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Underdiagnosis of botulism as a cause of tragedy: A case report

Vladimir V. Nikiforov[1, 2], Anastasia V. Kozhevnikova[1, 3], Igor N. Tyurin[3], Tatyana Y. Chernobrovkina[1], Olga A. Zykova[1], Natalia A. Antipyat[3], Ekaterina A. Lyapeykova[3]

[1] Pirogov Russian National Research Medical University, Moscow, Russia;
[2] Academy of Postgraduate Education of the Federal Research and Clinical Centre for Specialized Medical Care and Medical Technologies, Moscow, Russia;
[3] Infectious Diseases Clinical Hospital No. 1, Moscow, Russia

ABSTRACT

Botulism has unique clinical picture; however, some of its manifestations, when analyzed separately, are similar to the manifestations of other, both infectious and noncommunicable diseases. This contributes to the occurrence of diagnostic errors because botulism is not one of the most common infectious diseases; as a result, most practitioners are familiar with the clinical picture of botulism purely theoretically and clearly insufficiently. The article analyzes the course of botulism in a group of family diseases when, at the first visit to specialists, botulism was diagnosed in any of the patients not receiving medical care. In addition, the causes and effects of prolonged toxemia (20 days) in one of the patients are discussed.

Keywords: botulism; underdiagnosis; myasthenia gravis; encephalitis; prolonged toxemia; antibotulinum serum; case report.

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Гиподиагностика ботулизма как причина трагедии: случай из практики

В.В. Никифоров[1, 2], А.В. Кожевникова[1, 3], И.Н. Тюрин[3], Т.Я. Чернобровкина[1], О.А. Зыкова[1], Н.А. Антипят[3], Е.А. Ляпейкова[3]

[1] Российский национальный исследовательский медицинский университет имени Н.И. Пирогова, Москва, Россия;
[2] Академия постдипломного образования Федерального научно-клинического центра специализированных видов медицинской помощи и медицинских технологий, Москва, Россия;
[3] Инфекционная клиническая больница № 1, Москва, Россия

АННОТАЦИЯ

Ботулизм имеет свою, совершенно уникальную клиническую картину, однако некоторые его проявления, взятые по отдельности, сходны с проявлениями других, как инфекционных, так и неинфекционных, болезней. Это способствует возникновению диагностических ошибок, тем более что ботулизм не относится к числу часто встречающихся инфекционных заболеваний, ввиду чего основная масса практических врачей оказывается знакомой с клинической картиной ботулизма исключительно в теории и явно недостаточно. В статье даётся анализ течения ботулизма при групповом семейном заболевании, когда ни на одном этапе оказания медицинской помощи диагноз ботулизма при первичном обращении к специалистам ни у одного из заболевших диагностирован не был. Кроме того, обсуждаются причины и следствие длительной токсемии (20 дней) у одного из пациентов.

Ключевые слова: ботулизм; гиподиагностика; миастения; энцефалит; длительная токсемия; противоботулиническая сыворотка; клинический случай.

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ЭКО•ВЕКТОР

INTRODUCTION

Botulism is a unique disorder with a distinctive clinical presentation. However, it encompasses a wide range of signs and symptoms that can be separately found in different diseases (both infectious and non-infectious). At the same time, available botulism laboratory diagnosis techniques, such as toxin isolation and identification in body fluids and food using the classical procedure, with a neutralization reaction on muscles as the final stage, are time-consuming and cannot be performed at the point of care. Thus, the diagnosis of botulism is only based on clinical and epidemiological findings (at least during the first 2–3 days post-admission) [1]. As a result, clinicians must not only understand the primary manifestations of botulism, but also be able to differentiate between botulism and other disorders with similar manifestations.

However, the authors are profoundly cautious regarding the term *differential diagnosis* and its significance. If a clinician has deep knowledge in their therapeutic area, no differential diagnosis is required, because the diagnosis will already be obvious to an experienced specialist. However, if a clinician is less experienced and competent even within their therapeutic area, the knowledge in related areas will undoubtedly be far worse, offering no basis for differential diagnosis.

Botulism, in our opinion, has a completely unique course and clinical presentation. However, in real-world settings, especially during initial presentation to a general practitioner, this condition very frequently remains undiagnosed (or is misdiagnosed) both in Russia and around the world [2]. The analysis of botulism outbreaks in the US, where some cases were detected retrospectively (i.e., only after the patients were discharged with alternative diagnoses), indicates a high misdiagnosis rate [3, 4]. According to the literature, even classical botulism cases are frequently misdiagnosed as myasthenia, Guillain–Barré syndrome, and (more rarely) acute cerebrovascular accident, Lambert–Eaton myasthenic syndrome, meningitis, encephalitis, or tick-borne encephalitis [2, 5–9]. In the US, clinicians consider a wide range of classical and rare etiologies during the differential diagnosis of botulism. The chart analysis of 332 patients with suspected botulism, for which the physicians consulted the Centers for Disease Control and Prevention (CDC) between 1980 and 2016, revealed that attending physicians proposed an alternative diagnosis in 274 cases (83%). The most common possible diagnoses were Guillain–Barré syndrome (99 cases) and myasthenia (76 cases) [6].

