Case Report

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Treatment refractory acute necrotizing myelitis after COVID-19 vaccine injection: a case report

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Introduction and importance: Post-vaccination myelitis is a rare and debilitating clinical situation. There are few reports of post-COVID-19 infection and vaccination neurological sequela.

Case presentation: A 69-year-old lady was admitted to the emergency department due to weakness and hypoesthesia in her hands 1 week after the Sinopharm vaccine injection. MRI showed a cervicothoracic cord haemorrhagic lesion that deteriorated within 48 h. The clinical course was refractory to conservative treatments. She underwent an emergency cervical laminectomy as a salvage treatment. Intraoperative samples were in favour of acute necrotizing myelitis.

Discussion: In the review of the literature, the inflammatory storm, vasculitis, and many unknown etiologies are deemed to be the possible causes of encephalopathy and myelitis after COVID-19 infection and vaccination. There are few cases of post-COVID-19 myelitis and hematomyelia, but this case was the first report of post-vaccination necrotizing myelitis.

Conclusion: Post-vaccination necrotizing myelitis is a lethal medical situation requiring intensive and emergent neurosurgical vigilance. Early clinical diagnosis in the beginning and full neurosurgical-neurological treatment armamentarium options are cornerstones of treatment paradigms. Salvage treatment options such as extensive laminectomy may play a life-saving role in treatment refractory cases of acute necrotizing myelitis.

Keywords: acute necrotizing myelitis, adverse drug reactions, COVID-19, demyelinating diseases, laminectomy, post-vaccination myelitis, SARS-CoV-2, vaccine side effects

Introduction

SARS-CoV-2 or COVID-19 and its associated pneumonia had disastrous effects on global health systems. Cough, fever, and shortness of breath are cardinal manifestations of COVID-19 pneumonia. SARS-CoV-2 also causes extra-pulmonary manifestations. Cardiovascular, gastrointestinal, integumentary, and nervous systems are major system targets for the SARS-CoV-2 virus in the acute or subacute phase. Headache, dizziness, vertigo, neuropathy, encephalopathy, myelitis, seizure, and stroke are the main nervous system presentations of SARS-CoV-2[1,2]. Post-vaccination myelitis is a rare medical event that is associated with neurological sequela. Due to its rarity less is known about post-vaccine myelitis[3]. SARS-CoV-2 vaccines are a heterogeneous family of vaccines including inactivated SARS-CoV-2 virus (Sinopharm) to mRNA-containing ones (Moderna). They have different immunogenic mechanisms and were approved for emergency uses during the SARS-CoV-2 pandemic. Erythema, pain, fever, myalgia, and flu-like syndromes are the most common side effects of SARS-CoV-2 vaccines. They are relatively safe and effective but there are emerging reports on SARS-CoV-2 serious side effects including myelitis[4,5]. In general post-vaccination myelitis has a favourable clinical course but there are documented reports associated with mortality and severe disabilities[6]. Inflammation suppression with steroids and

HIGHLIGHTS

- Post-vaccination acute necrotizing myelitis is an insidious medical diagnosis in era of COIVID-19 due to its similarities with other intramedullary lesions.
- Emergent neurosurgical intervention and proper neurocritical care are essentials.
- Keen medical insight and in time interventions may prevent from unfavourable outcomes.

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Post-vaccination acute necrotizing myelitis is an insidious medical diagnosis in the era of COVID-19 due to its similarities with other intramedullary lesions. Early neurological deterioration, specially sensory-motor deficits are the cardinal manifestations on such a rare diseases. Keen medical insight, in time diagnosis and proper interventions may prevent from unfavourable outcomes.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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plasma exchange are the main treatment options for acute myelitis but the role of laminectomy as a salvage treatment remained debating and sometimes, life-saving.

In this report we present a case of post-vaccination acute necrotizing myelitis associated with Sinopharm anti-COVID-19 vaccine injection. The patient underwent extensive laminectomy as salvage treatment due to conservative treatment failure.

Case

This report was prepared considering the Consensus Surgical Case Report (SCARE) Guidelines[7].

