Case report of acute encephalitis following the AstraZeneca COVID-19 vaccine

Shu-Yuan Li | Hsin-Hua Chen | Po-Yu Liu | Zhi-Yuan Shi | Yu-Hui Lin | Che-An Tsai | Shih-Ping Lin

Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

Correspondence
Shih-Ping Lin, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung 40705, Taiwan. Email: poempin@vghtc.gov.tw

Abstract
Coronavirus disease 2019 (COVID-19) vaccines have proven to be safe, effective and life-saving. However, little information is available on the neurological complications of COVID-19 vaccine. Here, we report a case who developed acute encephalomyelitis 1 week after being vaccinated with AstraZeneca COVID-19 vaccine (AZ vaccine). Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) was also suspected. After intravenous dexamethasone and subcutaneous fondaparinux therapy, he returned to normal life without neurological sequelae. Four months later, he received Moderna COVID-19 vaccine without any sequelae.

KEYWORDS
COVID-19, encephalitis, vaccine

1 | INTRODUCTION

In December 2019, a novel coronavirus, SARS-CoV-2, first reported in the Wuhan city of China, soon spread around the world and caused substantial impact on health. As of March 2022, SARS-CoV-2 has infected ~400 million people worldwide and caused 6.07 million deaths. During the global COVID-19 pandemic, people in Taiwan maintained normal lives due to longstanding strategies of masking, personal hygiene, social distancing, quarantine measures and contact tracing. Unfortunately, the community outbreak of COVID-19 in Taiwan began in May 2021. To stop virus transmission, Taiwan Centers for Disease Control made an effort to increase COVID-19 vaccination coverage. Four types of vaccines, including Moderna, AstraZeneca (AZ), Pfizer-Biontech (BNT) and MVC COVID-19 Vaccine, are available in Taiwan. Headache is the most common neurological side effect after COVID-19 vaccination. In phase 3 clinical trials, the incidence of headache was 24%-35% and 46%-63% after first and second doses of Moderna vaccination; first and second doses of AZ vaccination; and 25%-42% and 39%-52% after first and second doses of BNT vaccination. In phase 2 clinical trial, the incidence of headache was 15.1% and 13.2% after first and second doses of MVC COVID-19 vaccination, respectively. However, some rare neurological disorders post-COVID-19 vaccine, like Bell’s palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis have been reported. Here, we report a case of new-onset acute encephalomyelitis after receiving the first dose of AZ vaccine.

2 | CASE REPORT

A 55-year-old man was admitted to hospital with fever and consciousness disturbance. The patient received the first dose of AZ vaccine 1 week before admission. Mild injection site pain was observed and subsided in the following 2 days. Two days before admission, the patient suffered from fever up to 39°C, nonproductive cough, general malaise and muscle soreness. One day before admission, progressive weakness and lowered consciousness and drowsiness developed. He had difficulty in sitting up from bed and changing clothes due to weakness. Due to progressive disorientation to people and place and slow response, he was referred to our hospital for help.
The patient had a history of hypertension, hyperlipidemia and sleep apnea and was currently under medication. He did not smoke tobacco, use illicit drugs, or drink alcohol. He lived in an urban area with his wife. He did not have a pet.

At the emergency department, body temperature was 37.9°C, blood pressure was 135/74 mmHg, pulse rate was 108 beats per minute, respiratory rate was 18 breaths per minute, and oxygen saturation was 97% on room air. Neurological examination disclosed Glasgow Coma Scale was 10 (E3V2M5), normal pupils with intact light reflex (3+/3+), intact blink reflex, symmetric muscle power (UE 3/3 and LE 3/3), down-going bilateral plantar reflex, impaired verbal expression (only could say simple words) and positive Kerning’s sign and Brudzinski’s sign.

