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Brief communications

Acute encephalomyelopolyradiculoneuropathy that occurred after BNT162b2 mRNA vaccination against COVID-19: A clinical case review

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SARS-CoV-2 and side effects of SARS-CoV-2 vaccination show tropism to nervous system structures. Neurological side effects from the central and peripheral nervous systems have been observed quite rarely after vaccination against COVID-19 compared to a large number of vaccinated individuals. The article presents a clinical case of simultaneous damage to the central and peripheral nervous systems in the form of acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy, which occurred after receiving the first dose of the BNT162b2 mRNA vaccine. The severe course of encephalomyelopolyradiculoneuropathy with peripheral tetraplegia, sensory disturbances, bulbar syndrome, and dysautonomia, followed by the occurrence of pneumonia, secondary bacterial meningoencephalitis, the need for long-term mechanical ventilation led to the occurrence of pneumothorax and multiple organ failure, which caused the patient's death after one and a half months of intensive therapy.

Thus, the acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy can be considered as a probable rare neurological complication of SARS-CoV-2 vaccination with mRNA-based vaccines. Encephalomyelopolyradiculoneuropathy can have a severe course, accompanied by multiple complications and leading to death. Establishing of the causal relationships of the occurrence of rare neurological pathological conditions close in time to vaccination against SARS-CoV-2 with mRNA-based vaccines requires additional further researches.

Keywords: SARS-CoV-2, BNT162b2 vaccine, acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy.

Introduction

Vaccination with modern vaccines against SARS-CoV-2 is a method of specific prevention of the occurrence of infectious disease and provides pronounced protection against both symptomatic and asymptomatic forms [1, 2]. An analysis of scientific works published in the E-Library, CrossRef, PubMed, Web of Science, Scopus databases was carried out in order to systematize data on the causes and frequency of occurrence, mechanisms of development, clinical forms of side effects from the nervous system that occur after vaccination against SARS-CoV-2 using MeSH keywords such as SARS-CoV-2, vaccination, BNT162b2, side effects, complications.

It is known that SARS-CoV-2 and adverse reactions to SARS-CoV-2 vaccination demonstrate tropism to nervous system structures [1, 3]. Neurological side effects from the central (CNS) and peripheral nervous (PNS) systems were quite rare after COVID-19 vaccination compared to a large number of vaccinated individuals. Dizziness, fatigue, headache, muscle pain, and paresthesia were most often noted as transient reactions to vaccination [1, 4, 5]. Strokes, acute disseminated encephalomyelitis, transverse myelitis [6,7,8], aseptic meningitis [8], acute inflammatory demyelinating polyneuropathy, cranial neuropathies, including Bell's palsy, tinnitus, diplopia, trigeminal neuralgia, peripheral neuropathies, dysautonomia, and herpes zoster reactivation [1, 5, 6, 8, 9-14] were less common. However, the causal relationship between the occurrence of rare pathological disorders of the nervous system and vaccination has not been fully established and requires further researches [6, 8]. To date, there is insufficient information on simultaneous damage to the central and peripheral nervous system close in time to vaccination against SARS-CoV-2 with mRNA-based vaccines.

Objective: The features of the clinical course, diagnosis, and treatment of acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy that occurred after receiving the first dose of the BNT162b2 mRNA vaccine based on a clinical case were studied.

Materials and Methods

A clinical case of acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy that occurred after receiving the first dose of the BNT162b2 mRNA vaccine is presented. The patient, born in 1976, was undergoing inpatient treatment at the Municipal Non-profit Enterprise of Lviv Regional Council "Lviv Regional Clinical Infectious Diseases Hospital" and the Municipal Non-profit Enterprise "Lviv Clinical Emergency Hospital". The patient underwent neurological examination, general and biochemical blood, urine, and CSF tests, coagulogram, arterial blood gasometry, blood test for D-dimer, ferritin, procalcitonin, microbiological examination of blood, CSF, sputum, nasopharyngeal smear for meningococcus. Total Ig A, Ig M, Ig G, and PCR levels were determined to detect COVID-19, cytomegalovirus, Epstein-Barr virus, herpes type 1, 2, 6, chlamydia, as well as blood IgG and IgM to SARS-CoV-2, Borrelia, hepatitis B and C, syphilis, cytomegalovirus, Epstein-Barr virus, herpes type 1, 2. Magnetic resonance imaging (MRI) of the brain with gadolinium contrast, electrocardiography, chest radiography, ultrasound examination of internal organs, and computed tomography of the chest and abdominal organs with tomohexol contrast and bronchoscopy (bronchofibroscopy) were used. After death, an autopsy, and morphological studies of organs and tissues were performed. During the treatment, written informed consent for the analysis and processing of personal data was received from the patient.