A 69-year-old female was admitted to the emergency department due to sensation and movement problems in her hands. She described that he had received her booster dose of Sinopharm anti-SARS-CoV-2 vaccine 7 days before symptom development. She complained that she could not feel and move her hands properly after receiving the vaccine shot which deteriorated within days. The problem was declared to be more severe in her left hand. She was a known case of a well-controlled mitral valve replacement and was on Warfarin, Valsartan, Concord®, and Aspirin. Her past medical and surgical histories were negligible except for mitral valve replacement surgery. There was no history of immunologic diseases or traumatic events. Her PT- international normalized rate for prothrombin time (INR-PT) was in the therapeutic range regarding her warfarin consumption (3-3.5, on multiple checks). PTT and platelet counts were in a normal range. The rest of the lab results had no remarkable findings. She was conscious and cooperative with a Glasgow coma scale score (GCS) of 15/15. The upper and lower right extremity forces in manual muscle strength testing (MMT) were ~3/5 and 4/5 but on the left side, these values were 2/5 and 3/5(ASIA C). On admission, cranial nerves examination had no obvious deficits. Hypoesthesia was compatible with quadriparesis distribution. Sphincter functions were impaired. Deep tendon reflexes (DTR) were absent (mute)in the upper extremities but exaggerated in the lower limbs (+ 3). The rest of the physical exam was unremarkable. He underwent an emergency brain computed tomography (CT) scan to rule out a stroke. The brain CT scan was normal. A whole neuroaxis MRI was obtained. The brain had no acute ongoing pathologic condition (Fig. 1). Cervical and thoracic MRI sequences showed signal hyperintensity in T1, T2, and short-tau inversion recovery (STIR) images. The major portion of the lesion originated from the brain stem extending to T2. Myelograms showed diminished cerebrospinal fluid (CSF) volumes around the cord with a partial CSF block. There was no obvious signal voids in cervical MRI sequences, compatible with absence of massive vascular malformations of the cord (Fig. 2). The findings were in favour of spontaneous intramedullary haematoma of cord or post-vaccination myelitis. Other diagnoses such as Guillain-Barre syndrome were less probable. She was transferred to the neurological ICU (NICU). Regarding both major clinical suspicion (hematomyelia or myelitis), she received full dose steroid therapy. Due to rapid clinical deterioration and poor response to conservative management, she was consulted with the neurosurgical team. Considering ongoing neurological deterioration, a high index of suspicion for intramedullary lesions such as hematomyelia, vascular malformations, and neoplasia, regarding poor response to high dose steroid therapy and CSF blockage, she and her family were recommended to an emergency decompressive laminectomy and tissue biopsy but they refused the surgery. Standard medical treatments regarding hematomyelia or myelitis were continued. According to cardiology consultation and her unpredictable situation, Warfarin was held and intravenous heparin was administered as antithrombotic. Despite full medical care in the NICU, within 2 days her muscle weakness progressed (ASIA B), lower cranial nerve deficits developed (C.N IX, X, XII, and XII), and she had difficulty maintaining effective breathing. Due to impending respiratory failure was intubated and a nasogastric tube was fixed. Another cervicothoracic MRI was obtained. The intramedullary lesion had been deteriorated and had advanced in both cranial (brain stem) and caudal (mid-thoracic) directions. Axial images showed complete cord signal intensity in MRI sequences. Myelograms showed significant cord oedema and obvious CSF blockage (Fig. 3). Another neurosurgical consultation was requested. Regarding the imaging findings and medical deterioration, CSF block, mass effect, and absence of proper clinical response to typical myelitis medical therapy and impending death the surgical team hypothesized that the lesion could be an expanding haematoma or neoplasia.