Lumbar puncture was performed and cerebrospinal fluid (CSF) testing showed the white cell count was 16/μL (reference range, 0–5), with a neutrophil/lymphocyte/monocyte count 3/4/7, red cell count was 1/μL (reference value, 0), the protein level was 97.3 mg/dL (reference range, 15 to 45) and positive antinuclear antibody (ANA; 1:2). Serum white cell count, platelet count and C-reactive protein were within normal range, and elevated D-dimer (1.19 mg/L fibrinogen equivalent units [FEU]) was noted. Other laboratory and serial CSF findings are shown in Tables 1 and 2.

Serology survey showed positive serum ANA (1:640), slightly elevated ferritin (351.02 ng/dL) and D-dimer (1.19 mg/1 FEU). Anti-platelet factor 4 (PF4) antibody was negative. Other autoimmune profiles are showed in Table 3. CSF bacterial, fungal and tuberculosis culture, CSF viral culture, BIOFIRE® FILMARRAY® Meningitis/Encephalitis Panel test and antibodies of paraneoplastic neurologic syndrome and limbic encephalitis were all negative findings. In addition, CSF and nasopharyngeal SARS-CoV2 polymerase chain reaction were negative. Magnetic resonance angiography of brain was done on day 4 after admission and showed pachymeningeal enhancement without definite abnormal signal intensity over brain parenchyma.

Under the impression of encephalomyelitis, empiric intravenous ceftriaxone and acyclovir were administered.

### Table 1  Serial cerebrospinal fluid (CSF) findings

|                              | Reference range | 25 June (admission d 1) | 28 June (admission d 4) | 5 July (admission d 11) |
|------------------------------|-----------------|-------------------------|-------------------------|-------------------------|
| Opening/closing pressure, cmH₂O | -               | 16.2/7.4                | 16/10                   | 3/2.5                   |
| Appearance                   | -               | Colorless, clear        | Colorless, clear        | Colorless, clear        |
| Red cell count per μL        | 0               | 1                       | 4                       | 6                       |
| White cell count per μL, differential count (neutrophil/lymphocyte/monocyte), % | 0-5            | 16 (N/L/M 3/4/7)        | 73 (N/L/M 9/62/2)       | 2 (N/L/M 0/1/1)         |
| Protein, mg/dL               | 15-45           | 97.3                    | 172.6                   | 102.4                   |
| Lactate, mg/dL               | 10-25           | 19.9                    | 14.7                    | 16.2                    |
| CSF glucose, mg/dL           | 40-70           | 69                      | 55                      | 60                      |
| Serum glucose, mg/dL         | 70-200          | -                       | 97                      | -                       |
| Adenosine deaminase, U/L     | <9              | 0                       | 1                       | -                       |
| Antinuclear antibodies       | -               | 1:2 (fine speckled)     | -                       | 1:8 (fine speckled)     |
| Venereal disease research laboratory test | -     | Non-reactive           | -                       | -                       |
| Immunoglobulin G index       | 0.34-0.58       | 0.404                   | -                       | -                       |
| Oligoclonal bands            | -               | Negative                | -                       | -                       |
| Bacterial culture            | -               | Negative                | Negative                | -                       |
| CSF polymerase chain reaction, VZV/Parvovirus B-19/HSV-1/HSV-II/EBV/CMV/HIV/SARS-CoV2 | -     | Negative                | -                       | -                       |

Abbreviations: CMV, cytomegalovirus; EBV, Epstein-Barr virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; VZV, varicella zoster virus.
Vaccine-induced immune thrombocytopenia and thrombosis (VITT) could not be excluded at that time due to post-vaccine and elevated D-dimer, so subcutaneous fondaparinux was administered. Due to suspected non-infectious causes of meningencephalitis (negative work up of infectious etiology and positive CSF/serum ANA). New-onset or flare of immune-mediated disease (IMD) following COVID-19 vaccine injection was of concern and intravenous dexamethasone 5 mg once daily was initiated on day 3 after admission. The fever subsided and consciousness level gradually improved. Treatment course and CSF protein change are summarized in Figure 1. He returned to normal life without neurological sequelae and was discharged on day 14 after admission. Four months later, he received BNT COVID-19 vaccine without any sequelae.