Results

A 45-year-old man had a fewer of 38.7°C three days after getting the first dose of the (14.07.2021) BNT162b2 vaccine. On the fifth day, he experienced numbness in the right half of the face, the right half of the tongue, and the right hand, swaying when walking, general weakness, and repeated vomiting. Since July 24, 2021, he received inpatient treatment at the Municipal Non-Profit Enterprise of Lviv Regional Council "Lviv Regional Clinical Infectious Diseases Hospital" (LRCIDH) with a diagnosis of acute encephalomyelitis. It is known from the medical history that the patient was diagnosed with chronic pancreatitis and chronic pyelonephritis in the stage of compensation. At the time of admission to LRCIDH, he did not take medication for the treatment of these diseases.

The condition at admission to LRCIDH was severe, the patient was conscious, and the fewer of 38.3°C persisted. Neurological examination revealed: rigidity of muscles in the back of the head +1 cm, reduced abdominal reflexes, reduced strength in the right arm, horizontal nystagmus. There were no changes in the general blood and urine tests, biochemical blood test (Table 1, Table 2). Cerebrospinal fluid was colorless and transparent, protein – 0.66 g/l, glucose – 3.8 mmol/l, cytosis – 117 in mm^3, with 95% of lymphocytes, 5% of neutrophils (Table 3). When performing CSF and blood culture, no microflora was detected. No growth was detected during the nasopharyngeal smear for

meningococcus (July 26, 2021). Starting from July 30, 2021, the full blood count showed an increase in white blood cells to 12×10^9/l, erythrocyte sedimentation rate (ESR) was up to 18 mm/h, the number of lymphocytes was 13.6%, monocytes – 6.3%, neutrophils – 80.1%. PCR for COVID-19 was negative. No changes on the electrocardiogram, ultrasound examination of internal organs, or chest X-ray were detected. MRI of the brain (July 29, 2021) showed damaged areas characteristic of encephalitis in the medulla oblongata, pons, and middle cerebellar peduncle on the right (Fig. 1).

Table 1

Indicators of the full blood count during the patient's treatment

Indicator	07/24/21	07/30/21	03/08/21	08/09/21	08/11/21	08/16/21	08/21/21	08/26/21	08/31/21	09/04/21
Hb, g/l	156	157	163	166	151	126	57	55	92	85
Leukocytes, 10^9/l	7.0	12	10.5	16.3	15.9	15.3	13.8	13.9	29.1	22.8
Lymphocytes, %	13.6	13.6	11.6	5	6	17	8.5	4.9	4	3.6
Neutrophils, %	76.4	80.1	82.1	88.9	88.9	78	84.9	89.6	94	88.9
Monocytes, eosinophils, basophils, %	10	6.3	6.3	6.1	5.1	5	6.6	5.4	2	7.5
Platelets, 10^9/l	239	195	206	223	187	106	170	136	243	256
ESR, mm/hour	5	18	2	10	13	25	70	-	84	-

