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SPINOCEREBELLAR ATAXIA TYPE 1 WITH CERVICAL DYSTONIA: CLINICAL POLYMORPHISM OR A COMBINATION OF TWO DISEASES? (CLINICAL CASES)

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Autosomal dominant spinocerebellar ataxias (AD SCA) can present with a wide variety of non-cerebellar symptoms, including movement disorders. In fact, movement disorders are common in many different subtypes of SCA, and they may be present, dominant, or even an isolated feature of the disease. In this article we describe 9 clinical cases of spinocerebellar ataxia type 1, the clinical picture of which includes cervical dystonia with laterocollis. In all cases, a mutation in the ATXN1 gene was detected.

Keywords: cerebellar ataxia; movement disorders; spinocerebellar ataxia; cervical dystonia.

Introduction. Spinocerebellar ataxias with an autosomal dominant pattern of inheritance are a heterogeneous group of hereditary progressive neurodegenerative diseases characterized by progressive cerebellar ataxia, dysarthria and a number of other variable neurological symptoms: pyramidal or extrapyramidal symptoms, ophthalmoplegia, cognitive dysfunction and peripheral neuropathy. Currently, more than 40 autosomal dominant spinocerebellar ataxias have been identified. AD SCA is a disease with a late onset, usually after 30-40 years, less often in childhood or in old age [1, 2]. Based on the fact that these diseases are disabling and affect mainly people of working age, the problem of research on SCA blood pressure is important in the healthcare and social care system [1]. The most common 6 types of progressive AD SCA are: 1, 2, 3, 6, 7, 17 and dentatorubro-pallidoluis atrophy (DRPA). In the Russian Federation, spinocerebellar ataxia type 1 (SCA1) has a high prevalence [4].

According to literary studies, the main neurodegenerative syndromes accompanied by muscular dystonia with an autosomal dominant type of inheritance are spinocerebellar ataxia type 3, Machado-Joseph disease, dentatorubro-pallidoluis atrophy, and Huntington's disease [1, 4, 7, 8].

Machado-Joseph disease in the modern classification is characterized as spinocerebellar ataxia type 3 (SCA3). The gene that causes this disease is located on chromosome 14 at the 14q24.3-q32 locus. The main clinical feature of SCA 3 is progressive ataxia due to dysfunction of the cerebellum and brainstem. Ataxia, however, never occurs in isolation. Numerous other clinical problems reflect progressive dysfunction of the brainstem, oculomotor system, pyramidal and extrapyramidal tracts, lower motor neurons, and peripheral nerves. The age of onset varies widely; Symptoms have been reported in individuals aged 5 to 70 years. This variability reflects differences in repeat size, with larger repeats on average leading to earlier disease development. Dystonia in the hands is often an extrapyramidal symptom; athetosis and parkinsonism are less common. A specific manifestation of the disease is the presence of the "bulging eyes" symptom, that is, the development of external ophthalmoplegia, which is observed in 30-50% of patients. When making a diagnosis, family history is important. DNA diagnostics helps to accurately determine the disease [4, 8].

Dentatorubropallidoluis atrophy is an autosomal dominant spinocerebellar ataxia caused by a CAG repeat expansion in the *ATN1* gene, which is located on chromosome 12p13 [2]. Pathological CAG repeats reach 48 or more repeats, and the age of onset and clinical severity of the disease correlates with the length of the CAG repeat. The symptoms of dentatorubro-pallidoluis atrophy are extremely polymorphic. The disease can begin between the 1st and 6th decades of life and manifests itself in the form of horseathetosis, ataxia, dementia, myoclonus, epileptic seizures, and less commonly, dystonia [2, 3]. An important role in diagnosis is played by DNA analysis and neuroimaging methods, which make it possible to identify atrophic changes in the tectum of the brain [4]. It is worth carrying out a differential diagnosis with Huntington's disease, which occurs in the juvenile Westphal variant, observed in 5-10% of cases. The core of the clinic is muscle rigidity; in adolescents, dystonia, myoclonus, athetosis, and convulsions may occur; hyperkinesis in the form of chorea may be absent or manifest only in the oromandibular muscles. Characterized by changes in behavior, memory loss, and criticism. An accurate diagnosis is esTableished after a molecular genetic study [4, 8].

In the available literature, we did not find clinical descriptions of SCA type 1 in combination with cervical dystonia. The presented clinical cases will help neurologists in their practical activities when making a diagnosis in such cases and developing a personalized approach to their management.

Material and research methods. Written informed consent for the study was obtained from all patients. The severity of ataxia was assessed using the Scale for Ataxia Assessment and Rating (SARA).

Research materials. Patients included in the registry of the YSC CMP for SCA type 1 (n=9)

Inclusion criteria:

1. The age of patients is over 18 years;
2. A molecular diagnosis confirmed in patients with a mutation in the *ATXN1* gene;

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3. Clinical picture with symptoms of cerebellar ataxia and muscular dystonia;
4. Voluntary informed consent for inclusion in the study.

Exclusion criteria:

1. Absence of a molecular diagnosis with a mutation in the *ATXN1* gene;
2. Absence of symptoms of muscular dystonia in the clinical picture of cerebellar ataxia;
3. Age less than 18 years;
4. Refusal of the patient to participate in a scientific study.

Research methods

1. Clinical method for identifying the onset and course of ataxia, the addition of symptoms of muscular dystonia;
2. Genealogical method to identify the type of inheritance;
3. Scale for Ataxia Assessment and Rating (SARA);
4. Statistical research method. Statistical processing was carried out using the IBM SPSS Statistics 27 application package using standard methods of variation statistics: medians (Me), quartiles (Q1; Q3) were calculated.