### 3 | DISCUSSION

AZ vaccine, developed at Oxford University, is a replication-deficient chimpanzee adenoviral vector vaccine containing the SARS-CoV-2 structural surface glycoprotein antigen gene. The phase 1 clinical trial in the UK was started in April, 2020. Since then, several randomized controlled trials were initiated to evaluate the safety and efficacy of AZ vaccine. The interim analysis showed 62.1% vaccine efficacy in 2 standard doses-vaccinated participants and 90.0% vaccine efficacy in a low dose followed by a standard dose-vaccinated group. Common adverse events reported in clinical trials included injection site reactions, fatigue, headache, muscle ache and feeling feverish.

After emergency approval of AZ COVID-19 vaccine in several countries, a wide spectrum of post-vaccination neurological adverse events were reported. Guillain-Barré syndrome (GBS) was reported in India (n = 7) and Britain (n = 1). GBS occurred mostly within 3 weeks of the first vaccination dose. The incidence was extremely low at about 5.8 per million. Most patients recovered well after intravenous immunoglobulin (IVIg) therapy. Other complications, including new-onset refractory status epilepticus and acute transverse myelitis were also reported. The recurrent seizures occurred 10 days after vaccination and were refractory to conventional antiepileptic drug therapy, which dramatically improved after steroid pulse therapy and plasma exchange. Vaccination-associated myelitis developed within 2 weeks after vaccination and symptoms were rapidly improved after initiation of high-dose corticoid therapy.

#### TABLE 2 Serum laboratory data

| Variable               | Reference range, adult | 25 June admission d 1 |
|------------------------|------------------------|-----------------------|
| White cell count, μL   | 3900-10 600            | 7670                  |
| Differential count (%) |                        |                       |
| Neutrophils            | 40-74                  | 82.1%                 |
| Lymphocytes            | 19-48                  | 12.1%                 |
| Monocytes              | 3.4-9                  | 5.6%                  |
| Eosinophils            | 0-7                    | 0.1%                  |
| Hemoglobin, g/dL       | 13.5-17.5              | 14.7                  |
| Platelet count, μL     | 150 000-400 000        | 240 000               |
| Alanine aminotransferase, U/L | 10-50 | 18 |
| Aspartate aminotransferase, U/L | 8-38 | 17 |
| Alkaline phosphatase, U/L | 50-190 | 68 |
| Total bilirubin, mg/dL | 0.2-1.2                | 0.8                   |
| Prothrombin time, s    | 9.5-11.7               | 10.8                  |
| Prothrombin time international normalization ratio | 0.85-1.15 | 1.02 |
| D-dimer, mg/L fibrinogen equivalent units | <0.55 | 1.19 |
| Ferritin, ng/mL        | 21.81-274.66           | 360.18                |
| Lactate dehydrogenase, U/L | 120-240 | 208 |
| C-reactive protein, mg/dL | <0.3 | 0.1 |
| Erythrocyte sedimentation rate, mm/h | 0-20 | 7 |
| Urea nitrogen, mg/dL   | 5-25                   | 13                    |
| Creatinine, mg/dL      | 0.7-1.4                | 1.30                  |
| Sodium, mEq/L          | 137-153                | 140                   |
| Potassium, mEq/L       | 3.5-5.3                | 4.2                   |
| Calcium, mg/dL         | 8.4-10.2               | 8.1                   |
| Lactic acid, mg/dL     | 3-12                   | 20.3                  |