Table 2

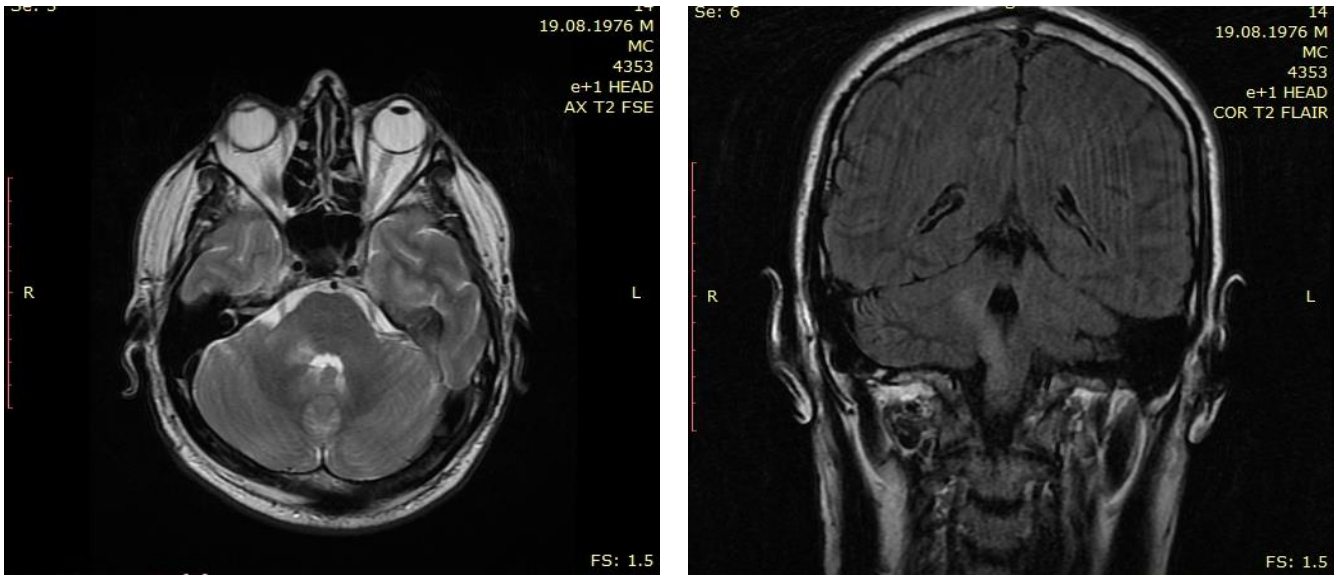
Indicators of biochemical blood tests during the patient's treatment

Indicator	07/24/21	08/12/21	08/16/21	08/21/21	08/25/21	08/31/21	09/04/21
Total protein, g/l	68	53.7	65	81	72	66.8	58
Total bilirubin, μmol/l	8.6	14.4	29	89.2	50	17.3	18
AST u/l	25.6	291.7	44.6	54	37	-	28
ALT u/l	22.7	1047	521	314	147	-	56
Urea, mmol/l	2.54	9.5	7.4	11	7.4	6.7	6.1
Creatinine, μmol/l	115.9	123	88	68	61	65	55
Glucose, mmol/l	6.6	8.8	12,6	13.4	12	16.7	9.4

Table 3

Indicators of cerebrospinal fluid during the patient's treatment

Indicator	07/26/21	08/02/21	08/12/21	08/18/21	08/21/21	08/26/21
Color	Colorless	Colorless	Light yellow	Light yellow	Yellow	Light yellow
Transparency	Transparent	Transparent	Transparent	Transparent	Faintly cloudy	Transparent
Protein, g/l	0.66	0.57	0.33	1.65	1.65	1.32
Cells, in mm^3	117	38	43	120	130	0
Lymphocytes, %	95	82	-	25	15	-
Neutrophils, %	5	18	-	75	85	-
Glucose, mmol/l	3.4	3.8	2.9	3.5	3.9	5
Microbiological research	Microflora wasn't detected	-	*Staphylococcus haemoliticus*	Microflora wasn't detected	-	-
Pandey's reaction	-	+	+	+++	+++	++++
Chlorides, mmol/l	-	-	124	115	112	152