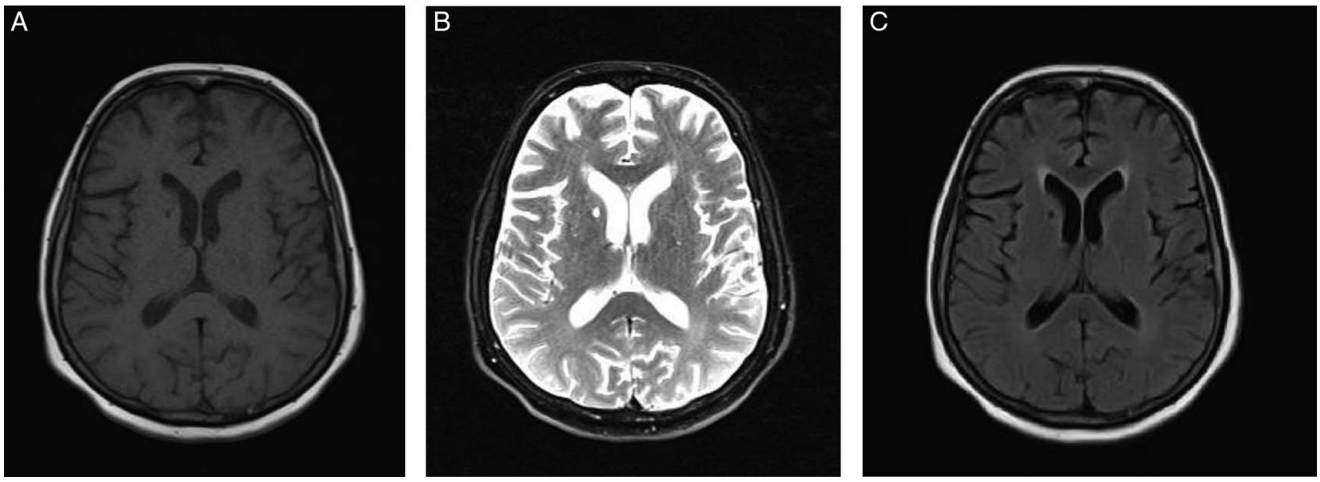

Figure 1. T1 (A), T2 (B) and fluid attenuated inversion recovery (FLAIR) (C) sequences of brain MRI showed no acute intracranial lesions.