#### TABLE 3 Autoimmune profile

| Antibody                                             | Result                  |
|------------------------------------------------------|-------------------------|
| Antinuclear antibody                                 | 1:640, fine speckled    |
| Anti-double-stranded DNA antibody                    | Negative                |
| Anti-Smith/ribonucleoprotein antibodies              | Negative                |
| Anti-Sjögren's syndrome A/B antibodies               | Negative                |
| Anti-neutrophil cytoplasmic antibodies/myeloperoxidase antibodies/ anti-proteinase-3 antibodies | Negative |
| Anti-cardiolipin IgM/IgG, anti-β2 glycoprotein I IgM/IgG, lupus anticoagulant | Negative |
| Complement 3, 87-200 mg/dL                          | 116.6 mg/dL            |
| Complement 4, 19-52 mg/dL                           | 37.6 mg/dL             |
| Anti-parietal cell antibody                          | Positive, 1:160         |
In Taiwan, severe adverse events are reported to Taiwan Vaccine Adverse Event Reporting System (Taiwan VAERS). Till September 2021, neurological adverse events included facial palsy, seizure, transverse myelitis, acute disseminated encephalomyelitis, GBS, myelitis, encephalitis and optic neuritis. A total of 116 cases in 13.6 million doses with a resulting incidence of almost 0.85 per 100,000 for post-vaccination neurological adverse effects has been recorded in Taiwan.

In our case, the symptoms of post-vaccination encephalitis onset occurred at day 7 after vaccination. Brain magnetic resonance imaging was performed with normal status of parenchyma. Significant improvement of the symptomatology was noted after steroid therapy. A first case of post-vaccination encephalitis was reported in Italy. Zuhorn et al. also reported 3 cases of acute encephalitis after AZ vaccine injection. We also summarize case reports of COVID-19 vaccine-related encephalomyelitis in Table 1. Similar to our case, the symptoms of encephalitis developed within 30 days after vaccination. After excluding alternative causes, vaccination-related autoimmune encephalitis was suspected and symptoms rapidly recovered after the initiation of immunosuppressive therapy. A new syndrome, VITT, with clinical features of thrombosis at unusual sites, elevated D-dimer, thrombocytopenia, coagulation abnormalities and positive antibodies to PF4, has emerged after wide vaccination. VITT is caused by antibodies that recognize PF4 bound to platelets. Anticoagulation therapy is primary therapy for VITT.

Our patient presented with neurological symptoms 1 week after vaccination and elevated D-dimer so VITT could not initially be excluded. Therefore, subcutaneous fondaparinux was initially administered. However, normal platelet count and absent evidence of thrombosis over brain imaging and negative anti-PF4 did not support the diagnosis of VITT. In this case, we gradually discontinued anticoagulation agents after neurological conditions improved.