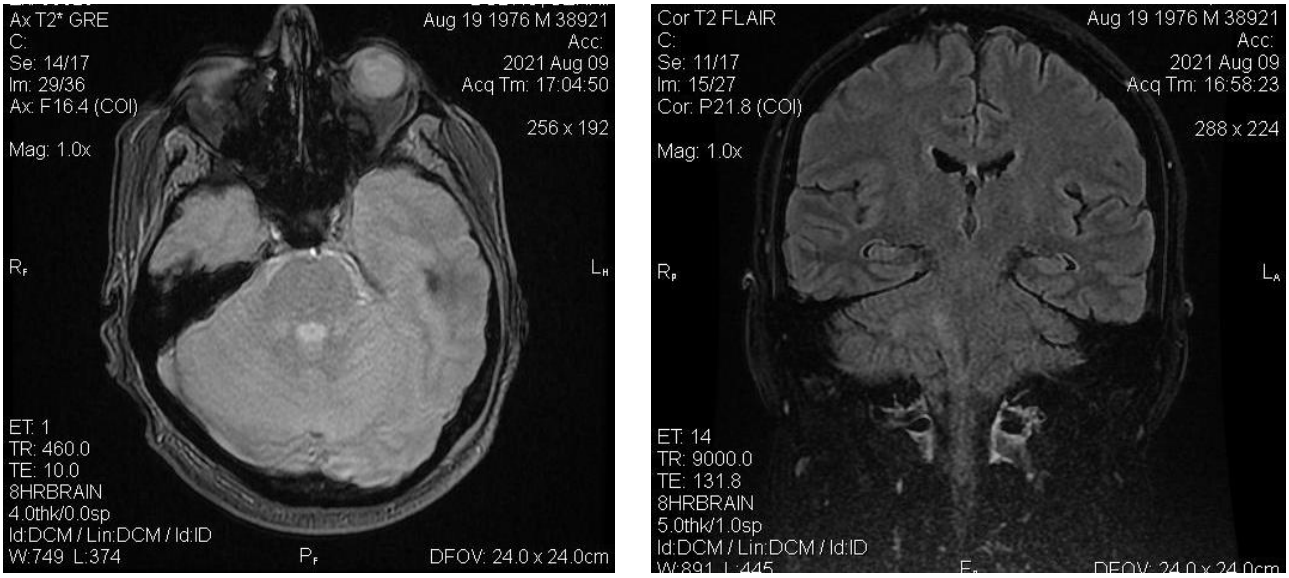


A B

Figure 1. MRI of the patient's brain, July 29, 2021: a) axial sections in T2 weighted image; B) frontal sections in FLAIR sequence. The area of damage in the medulla oblongata, pons, and right middle cerebellar peduncle

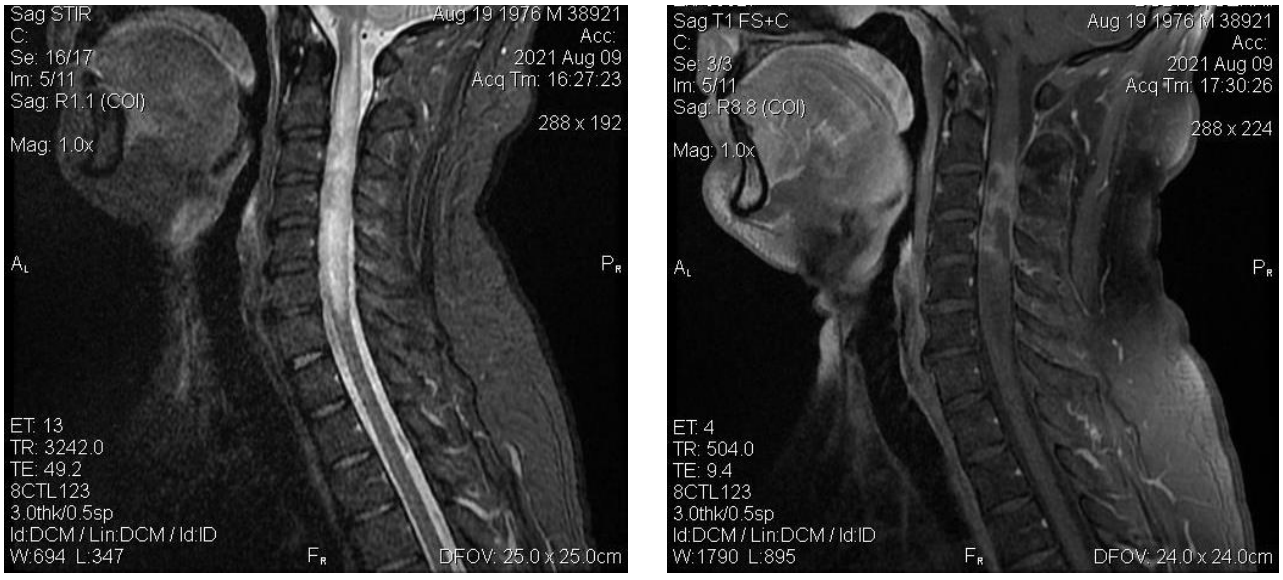
During the first 10 days of treatment with Acyclovir, Cefoperazone, Furosemide, Methylprednisolone, Diclofenac sodium, and Metoclopramide, meningeal symptoms regressed. The patient started walking independently, cytosis in the cerebrospinal fluid decreased to 38 mm^3 with a predominance of lymphocytes (Table 3). At the same time, on August 7, 2021, weakness, and sensitivity disorders of the right hand increased. On August 8, 2021, sensitivity disorders in the right leg and neck pain appeared. On August 9, 2021, weakness in the right leg and urination disorders were observed. On the second MRI scan of the head (Fig. 2) and the neck (Fig. 3), an increase in the size of the affected areas of the brain, changes in the spinal cord at the C_I-C_{VI} level – signs of the acute disseminated