To assess the nature and rate of misdiagnosis in botulism, we analyzed the records of the Infectious Diseases Clinical Hospital No. 1 of the Moscow Healthcare Department (IDCH No. 1) for the period between 2016 and 2020 (pre-COVID period). Moreover, we reviewed the historical records of the Botkin City Clinical Hospital and the Infectious Diseases Clinical Hospital No. 3 of the Moscow Healthcare Department (IDCH No. 3) for the period between 1975 and 2016. The assessment of botulism under-diagnosis rate, where botulism is misdiagnosed as a more or less hazardous infectious or non-infectious disease, is challenging and not always possible. This is because patients are frequently transferred to infectious diseases hospitals from other hospitals without a primary diagnosis in the accompanying documents (referral, discharge summary, etc.). Moreover, in group diseases, some patients are actively treated in infectious diseases hospitals, making under-diagnosis unlikely. The analysis of errors in botulism diagnosis is further complicated by the fact that some patients are unaware of the diagnosis made at the initial presentation. Despite these challenges, we performed a sampling analysis of the nature and rate of botulism under-diagnosis in 339 patients discharged from infectious diseases hospitals with a diagnosis of botulism. Unfortunately, during initial presentation, botulism was suspected (referral diagnosis: "botulism?") or immediately confirmed (referral diagnosis: "botulism") in only 149 patients (44%). Moreover, these included 37 patients whose diagnosis of botulism was known in advance, making the already grim picture even worse. Importantly, 40 of 339 patients were hospitalized for the primary condition following two or more diagnosis errors. The most common misdiagnosis is food-borne infection (as the first and only erroneous diagnosis in 59 patients, and as one of several diagnosis errors in 6 patients). The analysis suggests that the range of erroneous diagnoses is extremely wide, and clinicians' fantasies about language (such as "acute far-sightedness") dwarf even the worst ICD-10 stylistic howlers.

Acute cerebrovascular accident is the second most common diagnosis (23 cases), followed by neurocirculatory dystonia, hypertensive crisis, and brainstem encephalitis (5, 4, and 3 cases, respectively). Some unfathomable combinations of diagnoses and their language were discovered. The most spectacular examples included acute far-sightedness (2 cases); hypertensive crisis, brainstem encephalitis (2 cases); strep throat, myasthenia (1 case); hypertensive crisis, oropharyngeal diphtheria (1 case); neurocirculatory dystonia, acute far-sightedness, "?" (1 case); "?", laryngitis, functional paresis of the larynx, "?" (1 case); acute appendicitis, acute gastritis, spasm of accommodation, "?", "?" (1 case), and so on.[1]

In our perspective, difficulties in primary diagnosis of botulism are caused by quite trivial factors. Botulism is not a common infectious disease; thus, the majority of clinicians only have a theoretical understanding of its clinical presentation.

In this regard, we present an intriguing clinical case that may offer some insights to practitioners.

[1] The wording used for diagnosis in primary medical records was preserved. The sequence of erroneous diagnoses is denoted by ";". Cases where the diagnosis is unknown or not specified in the corresponding medical records, although botulism was not confirmed, are denoted by "?".

CASE DESCRIPTION

Patient A., a 30-year-old female, was admitted to the emergency room of IDCH No. 1 by ambulance on February 28, 2024, with a diagnosis of type A botulism.

The condition at admission was considered severe. The patient had a classical clinical presentation of botulism, with the toxin type (A) already identified.

However, the patient's journey to the specialized infectious diseases hospital was anything but simple.

The unfortunate chain of events began on February 3, 2024, in Shakhty (Rostov region). On the day in question, the family of three (patient's aunt I.V., 60 years old, patient's cousin A.S., 39 years old, and patient's nephew I., 11 years old) prepared and ate a vegetable salad with homemade canned cucumbers. These preserves were later found to contain botulinum toxin type A. The can with the leftover poisonous preserves was placed in the refrigerator. All three family members developed botulism of varying severity, which will be discussed in further detail later. The aunt became ill on the evening of February 3, 2024, and died on February 4, 2024.

Patient A. (who was healthy at the time) arrived from Moscow to attend her aunt's funeral during the night of February 4, 2024, to February 5, 2024. She stayed in her aunt's apartment and ate poisonous canned cucumbers on occasion beginning February 5, 2024. On February 6, 2024, she was joined by her late aunt's husband (61 years old). He also developed botulism, though later and in a milder form.