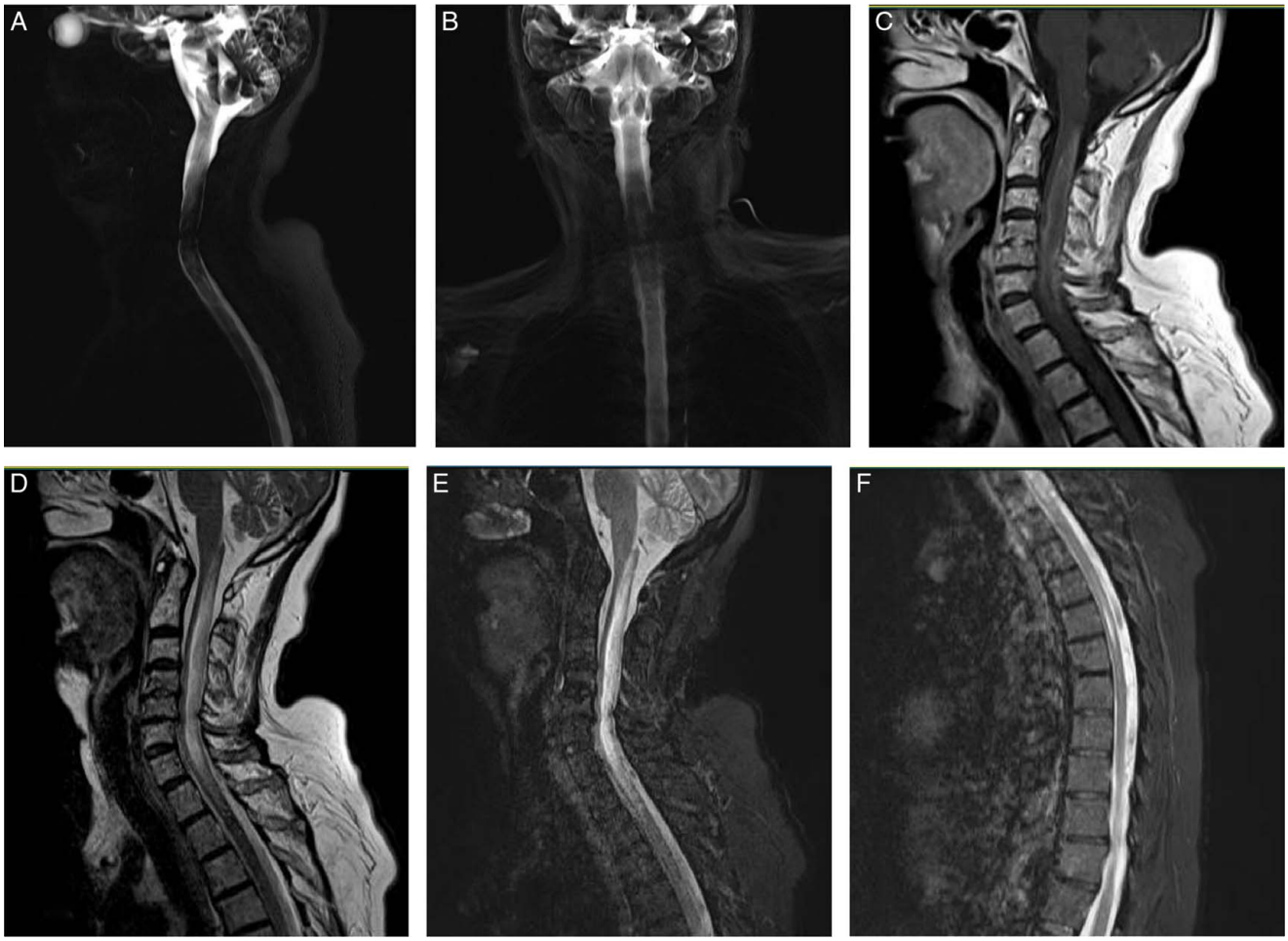

Figure 2. Cervical (A–E) and thoracic (F) MRI sequences demonstrating extensive cervicothoracic cord oedema compatible with both hematomyelia and myelitis of the cervical cord. Note the anterior segment of the cord is still spared.

Considering our previous experiences with similar cases, an explorative-decompressive laminectomy was deemed to be helpful[8]. The patient's first relatives agreed to a life-saving, not function-reversing emergency surgery regarding the fact that the surgery could be less beneficial compared to other neurosurgical pathologic conditions.

Operation

Under general anaesthesia and in prone position, after prep and drape in sterile fashion, using C-arm fluoroscopy cervical midline plane was incised and paravertebral muscles were stripped off the lamina. Using a high-speed drill a C2–T1 laminectomy was performed, then the dura was opened in the midline plane. The cervical cord was oedematous, pale, and poorly pulsatile. A small incision was made over the median raphe plane and minimized exploration showed no obvious haematoma collection or neoplasia. A tissue biopsy was obtained and sent to the neuropathology lab. After laminectomy and neural decompression, the wound was irrigated with copious amounts of warm, sterile normal saline. Expansion duraplasty was not necessary due to cord relaxation, thus dura was repaired continuously with a 4/0 Nylon suture. A submuscular drain was inserted and fixed. Paraspinal muscles, fascia, and skin were repaired in anatomic layers. The wound was dressed in a sterile fashion and the patient was transferred to the operation room recovery unit and then to the NICU.

Post-operation

She regained her full consciousness while remaining intubated (GCS 6T4). Her neurological and vital signs became stabilized. Routine post-operative neurosurgical care was followed and the drain was removed after 48 h. Neuropathological examination of tissue samples revealed glial reactions and many foamy macrophages compatible with acute necrotizing myelitis. No obvious vascular or tumoral anomaly was reported. She underwent a tracheostomy for a prolonged intubation period. 40 days post-operation a surgical wound dehiscence occurred and she underwent wound exploration and repair with desirable outcome.