Another possible mechanism of meningoencephalitis post-vaccination is autoimmune/inflammatory syndrome induced by adjuvants (ASIA). ASIA was proposed by Shoenfeld et al. in 2011. ASIA presents with a heterogeneous clinical picture including multiple system involvement. Around 13% severe ASIA cases harbored nervous system involvement. Watad et al. reported 27 cases of new-onset or flare of IMDs following COVID-19 vaccine injection. Among those IMDs cases, 78% had at least 1 underlying autoimmune disease prior the vaccination, and 80% of cases had excellent response after the use of steroid therapy. Connolly et al. conducted a prospective observational study to evaluate disease
| Age/gender | Dose/vaccine | Onset post-vaccination | Past history | Symptoms | Treatment | Outcome | Ref |
|------------|--------------|------------------------|--------------|----------|-----------|---------|-----|
| 77/M       | 1/AZ         | 2 d                    | 1. Sarcoidosis and polymyalgia rheumatica 2. COVID-19 5 mo ago | Agitation and confusion | Methylprednisolone for 4 d and taper to oral prednisolone | Complete remission | 17  |
| 21/F       | 1/AZ         | 5 d                    | Obesity      | Attention and concentration difficulties | Dexamethasone | Improved, with mild cognitive slowing | 18  |
| 63/F       | 1/AZ         | 6 d                    | Not available | Immobilizing opsoclonus myoclonus syndrome | Methylprednisolone for 5 d | Improved, with low-grade tremor | 18  |
| 63/M       | 1/AZ         | 8 d                    | Not available | Aphasia | Steroid was rejected by patient | Improved | 18  |
| 56/F       | 1/BNT        | 2 wk                   | Recurrent cutaneous herpes zoster | Hemi-ataxia and dysmetria | Corticosteroid 2 wk | Improved, with mild dysmetria and intention tremor | 19  |
| 63/M       | 1/AZ         | 12d                    | Diabetes, ischemic heart disease, and atrial fibrillation | Declining cognition, emerging disorientation and impaired attention | Corticosteroids and plasmapheresis | Expired | 20  |
| 34/M       | 2/Sputnik V  | 3 wk                   | Previously healthy | Acute confusional state and imbalance | Plasmapheresis | Improved | 21  |
| 88/F       | 2/BNT        | 29d                    | Diabetes and Alzheimer's disease | Impaired consciousness and gaze-evoked nystagmus | Steroid pulse therapy | Improved | 22  |
| 56/F       | 1/AZ         | 10d                    | Not available | Weakness of the lower limbs and slurred speech | Steroid pulse therapy | Marked improvement | 23  |
| 19/F       | 1/Moderna    | 2 wk                   | Atopic dermatitis and depression | Headache, fever, back and neck pain with nausea, vomiting and urinary retention | Corticosteroids and plasmapheresis | Complete remission | 24  |
| 36/F       | 1/AZ         | 14d                    | Not available | Bilateral optic neuritis | Corticosteroid | Improved | 25  |
| 64/M       | 1/AZ         | 10 d                   | Not available | Fever and drowsiness | Corticosteroids, plasmapheresis, and rituximab | Complete remission | 26  |
| 65/M       | 2/AZ         | 10 d                   | Not available | Behavioral changes and jerky movements | Corticosteroids and IVIG | Marked improvement | 26  |
| 64/M       | 2/AZ         | 20d                    | Not available | Ascending paresthesias in the legs and hand | Corticosteroids, IVG, and rituximab | Marked improvement | 26  |
| 46/M       | 1/AZ         | 4 d                    | Not available | Progressive lower limb weakness and numbness | Corticosteroids and plasmapheresis | Marked improvement | 26  |
| 42/F       | 1/AZ         | 5 d                    | Not available | Headache and photophobia | Corticosteroid | Marked improvement | 26  |
| 37/M       | 1/Sinopharm  | 1 mo                   | Previously healthy | Progressive muscle weakness in all limbs with dysphagia | Corticosteroids, plasmapheresis, and IVIG | Marked improvement | 27  |

Abbreviations: AZ, AstraZeneca; BNT, Pfizer-Biontech; IVIG, intravenous immunoglobulin.
flare-up and post-vaccination reaction among 1377 patients with rheumatic and musculoskeletal disease. The incidence of disease flares requiring treatment after 2-dose COVID-19 vaccination was 11%, with no reports of severe flares. Age-associated B cells (ABCs)-mediated autoimmunity (new-onset or flares) was thought to explain this autoimmune phenomena following COVID-19 vaccination. ABCs subset are known as double negative B cells in humans, which are hyperresponsive to Toll-like receptor 7 (TLR7) signaling. The use of TLR7/8 and TLR9 agonists, as adjuvants of COVID-19 vaccine, may trigger this post-vaccination autoimmune phenomena. Our patient fitted some features of ASIA: exposure to external stimuli prior to clinical manifestations and typical clinical manifestations (neurological manifestations and cognitive impairment). The patient receiving another COVID-19 vaccine (BNT) without adverse events might imply that special immune system activation resulting in neurological adverse events was triggered by AZ vaccine in our patient.