Patient A. became ill on February 9, 2024: in the morning, she developed blurry vision, double vision, and dry mouth. The following day (February 10, 2024) the patient started experiencing weakness, which gradually worsened. Patient A. consulted a neurologist in private practice for these complaints. The neurologist referred her to an infectious disease specialist and for a brain MRI, with a diagnosis of "meningitis?" (!). The examination performed on February 11, 2024, revealed no pathology, while the patient's condition continued to deteriorate. On February 11, 2024, the patient developed indistinct speech and difficulties swallowing dry, solid food. On February 13, 2024, the patient left Shakhty for Moscow. On February 14, 2024, she arrived home and immediately called an ambulance.

The actions taken by the patient (as recounted by her) and healthcare personnel (according to medical records) are listed in chronological order below. The grammar and spelling of medical records have been edited (while keeping their core) to meet the criteria of literary language. Moreover, the authors have the original medical records.

February 14, 2024, 3:44 pm. Examination by an emergency physician (record number: 40282098...). Emergency physician diagnosis: G45.0. Vertebro-basilar artery syndrome. Hospitalization was recommended; however, the patient declined for unknown reasons. The emergency call was reported to a local outpatient clinic. A general practitioner consulted the patient online as part of a voluntary health insurance program. The patient was advised to see a mental health counselor due to "cumulative stress."

February 14, 2024. Examination by a local general practitioner. No objective pathology detected. Medical opinion: G90.9. Disorder of autonomic nervous system, unspecified. Preliminary diagnosis: Vegetovascular dystonia, asthenoneurotic syndrome. Complication: H53.2. Diplopia. An electronic certificate of incapacity for work No. 910212185791 was issued for the period from February 14, 2024, to February 17, 2024. A referral for hospitalization to a neurology hospital No. 1970-1000032../2024 was issued.

February 14, 2024. Examination by a local ophthalmologist. Medical opinion: H35.0. Background retinopathy and retinal vascular changes.

February 15, 2024. The patient's condition continues to deteriorate. The voice is getting nasal, the speech is indistinct. Swallowing difficulties are becoming more severe.

February 16, 2024. The patient requested hospitalization at a neurology hospital; however, according to the patient, hospitalization was denied due to a "valid certificate of incapacity for work." By this time, neurological symptoms continued to worsen: the patient could barely open her eyes, occasionally experienced shortness of breath, and developed choking while drinking water. The patient returned to the local outpatient clinic.

February 16, 2024. Examination by a local general practitioner. Medical opinion: G45.9. Transient cerebral ischemic attack, unspecified. Transient ischemic attack of the left hemisphere? Neuralgia facialis vera on the right? An ambulance team was called.

February 16, 2024, 2:47 pm. Ambulance team. Record number: 40285355... Emergency physician diagnosis: G45.0. Vertebro-basilar artery syndrome. Vertebrobasilar insufficiency, acute cerebrovascular accident. The patient was admitted to the emergency room of a multidisciplinary city clinical hospital No. X (CCH No. X).

February 16, 2024, 4:06:00 pm. Examination by a neurologist in the emergency room.

Complaints: Headache, dizziness, double vision, bilateral ptosis, unsteady gait, speech impairment.

Diagnosis: I11.9. Hypertensive heart disease without (congestive) heart failure. Clinical diagnosis: Grade 2 hypertension, stage 3, cardiovascular risk 3.

The patient was transferred to the neurology department.

Examination at the neurology department. Complaints: Headache, dizziness, double vision, bilateral ptosis, unsteady gait, speech impairment.

Anamnesis morbi. According to the patient: The condition deteriorated in the morning of February 9, 2024, when the aforementioned complaints escalated. Head MRI of February 10, 2024: without pathological findings. On February 13, 2024, the patient developed speech impairment. On February 14, 2024, the patient presented to a healthcare facility, where treatment was prescribed and an electronic certificate of incapacity for work was issued. The patient received inosine + nicotinamide +

riboflavin + succinic acid (Cytoflavin), with no effect. On February 16, 2024, the patient again called an ambulance, received intravenous ethylmethylhydroxypyridine succinate (Mexidol), and was admitted to CCH No. X.

Anamnesis vitae. The patient is employed; an electronic certificate of incapacity for work was issued for the period from February 14, 2024, to February 17, 2024.

According to the patient, her cousin was diagnosed with myasthenia-like syndrome.

