cord from D1-D4 vertebral level showing T2 hyperintense signal marked by the arrow.

of the brain were performed to rule out demyelinating disorders. Following the comprehensive evaluation, the reports suggested TM secondary to a viral infection, with human Ad detected in the CSF PCR.

Treatment included the administration of antiviral drug acyclovir 500 mg intravenously thrice daily for five days, pulse steroid injections of Methyl Prednisolone (MPS) 1 g intravenously daily for three days and plasmapheresis for five days. Rigorous physiotherapy was initiated. After completing the pulse steroid therapy, five cycles of plasmapheresis and the antiviral course, the patient's power improved from 0/5 (no flickering movements) to 4/5 (active movements against gravity and resistance) in bilateral lower limbs. A follow-up MRI of the cervicodorsal spine (plain with contrast) before discharge showed improvement compared to the initial scan. Upon discharge, the patient was prescribed tapering doses of oral steroids, antidiabetic and antihypertensive medications, a steroid inhaler for asthma, and instructed to continue home physiotherapy.

DISCUSSION

The ATM is a spinal cord disorder characterised by the following key features: disruptions in sensory, motor, or autonomic functions associated with spinal cord involvement; bilateral symptoms or signs; a well-defined sensory level correlating with the spinal cord segment; absence of evidence for a compressive lesion; signs of inflammation, such as CSF pleocytosis, increased CSF immunoglobulin G index, and/or gadolinium enhancement on MRI; and rapid symptom progression, reaching its peak within a time frame of four hours to 21 days. There is a recurrence of systemic infection in 50% of idiopathic cases. Postinfectious ATM is triggered by inflammation after infection causing an autoimmune response [2]. The aetiology of TM includes systemic inflammatory conditions like systemic lupus erythematosus and sarcoidosis; demyelinating disorders such as multiple sclerosis; and postinfectious or idiopathic TM [3]. Ad type 21 has been linked to several fatal conditions of the respiratory system and widespread infection [4]. Neurological complications were not reported with Ad type 21, but the species B human Ad, especially Ad type 7, has been linked to various neurological issues like encephalitis and even TM [5-10].

Transverse myelitis has an estimated incidence of 1-8 cases per million per year worldwide [11], and ATM has an incidence of up to 3 per 100,000 patient years (0.003%) [12]. In an Indian study, the rate of Ad infection in immunocompromised individuals varied between 3% and 21%, while the associated mortality rate ranged from 7.7-38% [13]. Ad, being a common cause of viral infections of the upper respiratory tract, can cause rare neurological complications such as TM. A recent study in the United States found the prevalence of idiopathic TM to be 7.9 cases per 100,000 people from 2003 to 2016. In contrast, international studies from Israel and the United Arab Emirates reported annual TM prevalence rates of 1.34 per million and 0.18 per 100,000, respectively. However, these findings are constrained by varying diagnostic criteria and small sample sizes, often drawn from relatively uniform patient groups [14].

In the past century, only three cases of Ad causing TM worldwide have been reported. A 30-year-old female was diagnosed with TM, and PCR of bronchoalveolar lavage fluid was positive for Ad. She was initially treated with two days of high-dose steroids. However, after observing no neurological improvement, three daily sessions of plasmapheresis were initiated, resulting in a drastic improvement in her bilateral lower limb weakness [3]. Another case report from France described a patient with Ad-induced TM that resolved with treatment using high-dose methylprednisolone alone [15]. In a case study from the Netherlands, a nine-year-old male was diagnosed with TM following an upper respiratory tract infection caused by Ad [10].

The TM consortium working group suggests that to diagnose TM, the clinical presentation should be supported by evidence of contrast enhancement on an MRI of the spinal cord and/or elevated protein levels in the CSF, as was observed in the present case. An MRI is essential to exclude spinal cord compression, and an MRI of the brain should also be performed to rule out any brain lesions [16].

Current medical therapy for ATM includes pulse steroid injection, MPS 1 g i.v. daily for five days, and plasmapheresis [17], which was also administered to the present case patient. Since the patient responded well to steroids and plasmapheresis, the treatment was not escalated; however, cyclophosphamide has been identified in the literature as an alternative for patients with minimal and delayed responses or resistance to standard therapies [18].

In the present case involving an elderly patient, Ad was identified as the cause of TM, presenting with multiple regions of abnormal T2/FLAIR signal in the white matter and elevated CSF protein levels. This prompted an evaluation for possible autoimmune and viral causes. Aetiologies such as infections, neoplasms, vascular, or metabolic conditions have been thoroughly ruled out. The CSF PCR viral panel revealed human Ad in the present case patient, which is not a common finding in the literature. Treatment with pulse steroids injection, MPS 1 g intravenously daily for three days, plasmapheresis and antiviral acyclovir 500 mg intravenously thrice daily for five days led to rapid and remarkable improvement.