4 | CONCLUSION

We present a case of meningoencephalitis after AZ vaccine in Taiwan. Rational temporal association of COVID-19 vaccination, negative diagnostic work up of other meningoencephalitis etiologies and rapid clinical response after steroid treatment supported the possibility of CNS inflammation triggered by vaccination. Due to the COVID-19 pandemic, COVID-19 vaccine was quickly developed and put into clinical use. Safety of COVID-19 vaccination should be closely monitored and the benefit–risk balance should be reassessed. Further research is needed to study the mechanism of vaccine-related neurological adverse events.

AUTHOR CONTRIBUTIONS

Drs S-P Lin, S-Y Li, and H-H Chen were involved in the clinical care of the patient and planned the case report. Drs S-P Lin and S-Y Li wrote the first draft and created the tables and figures. Drs P-Y Liu, Z-Y Shi, Y-H Lin and C-A Tsai were responsible for clinical consultation. All authors reviewed and revised the manuscript and approved the final manuscript as submitted.

ACKNOWLEDGEMENTS

We are grateful to the patient and his family.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

ETHICS STATEMENT

No investigations or interventions were performed outside routine clinical care for this patient. The patient signed an approval for the publication of the case.

ORCID

Shih-Ping Lin https://orcid.org/0000-0002-2366-7022

REFERENCES

1. Baden LR, el Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384(5):403-416.
2. Falsey AR, Sobieszczyk ME, Hirsch I, et al. Phase 3 safety and efficacy of AZD1222 (ChAdOx1 nCoV-19) covid-19 vaccine. N Engl J Med. 2021;385(25):2348-2360.
3. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383(27):2603-2615.
4. Hsieh SM, Liu MC, Chen YH, et al. Safety and immunogenicity of CpG 1018 and aluminium hydroxide-adjuvanted SARS-CoV-2 S-2P protein vaccine MVC-COV1901: interim results of a large-scale, double-blind, randomised, placebo-controlled phase 2 trial in Taiwan. Lancet Respir Med. 2021;9(12):1396-1406.
5. Maramattom BV, Krishnan P, Paul R, et al. Guillain-Barre Syndrome following ChAdOx1-S/nCoV-19 vaccine. Ann Neurol. 2021;90(2):312-314.
6. Pagenkopf C, Sudmeyer M. A case of longitudinally extensive transverse myelitis following vaccination against Covid-19. J Neuroinmunol. 2021;358:577606.
7. Roman GC, Gracia F, Torres A, Palacios A, Gracia K, Harris D. Acute transverse myelitis (ATM): clinical review of 43 patients with COVID-19-associated ATM and 3 post-vaccination ATM serious adverse events with the ChAdOx1 nCoV-19 vaccine (AZD1222). Front Immunol. 2021;12:653786.
8. Maramattom BV, Lotlikar RS, Sukumaran S. Central nervous system adverse events after ChAdOx1 vaccination. Neurol Sci. 2022;43(6):3503-3507.
9. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet. 2020;396(10249):467-478.
10. Frater J, Ewer KJ, Ogbe A, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial. Lancet HIV. 2021;8(8):e474-e485.
11. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet. 2021;396(10267):1979-1993.
12. Madhi SA, Koen AL, Izu A, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in people living with and without HIV in South Africa: an interim analysis of a randomised, double-blind, placebo-controlled, phase 1B/2A trial. Lancet HIV. 2021;8(8):e568-e580.
13. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397(10269):99-111.
14. Patel SU, Khurram MK, Lakhan K, Quirk B, Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. BMJ Case Rep. 2021;14(4):e242956.
15. Aladdin Y, Shirah B. New-onset refractory status epilepticus following vaccination against COVID-19. QJM. 2021;114(8):591-593.
16. Singh Malhotra H, Gupta P, Prabhu V, Kumar Garg R, Dandu H, Agarwal V. COVID-19 vaccination-associated myelitis. QJM. 2021;114(8):591-593.
17. Baldelli L, Amore G, Monti A, et al. Hyperacusis reversible encephalopathy related to cytokine storm following COVID-19 vaccine. J Neuroinmunol. 2021;358:577661.
18. Zuhorn F, Graf T, Klingebiel R, Schäbitz WR, Rogalewski A. Postvaccinal encephalitis after ChAdOx1 nCoV-19. Ann Neurol. 2021;90(3):506-511.
19. Vogrig A, Janes F, Gigli GL, et al. Acute disseminated encephalomyelitis after SARS-CoV-2 vaccination. Clin Neurol Neurosurg. 2021;208:106839.