The general condition is satisfactory. The patient is fully conscious. Regular physique, well-nourished, normosthenic type. The skin and visible mucosa are clear, of normal color and moisture. Post-injection hematomas in the bends of elbows. No edema. No trophic disorders. Peripheral lymph nodes are not enlarged. Body temperature 36.5 °C. Fully conscious. No meningeal symptoms. Higher mental functions are normal. Cranial nerves: vision is preserved. Pupils D = S. Light reflexes are preserved. The eyes have full range of motion, no convergence. Bilateral ptosis. Double vision at a distance of 1–1.5 m from an object. The face is symmetrical. Facial sensitivity is preserved. Lateral gaze-evoked fine horizontal nystagmus. Hearing is preserved. Swallowing is preserved. Pharyngeal reflex is preserved on both sides. No dysarthria or dysphonia. Midline tongue protrusion. No limb paresis. Muscle tone of the extremities is normal, S = D. Moderate tendon and bone reflexes, S = D. No pathological plantar reflexes. No sensation disorders. Heel-to-shin and finger-to-nose tests: past-pointing on both sides. Romberg's maneuver: lateral deviation up to falling. Ataxic gait. No pain on paravertebral palpation or spinous processes percussion. Continent. Rankin 3, Rivermead 7.

Diagnosis by an admitting physician of the neurology department: I67.8. Other specified cerebrovascular diseases. Clinical diagnosis: Grade 2 chronic brain ischemia, vertebrobasilar insufficiency, decompensation, vestibulo-ataxic syndrome.

Concurrent diagnosis: Myasthenia?

February 16, 2024, 5:39 pm. Brain CT. Medical opinion: No CT findings indicating mass lesions and focal changes in the brain. No traumatic or destructive changes in skull bones.

February 16, 2024, 5:42 pm. Chest CT. Medical opinion: No CT findings indicating intrathoracic lymphadenopathy or focal and infiltrating pulmonary tissue lesions on both sides.

February 16, 2024, 8:03 pm. Contrast-enhanced brain MRI. Medical opinion: No MRI findings indicating brain infarction.

February 16, 2024, 9:40 pm. Contrast-enhanced CT angiography of intracranial vessels (arteries and veins). Medical opinion: No CT findings indicating aneurysm, arteriovenous malformation, or hemodynamically significant intracranial artery stenosis.

February 19, 2024, 1:17 pm. Assessment of neuromuscular transmission (repetitive nerve stimulation) before and after the proserin test. Description: Repetitive nerve stimulation was performed on *m. orbicularis oculi*, *m. nasalis*, digastric muscle, and *abductor digiti minimi*, on both sides. Supramaximal stimuli (3 V) were delivered to the corresponding nerve in a standard point. A decrease in the total muscle response amplitude (amplitude ratio of stimulus one to stimulus five) was detected in m. orbicularis oculi on the right (by 45%). Medical opinion: Repetitive nerve stimulation: positive.

February 20, 2024, 6:26 pm. Electroencephalography (EEG). Medical opinion: The basic activity is stable; frequency characteristics are age-appropriate. Functional tests revealed no significant changes in rhythmic cortical discharge. No EEG findings indicating paroxysmal activity.

February 20, 2024, 2:58 pm. Examination by an ophthalmologist. Medical opinion: OU: condition after keratorefractive (laser) surgery (moderate myopia –6.0 D/–5.0 D). Alternating divergent squint. OD incomplete blepharoptosis. OS partial blepharoptosis.

From February 16, 2024, to February 22, 2024, the patient was admitted to the neurology department of CCH No. X.

Discharge diagnosis. Principal diagnosis: G70.2. Congenital and developmental myasthenia. Clinical diagnosis: Myasthenia gravis, craniobulbar, MGFA 2A. OD incomplete blepharoptosis. OS partial blepharoptosis. Alternating divergent squint. Concomitant diseases: ICD-10 code: H52.1. Myopia; OU: condition after keratorefractive (laser) surgery (moderate myopia –6.0 D/–5.0 D).

Hospitalization outcome: improvement.

February 25, 2024. Examination by a local general practitioner. Complaints of double vision, numbness in the right arm, severe weakness, easy fatigability. Presented again with the same complaints: electronic certificate of incapacity for work No. 9102-1852-080..., from February 14, 2024, upon discharge from CCH No. X.