encephalomyelitis were observed. Over the next two days, the condition gradually worsened: Progressive peripheral tetraparesis with predominant damage to the right extremities, swallowing, and speech disorders developed. As of August 12, 2021, the patient was conscious, there were some movements in the left leg, neck pain persisted, urination was possible through a catheter, body temperature was 36.7 °C, and respiratory disorders (difficulty breathing, reduced saturation to 88%, respiratory rate of 24/min) were corrected by oxygen insufflation through a non-reflux mask. Microbiological analysis of the cerebrospinal fluid revealed the presence of *Staphylococcus Haemoluticus* (Table 3). On the same day, the patient was hospitalized at the Lviv Clinical Emergency Hospital. Computed tomography of the chest and abdominal organs with contrast revealed subsegmental atelectasis of the basal parts of both lungs, and a trace amount of free fluid in the right pleural sinus (Fig. 4).



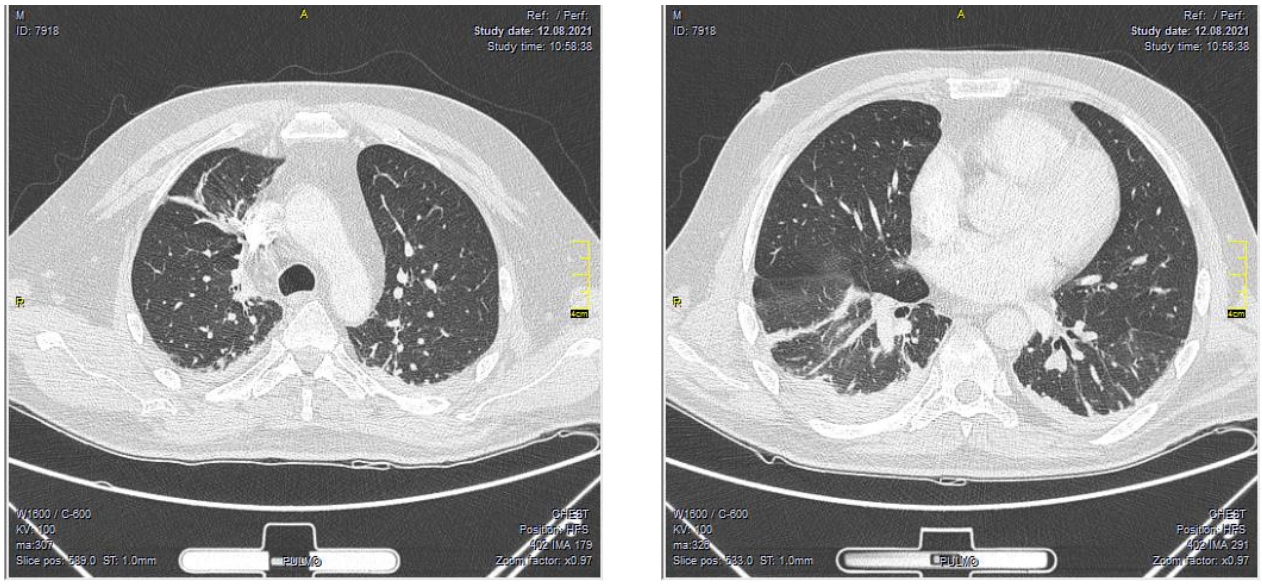
A B

Figure 2. MRI of the patient's brain, July 29, 2021: a) axial sections in T2 weighted images; B) frontal sections in FLAIR sequence. The area of damage in the medulla oblongata, pons, and right middle cerebellar peduncle



A B

Figure 3. MRI of the patient's cervical spinal cord, August 9, 2021: a) sagittal sections in T2 weighted images; B) sagittal sections in T1 weighted images with contrast. The damaged area in the spinal cord at the level C_I- C_{VI} vertebrae with spread to the brain stem



A B

Figure 4. CT scan of the patient's lungs. a) fibroatelectasis is visualized in the upper lobe of the right lung; B) in the basal parts of both lungs, areas of consolidation, subsegmental atelectasis, and a trace amount of free fluid in the right pleural sinus are found

During further intravenous treatment with immunoglobulins, antibiotics, anticholinesterase drugs, and B vitamins, leukocytosis in the full blood count was retained with an increased number of neutrophils (Table 1). There was an increase in blood glucose in the range of 8.8-11.6 mmol/l. A blood test was performed for ferritin (more than 500 ng/ml), D-dimer (2.29 mg/L), C-reactive protein (less than 5 mg/l), procalcitonin (0.14 ng/ml), IgG and IgM to SARS-CoV-2 (3,144 Abs and 1,081 Abs, respectively).