Follow-up

She remained in the hospital because of her unfavourable medical situation. There was no CSF leak, no infectious process, and no wound dehiscence in the 2-week follow-up. After 2 months of surgery, her neurological evaluation showed no change

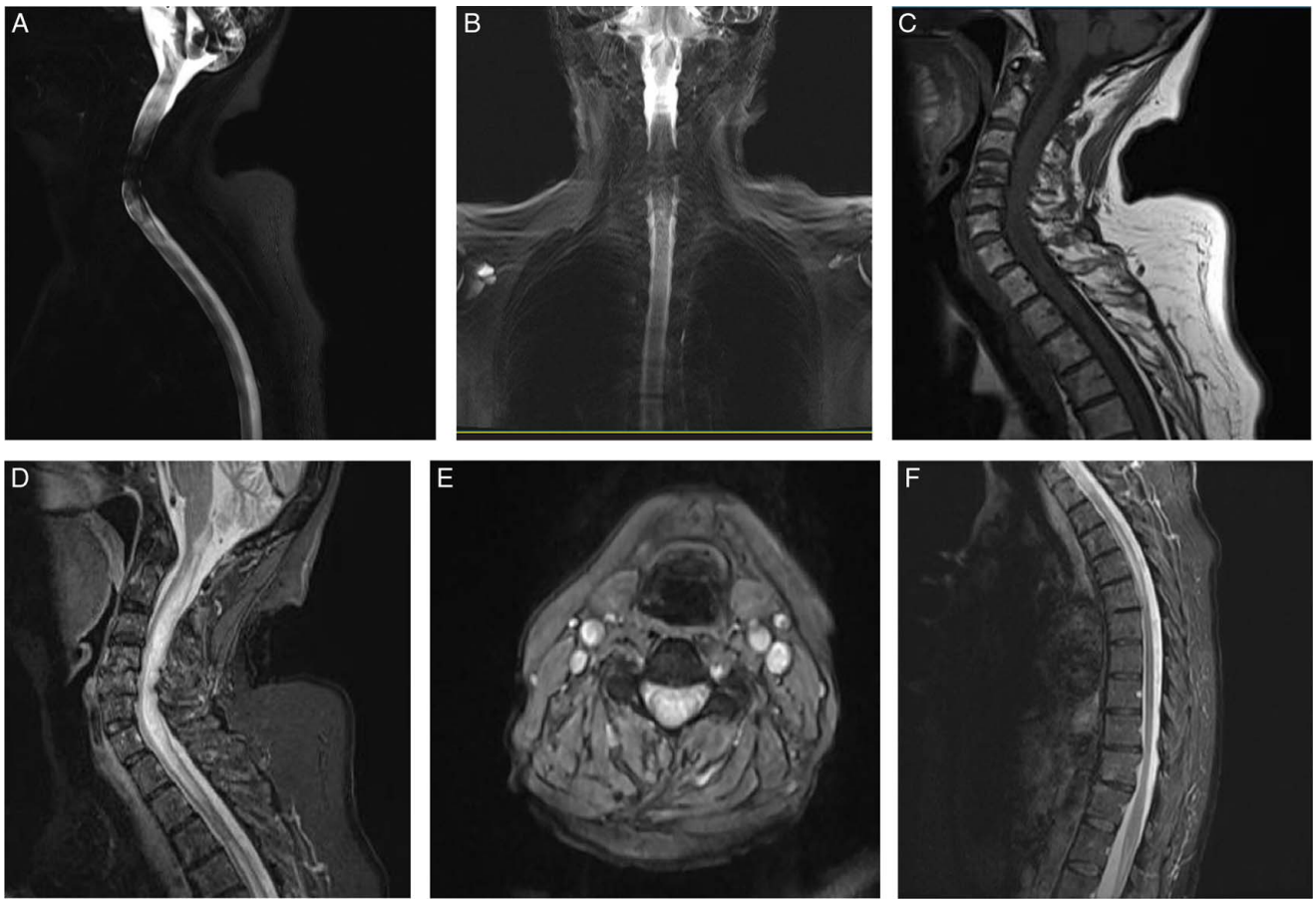

Figure 3. Control MRI after 24 h showed severe progressions of cervical and thoracic oedema and signal intensity in T1, T2, and short-tau inversion recovery sequences. Please note anterior cord was involved (holocord lesions) (A, B) Myelograms, (C) T1 sequence, (D, E) short-tau inversions recovery sequences, and (F) upper thoracic extension of the lesion.

compared to her preoperative status (ASIA B). On day 60 of her hospitalization, she experienced cardiopulmonary arrest, resuscitated but unfortunately expired.