Physical examination: blood pressure (BP) 125/70 mm Hg, body temperature 36.5 °C. The general condition is satisfactory. The patient is fully conscious. Neuropsychological status: oriented times 3. Heart rate 78 bpm, regular rhythm. Oral cavity: the oropharynx is clear, pink. Tongue: moist, no plaque. Respiratory organs: unobstructed nasal breathing. Lungs: vesicular breathing, no rales. The abdomen is soft and painless on palpation. Urination: unimpeded, painless; costovertebral angle tenderness: negative. Stool: once daily, no pathological admixtures in feces. Neurological status: alert and oriented. No meningeal signs. Brudziński cheek, symphyseal, and neck signs: negative; Kernig's sign: negative. No dysarthria; hearing is not impaired; the sense of smell is preserved. The olfactory nerve function is normal. Pupils D = S. The right eye fails to have full range of motion. No nystagmus; double vision. Facial paresis on the right. Midline tongue protrusion. Swallowing is unobstructed. Tendon reflexes D = S; Achilles reflexes are preserved, D = S, brisk. No sensation disorders. Muscle strength in the arms and legs is preserved; the patient can walk without assistance. No pelvic organ dysfunction. Romberg's maneuver: wobbling. Tandem gait test: tilts to the right. Upper extremities diadochokinesis test: successful; Stewart–Holmes sign: negative; dysmetria test: negative.

Principal diagnosis: G70.2. Congenital and developmental myasthenia.

The general practitioner requested that the medical board extend the electronic certificate of incapacity for work from February 24, 2024, to February 25, 2024 (3 days), and from February 26, 2024, to February 28, 2024.

February 25, 2024. The patient learned that botulism was suspected in her family in Shakhty, where she attended the funeral, and immediately called an ambulance.

February 25, 2024, 5:47 pm. Record number: 414705328. The ambulance team did not confirm the diagnosis of botulism. Diagnosis: ICD-10 code: I11.9. Hypertensive heart disease without (congestive) heart failure. The patient was not hospitalized; instead, she was instructed to visit an outpatient clinic (or another healthcare facility).

February 26, 2024. The patient asked for a referral to an infectious disease specialist. Examination by a general practitioner: According to the patient, her cousin was diagnosed with myasthenia-like syndrome. According to the patient, she was in the Rostov region beginning February 4, 2024. She attended the funeral, where several people were hospitalized for poisoning after a funeral banquet. The Russian Consumer Rights Protection Agency called and informed the patient that the poisoning was caused by botulinum toxin type A.

Principal diagnosis: Z03.9. Observation for suspected disease or condition, unspecified. Confirmed diagnosis: Myasthenia.

Recommendations: Outpatient follow-up. Other recommendations: Consultation by an infectious disease specialist at the patient's request, to rule out the pathology.

Next visit: February 28, 2024.

The patient was referred to an infectious disease specialist (the local outpatient clinic does not have one).

February 26, 2024. The patient saw an infectious disease specialist in private practice. Medical opinion: Condition after botulism cannot be ruled out. Consultation at IDCH No. 1 was recommended.

February 26, 2024. Examination by a local neurologist. Complaints of persistent arm and leg weakness, headache, dizziness, double vision, bilateral ptosis, unsteady gait, speech impairment.

Anamnesis morbi. The patient reported eating homemade preserves between February 4, 2024, and February 9, 2024. Her condition deteriorated in the morning of February 9, 2024, when the aforementioned complaints escalated.

Inpatient treatment in CCH No. X from February 16, 2024, to February 22, 2024. Diagnosis: G70.2. Congenital and developmental myasthenia. The patient saw an infectious disease specialist in private practice. Medical opinion: Condition after botulism cannot be ruled out.

Physical examination. General condition: no cerebral symptoms. Cranial nerves: bilateral ptosis, double vision, dysphonia, dysphagia. Motor sphere: a symmetrical decrease in muscle strength and tone in the arms and legs. Low tendon reflexes in the upper and lower extremities, D = S. No pathological reflexes. No sensation disorders. Coordination tests: satisfactory. Romberg's maneuver: completely steady.

Principal diagnosis: A05.1. Botulism (preliminary).

Other recommendations: follow-up by an infectious disease specialist and general practitioner.

February 28, 2024. Examination by an infectious disease specialist at an outpatient clinic No. ... Complaints of muscle weakness (unable to lift her arms), ptosis, speech impairment, double vision, numbness in the right arm, unsteady gait. Difficulties swallowing, weight loss. Has been ill for 3 weeks. The patient reported eating homemade preserves between February 4, 2024, and February 9, 2024. Her condition deteriorated in the morning of February 9, 2024, when the aforementioned complaints appeared and escalated. The patient presented to a local outpatient clinic and was not hospitalized. Inpatient treatment in CCH No. X from February 16, 2024, to February 22, 2024. Diagnosis: G70.2. Congenital and developmental myasthenia.

On February 26, 2024, botulinum toxin type A was detected in the blood of the patient's nephew.

Physical examination. Body temperature 36.6 °C. The general condition is satisfactory. Muscles: weakness of all muscle groups. Tongue: moist, with white plaque. Laryngeal edema. Vesicular breathing, no rales. Dyspnea; struggles for breath in lying position. The abdomen is soft and painless. The liver is palpable along the costal margin; painless; soft and elastic. The spleen is not palpable. Stool: constipation.