On August 13, 2021 signs of respiratory failure increased. An X-ray of the lungs showed right-sided lower-lobe pneumonia. Due to the deterioration of the patient's condition, artificial ventilation was arranged. On August 14, 2021, during bronchoscopy, endobronchitis and atelectasis of the right lower part of the bronchus were detected. Over the following days, an increase in total bilirubin (29 mmol/L), alanine aminotransferase (214 u/L), and aspartate aminotransferase (44.6 u/l) was detected in the blood (Table. 2), alpha-amylase (213.9 MG/sL), urinary alpha-amylase (128 u/l). The total IgM level was 0.03, IgA – 1.22, and IgG – 13.1. SARS-CoV-2 IgM was 0.08 and IgG was 6.1. During an ultrasound examination of internal organs, diffuse changes in the pancreas were detected. Cerebrospinal fluid 18.08.2021 – light yellow, transparent, protein 1.65 g/l, cytosis 120/μL, red blood cells unchanged 25-30/μL, neutrophils 75%, lymphocytes 25%, Pandy reaction +++, glucose 3.5 mmol/l, chlorides 115 mmol/l (Table 3). Microbiological examination of sputum revealed *Acinetobacter baumannii*.

During the treatment period, IgG, IgM for Borrelia, hepatitis B and C, syphilis, PCR for COVID-19, cytomegalovirus, Epstein-Barr virus, and herpes type 1, 2, 6 were determined – no changes were detected.

From August 18 to August 31, total bilirubin (37-81 mmol/L), and glucose (11.2-16.7 mmol/l) in the blood increased (Table 2). Ultrasound showed signs of hepatosis. On August 25, 2021, the level of procalcitonin was 1.49 ng/mL, and on August 31, 2021 – 0.6 ng/mL. Blood and CSF culture – no microflora was detected. There were signs of peripheral tetraplegia, sensory, urination, and breathing disturbances. Bilateral lower lobe pneumonia was noted.

Since the beginning of September 2021, the patient's condition was severe with negative dynamics, there were repeated fluctuations in blood pressure and heart rate during the day, increased sweating, and peripheral tetraplegia was maintained with minimum movements in two fingers of the left hand, superficial and deep sensitivity from the neck level on both sides was reduced. Consciousness level – stupor. Body temperature 37.1 °C. Ultrasound showed

signs of moderate hepatomegaly and diffuse changes in the pancreas and kidneys. On September 2, 2021, a chest X-ray showed right-sided lower lobe pneumonia and right-sided hydrothorax.

Since September 3, due to unstable hemodynamics, and frequent drops in blood pressure, the patient was treated with catecholamines. The next day, according to vital signs, thoracocentesis and Bulau drainage were performed to eliminate right-sided pneumothorax. Despite all the intensive care, the patient died on the evening of the same day.

Treatment: Antibiotics, antiviral, anti-cholinesterase, diuretics, non-steroidal anti-inflammatory drugs, corticosteroids, non-glycoside cardiotonic agents, intravenous immunoglobulins, artificial ventilation, thoracocentesis with drainage of the right pleural cavity.

Final diagnosis: Acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy, Guillain-Barre syndrome, ascending Landry type with peripheral tetraplegia, bulbar syndrome, signs of dysregulation of the autonomic nervous system (dysautonomia). Bilateral pneumonia caused by Acinetobacter baumanii (sputum microbiological examination of August 26, 2021). Right-sided spontaneous pneumothorax (condition after drainage of the right pleural cavity on September 49 at 19.50-20.00, 21.30-2.40), multiple organ failure (acute cardiac, respiratory, cerebral). Chronic pancreatitis. Chronic pyelonephritis.

An autopsy was performed where changes in organs and tissues were detected. Histological examination of the pia mater's necroptates revealed the dilation of small caliber vessels, minor perivascular leukocyte-macrophage infiltrate; in other areas, minor lymphocytic-leukocyte infiltrate in loose granulation tissue. In the gray and white matter of the brain – small foci of colliquative necrosis, focal minor perivascular and intravascular leukocyte infiltrate, perivascular and pericellular edema, hyperemia, dilatation of the lumen of small-caliber arteries, and there are small accumulations of white blood cells, alterative changes in neurons in the pons and stem.