Discussion

SARS-CoV-2 neurological manifestations are relatively common during the acute or subacute phase of the disease. Headache, dizziness, encephalomyelitis, psychological presentations, Guillain-Barre syndrome, intracerebral haemorrhage, ischaemic strokes, cerebral vasculitis, and neuropathy are amongst the most reported nervous system presentations of SARS-CoV-2 virus[1,9].

spontaneous epidural and intramedullary haematoma are infrequent presentations following SARS-CoV-2[10–12]. In a recent systematic review, Sourani and colleagues investigated the association of spontaneous spinal haemorrhage following COVID-19. According to their results, the majority of the bleedings were epidural haematomas while intramedullary haematomas were less common. They found sensory-motor deficits were the most common presentations of the post-COVID-19 spinal haemorrhage while the worst response rate belonged to sphincter dysfunction. Considering their data, the poor preoperative neurological status (ASIA A-C) was associated with poor long-term neurological outcomes[13].

Shah and colleagues conducted a systematic review on the development of transverse myelitis (TM) after vaccination based on data from the Vaccine Adverse Event Reporting System (VAERS) from 1985 to 2017. According to their review, post-vaccination TM had female predominance, occurring within 8 weeks post-vaccination (40%) or longer intervals (60%). Hepatitis B and human papillomavirus (HPV) 4 were the most reported vaccines associated with TM[14].

The exact pathophysiology of myelitis and other demyelination diseases after SARS-CoV-2 vaccination is not well understood. These mechanisms may also share common pathogenesis with SARS-CoV-2-associated myelitis and other demyelinating syndromes as well. Immune-complex type reactions, neural-tissue molecular surface antigen adhesion-transportation pathways, virus re-activation after live-attenuated vaccine injection, virus neurotropism, cytokine-associated responses, and molecular mimicry are the most discussed molecular pathogenesis associated with post-vaccination/infectious myelitis[4,6,15]. Post infectious processes, inflammatory storm, abnormal interleukin and cytokine levels in the circulation and aquaporin disturbance can lead to cord oedema and myelitis[16,17]. Besides that, vector glycoprotein antigen or its chimpanzee adenovirus adjuvant have been tagged with possible immune system triggering cascades[18].

Roman and colleagues review 46 cases of post-SARS-CoV-2 vaccination or post-infection acute transverse myelitis (ATM)

and found almost the same neuropathogenesis in both groups in developing post-exposure ATM. It is important to mention that their results were extracted from Vaxzevria - AstraZeneca COVID-19 (AZD1222) (ChAdOx1 nCov-19) (C19VAZ) vaccine databases[19]. Khan *et al.* reported a 67-year-old patient developing ATM after the Moderna anti- SARS-CoV-2 Vaccine who was treated conservatively with acceptable clinical outcomes[5].

Ismail and Salma conducted a systematic review on SARS-CoV-2 vaccine-associated demyelinating presentations.32 cases were associated with SARS-CoV-2 vaccines and myelitis was the most common nervous system demyelinating side effect. The interval between vaccine injection to presentation was 1–30 days (median: 9 days), 78% of the events occurred after the first dose while 28% occurred after booster doses. Based on their data, mRNA-based vaccines and vector-type vaccines were the most reported cases of post-vaccine transverse myelitis[6].

Sepehrvand *et al.*[20] reported a transverse myelitis episode after Covilo; BIBP-CorV or Sinopharm anti-COVID-19 vaccine injection presented with acute hemi cord syndrome.