Principal diagnosis: A05.1. Botulism (preliminary). An ambulance was called, and the patient was hospitalized to IDCH No. 1.

February 28, 2024, 1:03 pm. The patient was admitted to IDCH No. 1 by ambulance. Record number: 414751423.

February 28, 2024. Examination at the emergency room of IDCH No. 1. The condition at admission was considered severe.

Admission diagnosis. Principal diagnosis: A05.1. Severe botulism.

From February 28, 2024, 3:49 pm, to February 29, 2024, the patient was admitted to the intensive care unit (ICU). On February 28, 2024, 8:00 pm, after a skin test (negative), the patient received antibotulinic serum (ABS) type A at a single intravenous dose of 10,000 IU. Appropriate therapeutic interventions allowed stabilizing the patient's condition, preventing respiratory decompensation, and avoiding mechanical ventilation.

February 29, 2024, 1:29 pm. Consultation by a neurologist. Medical opinion: Given the epidemiological anamnesis, disease course and clinical presentation, and inefficacy of acetylcholinesterase inhibitors, the diagnosis of myasthenia appears unlikely. Positive findings of repetitive nerve stimulation are associated with decreased acetylcholine levels in the synaptic cleft, which is also observed in botulism. Myasthenia was ruled out.

Laboratory findings: Complete blood count of February 28, 2024: normal, C-reactive protein 1 mg/L. Electrocardiography of February 29, 2024, echocardiography of February 28, 2024, abdominal and kidney ultrasound of February 28, 2024, Doppler ultrasound of lower extremity veins of February 28, 2024: without pathological findings.

February 29, 2024. Given the improved condition, the patient was transferred to the infectious diseases department No. 10. Following that, neurological symptoms subsided. On March 5, 2025, the patient was discharged with a valid electronic certificate of incapacity for work (next visit: March 6, 2024), to be followed up by a local general practitioner, neurologist, and ophthalmologist.

Discharge diagnosis. Principal diagnosis: A05.1. Botulism (clinical and epidemiological, moderate).

The situation was even worse for the patient's relatives. As previously mentioned, relatives of patient A. (her aunt I.V., cousin A.S., and nephew I.) ate a salad with canned cucumbers on February 3, 2024. According to A.S., I.V. "felt unwell" on the evening of February 3, 2024. An ambulance was called, and a blood pressure increase up to 200/100 mm Hg was discovered; I.V. received an intravenous antihypertensive drug and was not hospitalized. The blood pressure decreased to 150/... mm Hg after some time; however, I.V. developed dizziness, blurry vision, and double vision. A.S. took her mother to a hospital in Shakhty, where an acute cerebrovascular accident (stroke) was suspected. I.V. was hospitalized; however, on the morning of February 4, 2024, A.S. was informed of her mother's death. According to the family, the cause of death was pulmonary embolism.

The patient's nephew I. (11 years old) felt unwell on February 4, 2024. The symptoms included dry mouth, recurrent vomiting, and visual impairment. The boy openly refused to go to a hospital. On February 5, 2024, his condition worsened. He developed indistinct speech and severe atony. His mother, A.S., took him to a hospital in Shakhty. The hospital personnel suspected a subarachnoid hemorrhage based on the boy's clinical presentation and a small hematoma on his forehead (from a ball game a few days prior). However, an urgent brain CT revealed no pathology. On the morning of February 6, 2024, the boy was transferred to the Rostov Regional Children's Clinical Hospital (RCCH) for further examination and treatment, with a diagnosis of acute cerebrovascular accident, unspecified (medical record No. 1240706).

At this point, his mother, A.S., had dry mouth, blurry vision, and double vision. However, she did not give it much thought due to her family's difficult situation.

The boy was admitted to RCCH with dizziness, indistinct speech, lethargy, somnolence, and severe weakness; he refused to eat or drink due to difficulties swallowing. He was examined by a neurologist and infectious disease specialist. A follow-up brain CT was performed, which revealed no pathology. A survey X-ray of the lungs revealed signs of left-sided pneumonia. The boy was transferred to the neurology department, where his condition continued to deteriorate; he developed progressively worsening signs of acute respiratory failure. Three hours after hospitalization, he developed dyspnea and generalized convulsions (probably due to hypercapnia). The boy was transferred to the ICU for urgent intubation and mechanical ventilation.

February 6, 2024. Consultation by a neurologist. Medical opinion: Toxic syndrome. Bulbar syndrome, unspecified. An autoimmune process (Bickerstaff brainstem encephalitis) cannot be ruled out.