CONCLUSION(S)

Early diagnosis and detection of the aetiology of TM is required to prevent the patient from experiencing respiratory involvement and debilitating complications. Patients should always be evaluated for other causes of autoimmunity and bacterial/fungal infections. A viral panel of CSF helped in better understanding the Ad, even though the patient had minimal systemic manifestations of respiratory tract infections. Immediate treatment, simultaneously with antivirals such as acyclovir 500 mg intravenously thrice daily for five days, pulse steroids-injection MPS 1 g intravenously daily for three days, and plasmapheresis cycles along with rigorous physiotherapy helped us to get the patient back to day-to-day activities in five days.

REFERENCES

[1] American Board of Internal Medicine. ABIM laboratory test reference ranges-January 2024 [Internet]. Philadelphia (PA): American Board of Internal Medicine; 2024. Available from: https://www.abim.org/laboratory-test-reference-ranges.
[2] Yeshokumar AK, Waubant E. Post-infectious acute transverse myelitis. In: Pediatric demyelinating diseases of the central nervous system and their mimics. 2017:215-24. ISBN: 978-3-319-61405-2.
[3] Memon SB, Shaib F. Adenovirus as a cause of transverse myelitis in the intensive care unit. Chest. 2008;134(4):36C. Doi: 10.1378/chest.134.4_MeetingAbstracts.c36002.
[4] Horwitz MS, Knipe DM, Howley PM. Adenoviruses. In: Fields Virology. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 2301-26.
[5] Kelsey DS. Adenovirus meningoencephalitis. Pediatrics. 1978;61(2):291-93.
[6] Simila S, Jouppila R, Salmi A, Pohjonen R. Encephaloningitis in children associated with an adenovirus type 7 epidemic. Acta Paediatr Scand. 1970;59(3):310-16.
[7] Straussberg R, Harel L, Levy Y, Amir J. A syndrome of transient encephalopathy associated with adenovirus infection. Pediatrics. 2001;107(5):69.
[8] Ladisch S, Lovejoy FH, Hierholzer JC, Oxman MN, Strieder D, Vawter GF, et al. Extrapulmonary manifestations of adenovirus type 7 pneumonia simulating Reye syndrome and the possible role of an adenovirus toxin. J Pediatr. 1979;95(3):348-55.
[9] Chou SM, Roos R, Burrell R, Gutmann L, Harley JB. Subacute focal adenovirus encephalitis. J Neuropathol Exp Neurol. 1973;32(1):34-50.
[10] Linssen WH, Gabreels FJ, Wevers RA. Infective acute transverse myelopathy: Report of two cases. Neuropediatrics. 1991;22(2):107-09.
[11] Kilbertus S. Acute transverse myelitis attributed to SARS-CoV-2 infection presenting as impaired mobility: A case report. Can J Emerg Med. 2021;23(4):551-52. Doi: 10.1007/s43678-021-00104-z.
[12] West TW, Hess C, Cree BA. Acute transverse myelitis: Demyelinating, inflammatory, and infectious myelopathies. Semin Neurol. 2012;32(2):97-113. Doi: 10.1055/s-0032-1322586.
[13] Sarker R, Roknuzzaman A, Nazmunnahar, Islam MR. Risk evaluation and mitigation strategies for potential outbreaks of adenovirus infection: Evidence from the recent incidences in West Bengal, India. Clin Pathol. 2023;16:2632010X231205672. Doi: 10.1177/2632010X231205672.
[14] Abbatemarco JR, Galli JR, Sweeney ML, Carlson NG, Samara VC, Davis H, et al. Modern look at transverse myelitis and inflammatory myelopathy: Epidemiology of the National Veterans Health Administration population. Neurol Neuroimmunol Neuroinflamm. 2021;8(6):e1071. Doi: 10.1212/NXI.0000000000001071.
[15] Breteau G, Stojkovic T, De Seze J, Gauvrit J, Pruvo J, Vermersch P. Adenovirus myelitis and Epstein-Barr myelitis: Two unusual viral causes with similar presentations. Rev Neurol. 2000;156(8-9):786-89.
[16] Goh C, Desmond PM, Phal PM. MRI in transverse myelitis. J Magn Reson Imaging. 2014;40(6):1267-79. Doi: 10.1002/jmri.24563.
[17] Weinshenker BG, O'Brien PC, Petterson TM, Noseworthy JH, Lucchinetti CF, Dodick DW, et al. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. Ann Neurol. 1999;46(6):878-86. Doi: 10.1002/1531-8249(199912)46:6<878: AID-ANA10>3.0.CO;2-Q.
[18] Ayed H, Chaudhary MW, AlBaradie R, Mir A. Use of cyclophosphamide in a child with fulminant acute disseminated encephalitis. Child Neurol Open. 2018;5:2329048X18754631. Doi: 10.1177/2329048X18754631.

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