20. Permezel F, Borjevic B, Lau S, de Boer HH. Acute disseminated encephalomyelitis (ADEM) following recent Oxford/AstraZeneca COVID-19 vaccination. Forensic Sci Med Pathol. 2022;18(1):74-79.

21. Badrawi N, Kumar N, Albastaki U. Post COVID-19 vaccination neuromyelitis optica spectrum disorder: case report & MRI findings. Radiol Case Rep. 2021;16(12):3864-3867.

22. Shimizu M, Ogaki K, Nakamura R, et al. An 88-year-old woman with acute disseminated encephalomyelitis following messenger ribonucleic acid-based COVID-19 vaccination. eNeurologicalSci. 2021;25:100381.

23. Al-Quiliti K et al. Acute demyelinating encephalomyelitis post-COVID-19 vaccination: a case report and literature review. Diseases. 2022;10(1):13.

24. Kania K, Ambrosius W, Tokarz Kupczyk E, Kozubski W. Acute disseminated encephalomyelitis in a patient vaccinated against SARS-CoV-2. Ann Clin Transl Neurol. 2021;8(10):2000-2003.

25. Nagaratnam SA, Ferdi AC, Leaney J, Lee RLK, Hwang YT, Heard R. Acute disseminated encephalomyelitis with bilateral optic neuritis following ChAdOx1 COVID-19 vaccination. BMC Neurol. 2022;22(1):54.

26. Yazdanpanah F, Iranpour P, Haseli S, Poursadeghfard M, Yarmahmoodi F. Acute disseminated encephalomyelitis (ADEM) after SARS-CoV-2 vaccination: a case report. Radiol Case Rep. 2022;17(5):1789-1793.

27. Pavord S, Scully M, Hunt BJ, et al. Clinical features of vaccine-induced immune thrombocytopenia and thrombosis. N Engl J Med. 2021;385(18):1680-1689.

28. Shoenfeld Y, Agmon-Levin N. ‘ASIA’ - autoimmune/inflammatory syndrome induced by adjuvants. J Autoimmun. 2011;36(1):4-8.

29. Jara LJ, Garcia-Collinot G, Medina G, et al. Severe manifestations of autoimmune syndrome induced by adjuvants (Shoenfeld’s syndrome). Immunol Res. 2017;65(1):8-16.

30. Watad A, de Marco G, Mahajna H, et al. Immune-mediated disease flares or new-onset disease in 27 subjects following mRNA/DNA SARS-CoV-2 vaccination. Vaccines (Basel). 2021;9(5):435.

31. Connolly CM, Ruddy JA, Boyarsky BJ, et al. Disease flare and reactivation in patients with rheumatic and musculoskeletal diseases following two-dose SARS-CoV-2 messenger RNA vaccination. Arthritis Rheumatol. 2022;74(1):28-32.

32. Sachinidis A, Garyfallos A. COVID-19 vaccination can occasionally trigger autoimmune phenomena, probably via inducing age-associated B cells. Int J Rheum Dis. 2022;25(1):83-85.

33. Jenks SA, Cashman KS, Zumaquero E, et al. Distinct effector B cells induced by unregulated toll-like receptor 7 contribute to pathogenic responses in systemic lupus erythematosus. Immunity. 2018;49(4):725-739. e6.