February 7, 2024. A lumbar puncture was performed. It produced 2.0 mL of a clear, slightly opalescent fluid. Protein 0.39 g/L, glucose 4.3 mmol/L, chlorides 117 mmol/L, cytosis $1{,}0\times10^6$/L.

PCR with CMV, EBV, HSV-1, HSV-2, and virus GH-6 DNA: negative.

February 7, 2024. Follow-up consultation by a neurologist. Medical opinion: Brainstem encephalitis. Miller Fisher syndrome? Bulbar syndrome, seizure syndrome.

February 15, 2024. Follow-up consultation by a neurologist. Medical opinion: Autoimmune Bickerstaff brainstem encephalitis? Bulbar syndrome, seizure syndrome. Spastic tetraparesis, bilateral ptosis.

During this period, the patient's condition did not improve; a tracheostomy was performed, and mechanical ventilation was continued.

At the same time, A.S. (patient I.'s mother and patient A.'s cousin) began investigating the cause of her sudden visual impairment and weakness. She saw neurologists in private practice several times and received the same diagnosis of myasthenic syndrome or myasthenia-like syndrome. Brain CT was performed on February 10, 2024, without pathological findings. Anti-acetylcholine receptor antibodies (outpatiently) 0.03 nmol/L.

The ordeal of patient A.S. came to an end thanks to L.A. Fomina-Chernousova, a neurologist from Rostov-on-Don. On February 21, 2024, during an outpatient consultation, she immediately suspected botulism in patient A.S. (and, thus, other affected family members). Patient A.S. promptly informed her son's attending physicians. However, it was not until February 23, 2024, on Day 17 of treatment, that the ICU physicians confirmed the possibility of botulism in patient I. based on the epidemiological anamnesis and clinical presentation. Tests for botulinum toxin were performed, and the patient received a single intravenous dose of ABS type A, B, and E, respectively. On February 26, 2024, the Center of Hygiene and Epidemiology (Rostov region) reported that botulinum toxin type A was detected in the blood of patient I. (study No. 11, sampling date: February 23, 2024).

Notably, detecting botulinum toxin in the patient's blood after 20 days of disease is uncommon.

On February 26, 2024, patient A.S. was admitted to the infectious diseases department of the Semashko Central City Hospital (Rostov-on-Don) with a diagnosis of botulism (clinical and epidemiological, mild) (*author's note*: according to the discharge summary). The patient was hospitalized until

March 5, 2024. Medical record number: 160595... The patient received pathogenetic therapy; on February 26, 2024, the patient received a single intravenous dose of ABS type A, B, and E, respectively.

She was discharged on March 5, 2024, to be followed up by a local general practitioner.

The authors know little about the husband of deceased patient I.V. It is known that he experienced visual impairment (double vision). After February 26, 2024, he was invited to the infectious diseases department of the city hospital (Shakhty) and received ABS.

After receiving ABS, the condition of patient I. gradually improved. Since March 15, 2024, the requirement for mechanical ventilation gradually diminished. Beginning March 18, 2024, the patient could breathe spontaneously with a tracheostomy cannula, which was removed on March 19, 2024. On March 21, 2024, the patient was transferred to the infectious diseases department.

The patient was discharged on March 22, 2024, to be followed up by a local pediatrician and neurologist. It was advised that the patient be readmitted to the neurology department of RCCH for rehabilitation on June 3, 2024.

Discharge diagnosis: Botulism caused by botulinum toxin type A, food-borne, severe. ICD-10 code: A05.1. Complication: Grade 3 respiratory failure, aspiration pneumonia. Concurrent diagnosis: Condition after decannulation (April 19, 2024) (*author's note*: according to the discharge summary).

After discharge, patient A. has been regularly followed up by phone. As of late April 2024, the patient had persistent weakness and visual impairment (inability to read small print). Her condition did, however, improve gradually.

DISCUSSION

Two critical questions arose from our interactions with patient A. and the review of available medical records. The first question is addressed to healthcare professionals who were in charge of the patients featured in this article. How is it possible that all the physicians who treated five members of the same family who became ill almost simultaneously failed to see a pattern in a previously healthy 60-year-old woman's sudden death, a "stroke" in an 11-year-old boy (which is an extremely uncommon diagnosis for this age), cousins who developed "myasthenia" at the same time, and the deceased patient's husband's sudden visual impairment? None of the physicians bothered to check the family history. According to Professor Vladimir Oppel, "to make a diagnosis, one must first recall the diagnosis." However, in this case, there was most likely nothing to recall.

The second question is in an altogether different area. It has a scientific and practical significance, referring to the time when botulinum neurotoxin (BoNT) type A was isolated from the blood of patient I. (11 years old).