Table 1 shows the median age of onset in the studied patients and the manifestations of their clinical syndromes of the disease. The data from the Table corresponds to the indicators of other scientific studies on SCA1 [1, 2, 3].

Table 1

Clinical characteristics of the examined group of patients with spinocerebellar ataxia type 1

Indicator	Median age M(Q1;Q3)
Age of disease onset (years)	53(44;59)
Duration of disease (years)	14(9;19)
Age of onset of cerebellar syndrome (years)	32(24;42)
Age of onset of dystonic syndrome (years)	45(32;52)
SARA scale (points)	20(16;25)
Number N of repetitions	30(27;30)
Number of pathological repetitions	48(42;50)

Table 2

Symptoms of cerebellar and dystonic syndrome

Symptoms of cerebellar syndrome	Number of patients N	Symptoms of dystonia in patients with cerebellar syndrome	Number of patients N
Ataxia of the limbs and trunk, slow saccades, scanned speech, dysarthria, dysphagia	9	Laterocollis Laterocollis with corrective gesture Laterocollis with dystonic head tremor	4 1 3

From Table 2 it follows that all patients had clinical manifestations of both cerebellar syndrome and dystonic syndrome. At the same time, dystonic syndrome manifested itself only as a focal form of muscular dystonia – cervical dystonia with laterocollis. In one patient it was accompanied by a corrective gesture, in three patients it was accompanied by dystonic head tremor.

Table 3

Manifestations of dystonic syndrome in the parent and siblings

Пациент	Number of sick sibs in the family	Manifestations of dystonia syndrome in parents and siblings	Gender	Type of inheritance	Place of birth of parent\place of residence	Number of CAG repeats	Botulinum therapy
1	0	Нет	Ж	ADT of inheritance through the mother	Namsky district\ Amginsky district	28/48	no
2	0	Нет	Ж	ADT of inheritance through the father	Abyisky district/ Abyisky district	30/52	no
3	3	Нет	М	ADT of inheritance through the mother	Abyi district. Yakutsk	27/43	Yes (with good effect)
4	4	Нет	Ж	ADT of inheritance through the mother	Ust-Aldansky district / Ust-Aldansky district	Unknown, because the result was lost by the patient	no
5	0	Нет	Ж	ADT of inheritance through the father	Lensky district/ Namsky district	25/42	Yes (with reduction of dystonic tremor)
6	1	Yes, his sister has SCA type 1	М	ADT of inheritance through the father	Tattinsky district / Tattinsky district	30/53	no
7	1	Yes, her brother has SCA type 1	Ж	ADT of inheritance through the father	Tattinsky district / Tattinsky district	30/53	no
8	2	Нет	Ж	ADT of inheritance through the mother	Tattinsky district / Tattinsky district	29/40	no
8	0	Нет	Ж	ADT of inheritance through the mother	Abyisky district / Yakutsk	28/43	Yes (no significant effect)

Table 3 shows the results of the genealogical research method, which show the manifestations of dystonic syndrome in parents and siblings of patients with SCA type 1. Patients 6 and 7 are siblings. However, the father did not experience symptoms of cervical dystonia, who died at the age of 59 years. It is worth noting that in patient No. 7, cervical dystonia was diagnosed before the symptoms of ataxia. In the remaining patients, no hereditary form of SCA type 1 with dystonia was observed in relatives. According to genealogical inheritance, the mutation in the *ATXN1* gene was transmitted through the maternal line in 5 cases. On the paternal side in 4 cases. There were more natives from the Abyisky and Tattinsky districts, which are geographically located at a distance of 1800 km from each other. Abyisky ulus is located in the tundra arctic zone, and Tattinsky in the central zone of the Republic of Sakha (Yakutia). Botulinum therapy was performed in 3 patients, with a positive effect in 2 cases. The rest were not carried out due to the severity of the condition and the patients' disagreement with the procedure.

Conclusion. Thus, the study showed that in hereditary SCA type 1, manifestations of muscular dystonia may occur in the form of its focal form - cervical dystonia. Is this a manifestation of clinical polymorphism or is it a combination of two neurodegenerative diseases, when the olivopontocerebellar neurodegenerative process is a trigger for the development of further neurodegeneration in a certain area of the extrapyramidal system? The answer to this question can be provided by further molecular genetic studies, namely whole-genome sequencing. Considering the positive effect of botulinum therapy for cervical dystonia in practical medicine, this treatment method may become promising in the management of patients with SCA type 1 and improve their quality of life.

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A CLINICAL CASE OF THE EFFECTIVE USE OF VALVE BRONCHOBLOCATION IN THE COMPLEX TREATMENT OF A PATIENT WITH CASEOUS PNEUMONIA WITH MULTIDRUG RESISTANCE OF THE PATHOGEN TUBERCULOSIS

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Valvular bronchoblocation is a minimally invasive non–drug method of treating pulmonary tuberculosis and its complications. The method is based on the creation of therapeutic hypoventilation in the affected area of the lung while maintaining the drainage function of the bronchus by installing an endobronchial valve in its lumen. The article describes a case of effective application of the valvular bronchoblocation method in an acute progressive form of tuberculosis - caseous pneumonia, in a patient with multidrug-resistant tuberculosis pathogen (MDR MBT).

Keywords: tuberculosis, method of treatment, valvular bronchoblocation, effectiveness of treatment, multidrug resistance, causative agent of tuberculosis.

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Introduction: One of the main obstacles to achieving success in eliminating tuberculosis is multidrug-resistant tuberculosis (MDR-TB) [4]. Valvular bronchoblocation (CBB) is a minimally invasive non–drug method used in the complex treatment of pulmonary tuberculosis and its complications. The method is based on the creation of therapeutic hypoventilation in the affected area of the lung while maintaining the drainage function of the bronchus by installing an endobronchial valve (EC) into its lumen. The EC is designed in such a way that with