Based on clinical and pathomorphological data, a pathologic and anatomical diagnosis was established:

I. The main disease: Diffuse, serous-purulent meningoencephalitis with damage to the hemispheres and brain stem, organization of exudate. Myelopolyradiculoneuritis (Guillain-Barre syndrome) according to clinical data.

II. Complications of the underlying disease: Prolonged mechanical ventilation. Purulent-ulcerative tracheitis. Bilateral subtotal polysegmental purulent, abscessing bronchopneumonia. Focal obturating thrombosis in the lumen of the branches of the pulmonary medium caliber artery

Bilateral exudative purulent-fibrinous pleurisy of the lungs` lower lobes. Spontaneous right-sided pneumothorax. The focal right-sided collapse of lung tissue. Small-focal interstitial serous myocarditis. General venous hyperemia and alterative changes in parenchymal organs: Diffuse central particles necrosis of hepatocytes; focal tubulonecrosis. Focal erosions of the stomach. Edema of the upper lobes of the lungs. Edema-swelling of the brain.

Discussion

The term encephalomyelopolyradiculoneuropathy is used to describe cases with damage to the CNS and PNS, with clinically predominant PNS deficiency in most cases [15]. It is often an immunologically mediated demyelinating disorder, which features manifestations of acute disseminated encephalomyelopathy and Guillain-Barre syndrome.

In the case of the 45-year-old man we described, acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy developed, an ascending type of Landry, which was manifested by peripheral tetraplegia, bulbar syndrome, sensitive disorders, disorders of pelvic organ function, respiration, and cardiovascular activity (signs of dysautonomia). The diagnosis was made based on the clinical picture, which developed gradually from increased body temperature, meningeal symptoms, and right-hand paresis to peripheral tetraplegia, sensitive disorders, bulbar syndrome, and dysregulation of the autonomic nervous system. Multifocal changes, hyperintensive on T2-weighted image in the white matter of the cerebral hemispheres, cerebellum, brain stem, and spinal cord on MRI, protein cell dissociation in the cerebrospinal fluid confirmed the diagnosis. The occurrence of bilateral subtotal polysegmental purulent bronchopneumonia over time, as a complication, most likely caused additional secondary bacterial damage to the brain and meninges.

Acute polyradiculoneuropathy and disseminated encephalomyelitis are known as rare complications of vaccination for both SARS-CoV-2 and other infections [1, 5, 6, 8, 9, 10]. Ismail I. I. and Salama S. (2022) noted that demyelinating processes of the central nervous system develop mainly after the first administration of the vaccine, on average after 9

days [16]. Most of them occurred after vaccination with mRNA-based vaccines. The average age of patients was about 44 years, and women predominated.

In our case, simultaneous immune-mediated damage to the CNS and PNS occurred 3 days after vaccination with the first dose of the BNT162b2 mRNA vaccine in the form of acute encephalomyelopolyradiculoneuropathy. Despite the treatment, encephalomyelopolyradiculoneuropathy with peripheral tetraplegia, sensitive disorders, bulbar syndrome, vegetative disorders, the need for prolonged artificial ventilation, followed by the occurrence of bilateral abscessed bronchopneumonia, which additionally caused secondary bacterial meningoencephalitis, led to the occurrence of pneumothorax, multiple organ insufficiency, severe dysautonomia, which led to the death of the patient. The presence of chronic pancreatitis and chronic pyelonephritis in the life anamnesis could also negatively affect the development and severity of the course of the disease. Since the causal relationship between the occurrence of rare pathological disorders of the nervous system and vaccination against SARS-CoV-2 with mRNA-based vaccines has not been fully established [6, 8], there is also the possibility that this case may be a coincidence .

In conclusions: Acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy can be considered as a probable rare neurological complication of SARS-CoV-2 vaccination with mRNA-based vaccines.

Acute autoimmune inflammatory encephalomyelopolyradiculoneuropathy can have a severe course, accompanied by multiple complications leading to death.

Further additional research is needed to establish causal relationships and the exact mechanisms of simultaneous CNS and PNS damage close in time to vaccination against SARS-CoV-2 with mRNA-based vaccines.

Informed Consent Statement: During the treatment, written informed consent for the analysis and processing of personal data was received from the patient.

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