According to the literature, circulating botulinum toxin can be found in untreated patients 12–25 days after it enters the body with food [10]. This clinical case refers to a female patient with moderate botulism, hospitalized (without a medical order) to IDCH No. 3 on Day 23 of the disease, with BoNT type A isolated from the blood at admission [1]. Toxemia of such duration definitely cannot be explained by the initial extra-high dose of the toxin. Individual characteristics of the patient could result in very slow absorption of ingested toxin or the formation of a *Clostridium botulinum* colony that produces botulinum toxin in the intestine after consuming contaminated food containing both the toxin and the pathogen.

The long-term persistence of circulating botulinum toxin in the blood of patient I., which was detected on Day 20 of the disease, can only be explained by ongoing BoNT synthesis *in vivo, in situ*. Given the short incubation period and very severe course of the disease, the initial toxin dose was high. However, it is difficult to picture BoNT remaining in the patient's blood for nearly three weeks without its additional supply from the intestine. Taking into account the patient's generally severe condition, which required mechanical ventilation and other intensive care measures, it is fair to suspect that vegetative forms of the pathogen were activated due to intestinal paresis. This is the case in the so-called intestinal colonization [11, 12] by *C. botulinum*, which is an extremely rare form of botulism in severe somatic disorders (most frequently cancer) in patients with intestinal lesions prior to botulism. This suggestion is supported by the fact that patient I.'s condition did not improve at all during his hospital stay before ABS administration. An assessment of the worsening of neurological symptoms caused by additional BoNT doses was impossible, because the patient's symptoms were already at their peak severity, and he was on mechanical ventilation.

CONCLUSION

In history, there are no givens. However, one cannot help but question whether the first affected family member (patient I.V., 60 years old) could have been saved if the diagnosis of botulism was confirmed shortly after her admission to the hospital in Shakhty. What would happen if the leftover salad and canned cucumbers were discarded, while other family members received ABS as a preventive measure? We hope that after reading this article, our colleagues will pay closer attention to each patient and their medical history. As Gustave Flaubert put it, "God is in the details." However, more often than not, the devil is in the details.

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AUTHORS' INFO

*** Vladimir V. Nikiforov**, MD, Dr. Sci (Medicine), Professor;
address: 1 Ostrovityanov street, 117997 Moscow, Russia;
ORCID: 0000-0002-2205-9674;
eLibrary SPIN: 9044-5289;
e-mail: v.v.nikiforov@gmail.com

Anastasia V. Kozhevnikova;
ORCID: 0009-0009-2606-7071;
e-mail: ice1234@yandex.ru

Igor N. Tyurin, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0000-0002-5696-1586;
eLibrary SPIN: 6755-0576;
e-mail: ikb@zdrav.mos.ru

Tatyana Y. Chernobrovkina, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0009-0008-3853-4792;
eLibrary SPIN: 1582-1930;
e-mail: Tanyura541@mail.ru

Olga A. Zykova, MD, Cand. Sci. (Medicine), Assistant Professor;
ORCID: 0009-0004-6668-2144;
eLibrary SPIN: 3146-1468;
e-mail: ozpenza @yandex.ru

Natalia A. Antipyat;
ORCID: 0000-0001-8578-2838;
e-mail: ikb@zdrav.mos.ru

Ekaterina A. Lyapeykova;
ORCID: 0000-0002-5071-6328;
e-mail: ikb@zdrav.mos.ru

ОБ АВТОРАХ

*** Никифоров Владимир Владимирович**, д-р мед. наук, профессор;
адрес: 117997, Россия, Москва, ул. Островитянова, д. 1;
ORCID: 0000-0002-2205-9674;
eLibrary SPIN: 9044-5289;
e-mail: v.v.nikiforov@gmail.com

Кожевникова Анастасия Владимировна;
ORCID: 0009-0009-2606-7071;
e-mail: ice1234@yandex.ru

Тюрин Игорь Николаевич, канд. мед. наук, доцент;
ORCID: 0000-0002-5696-1586;
eLibrary SPIN: 6755-0576;
e-mail: ikb@zdrav.mos.ru

Чернобровкина Татьяна Яковлевна, канд. мед. наук, доцент;
ORCID: 0009-0008-3853-4792;
eLibrary SPIN: 1582-1930;
e-mail: Tanyura541@mail.ru

Зыкова Ольга Алексеевна, канд. мед. наук, доцент;
ORCID: 0009-0004-6668-2144;
eLibrary SPIN: 3146-1468;
e-mail: ozpenza @yandex.ru

Антипят Наталья Александровна;
ORCID: 0000-0001-8578-2838;
e-mail: ikb@zdrav.mos.ru

Ляпейкова Екатерина Александровна;
ORCID: 0000-0002-5071-6328;
e-mail: ikb@zdrav.mos.ru

* Corresponding author / Автор, ответственный за переписку