Sotoca *et al.*[21] reported a 69 years old woman presented with acute necrotizing myelitis(ANM) after COVID-19 infection in the cervical region that was treated conservatively. Guada and colleagues reported a surgically treated ANM following COVID-19 infection. Their indication for surgical intervention was medical treatment failure, respiratory compromise, and aggressive progression of the disease[22]. In an interesting report, Sourani and colleagues presented the first case of hematomyelia following first shot of the Sinopharm COVID-19 vaccine. The patient underwent conservative management with acceptable outcomes[8].

In our case, the patient had received a booster dose of the Sinopharm vaccine and within days the myelitis became clinically evident. Her primary MRI had undistinguishable features between subacute stages of hematomyelia and myelitis. The clinical and radiological deterioration despite full dose steroid therapy and medical treatment for transverse myelitis, leads to mass effect, extension of the lesion, CSF block, brain stem dysfunction, respiratory failure, and life-threatening conditions. Considering all together this medical scenario increased the clinical suspicion for hematomyelia or underlying neoplasia/vascular malformation, thus surgical exploration was regarded for possible clinical advantages. Unfortunately, the clinical suspicion for hematomyelia or other intramedullary lesions after surgical exploration and pathological examination was not confirmed thus lowering the rationale for surgical intervention. The authors had previously discussed this possibility with the patient's family but it is worth mentioning that myelitis especially necrotizing myelitis can mimic hematomyelia and mislead the surgical team over the decision-making process. There is almost no place for cervical decompression in the treatment of transverse myelitis but the clinical scenario was based on intramedullary lesions possibility. Guada *et al.*[22] reported surgical intervention for life-threatening conditions such as respiratory failure and atypical clinical course, the role of surgical intervention for ANM remains for late stages of clinical approach. The authors would like to share the fact that the operation prevented the clinical and neurological deterioration and stopped the impending death both in our study and in Guada's[22] .This point is of great pedagogical value for future encounters that the surgeons should be vigilant about the clinical and radiological similarities between acute necrotizing myelitis and other intramedullary lesions. However, pathological examination showed no hematomyelia but the authors would like to share the fact that there was no need for further intramedullary exploration for possible hidden haematoma in the cervical cord during the surgery. The rationale behind this was that there could be diffused haemorrhagic transformations across the cervical cord that were not surgically necessary to explore or evacuate. The authors would like to emphasize they are merely reporting the coincidence of necrotizing myelitis and vaccination logically, this report neither confirms nor denies this association. Further reports and molecular research are required.

Limitations

Although the surgical intervention was based on hematomyelia in a rare clinical scenario and prevented impending death and further clinical deterioration, cervical decompression had low medical indication in necrotizing myelitis.

Conclusion

Post-vaccination myelitis after COVID-19 is a potentially serious complication with unpredictable clinical outcomes. The authors would like to share their experience that hematomyelia and necrotizing myelitis can mimic each other, making clinical judgment more challenging.

Healthcare providers and patients need to be more vigilant about new neurological manifestations after every vaccine dose. Each new neurological manifestation requires a thorough clinical investigation.

Ethical approval

None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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None.

Author contribution

M.R. contributed to patient treatment, funding processes, final approval of the manuscript and agreed to be accountable for all aspects of the work. M.M. contributed to patient treatment, funding processes, final approval of the manuscript and agreed to be accountable for all aspects of the work. A.S. contributed to the conception of the work, data search, data gathering, patient treatment, manuscript preparation, manuscript revision, final approval of the manuscript and agreed to be accountable for all aspects of the work. He is corresponding author. M.F. contributed to patient treatment, funding processes, final approval of the manuscript and agreed to be accountable for all aspects of the work. S.B.M. article preparation, funding processes, final approval of the manuscript and agreed to be accountable for all aspects of the work. R.N. contributed to article preparation, final approval of the manuscript

and agreed to be accountable for all aspects of the work. A.S. contributed to article preparation, final approval of the manuscript and agreed to be accountable for all aspects of the work.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

None.

Guarantor

Arman Sourani.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. Some data may not be made available because of privacy or ethical restrictions.

Provenance and peer review

None.

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