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LETTER TO THE EDITOR

Fulminant amyotrophic lateral sclerosis manifesting in a young woman during pregnancy

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Dear Editor,

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects upper and lower motor neurons. The incidence rate of ALS is age dependent, increasing from 40 years and peaking at 65–67 years [1]. Young-onset cases are commonly attributed to familial disease, which takes 10% of all cases; however, sporadic cases of young-onset ALS have been also reported [2]. In addition, the disease displays male predominance [1].

Given such epidemiological background, ALS is an extremely rare entity in obstetric care. As clinical cases report both favorable and unfavorable courses of ALS in pregnant women, there is no definite trend regarding the effect of pregnancy on the manifestation and course of the disease [3, 4]. Here, we describe a case of fulminant ALS with a definite clinical diagnosis as per revised El Escorial criteria manifesting during pregnancy in a woman without a family history of ALS.

Clinical case

A 25-year-old woman presented with marked weakness of her hands and legs resulting in gait abnormalities and impaired self-service. She also complained of involuntary twitching and cramping in the muscles of the trunk and limbs, widespread muscle wasting, feeling of "a lump in the throat," dyspnea, and fatigue. Her history was unremarkable for any personal or family history of neurological diseases. She held a Bachelor's Degree in Mine Engineering but had never been employed in the related fields.

She first noted weakness in her hands, the left more than the right, in June 2018, in the 6th month of her pregnancy. In the 8th month of pregnancy, the patient developed dyspnea, weakness in the lower limbs, and difficulties walking. She was thoroughly evaluated by a neurologist; her neuroimaging was unremarkable, and nerve conduction study showed signs of demyelination. She was diagnosed with chronic inflammatory demyelinating polyneuropathy. At week 38 of the pregnancy, the patient delivered a healthy baby by a scheduled cesarean section and received pulse IV methylprednisolone, with no clinical improvement. She was re-diagnosed with multifocal motor neuropathy and treated with a course of IV immunoglobulin, which resulted in no improvement.

The patient was then redirected to our clinic for reevaluation and treatment. On examination, she had dyspnea with visible recruitment of thoracic musculature, which was aggravated by talking and mild physical activity. Cranial nerve examination was normal. There was gross atrophy of the shoulder girdle and upper limb muscles, most prominent in the hands, with widespread spontaneous fasciculations. The muscle strength was 3/5 in the upper limbs and 4/5 in the lower limbs bilaterally; the tone was symmetrically reduced in all limbs.

The reflexes in the upper and lower extremities were brisk with the right predominance in the lower extremities and the left predominance in the upper extremities. Pathological upper limbs reflexes and Babinski sign were present bilaterally. The patient had paretic gait with right leg favoring. There were neither sensory nor coordinative and pelvic floor disturbances, as well as no meningeal signs.

Careful scrutiny of the available brain MRI scans revealed a previously omitted finding of symmetrical areas of the

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hyperintense signal in T2 and FLAIR in the internal capsule, which might correspond to pronounced degenerative changes in the corticospinal pathways. EMG was remarkable for fibrillation potentials and positive sharp waves in examined muscles of cervical, thoracic, and lumbosacral regions. There was no evidence of demyelination or conduction blocks according to nerve conduction study. Ganglioside antibody panel, screening tests for gangliosidoses, and workup for systemic lupus erythematosus were all negative.

The patient was diagnosed with a clinically definite ALS according to the revised El Escorial criteria (UMN signs in the bulbar region and at least 2 spinal regions or the presence of LMN and UMN signs in 3 spinal regions) with an ALS-FRS score of 27. She refused pathogenetic treatment with riluzole and edaravone. Her motor symptoms progressed to near-complete quadriplegia. Two months after the presentation to our clinic (6 months after the onset of symptoms), she passed away due to respiratory failure.

Discussion

Since ALS most commonly occurs in the later-midlife and elderly population and shows male predominance, literature accounts on ALS course in pregnant women are scarce. We could identify 35 clinical cases of ALS in pregnant women reported in different sources since 1977. Hancevic et al. report yielding description of 45 such cases published in the scientific literature since 1920 [3]. To our knowledge, the case we present is the first such report from the Eastern Europe.

Available literature features different scenarios of the progression of ALS manifested during pregnancy. For example, Chiò et al. describe three cases of relatively benign course with slow progression during and after pregnancy and one case of almost fulminant ALS with 5 months between the onset and death of the patient [5]. Hancevic and coauthors discuss another variant of obstetric ALS course: in their three-case series, the patients were stable during the pregnancy and progressed rapidly after the delivery [3]. Our case seems to follow the latter scenario, with a dramatic acceleration after the delivery.

Sex-related factors, such as hormones, may play a role in the progression of the disease. Both estrogens and progesterone, the concentration of which increases in pregnancy and abruptly decreases after delivery, show a protective effect in mice ALS models [6]. The data about the effect of these two hormones in human individuals are conflicting. Earlier population studies found no effect of estrogen replacement therapy in postmenopausal women on ALS risk or progression [7, 8]. A more recent case-control study held in Ireland, Italy, and the Netherlands reports decreased odds of ALS in women on estrogen-progesterone hormone replacement therapy in the Netherlands, but not in the other two countries [9].

In summary, we present a case of ALS manifesting in a pregnant woman, which is a rare and challenging to diagnose and manage neurological condition in the obstetric population. Pregnancy has been associated with slowing the progression of the disease in some reports, while in others, similarly to the case described by us, a rapid deterioration of the neurological status was noted after delivery. Since estrogen and progesterone exert a neuroprotective effect in animal models and some human studies, a change in levels of these reproductive hormones during and after pregnancy might affect the clinical course of ALS.

Author contribution Conceptualization, Anastasiia Kobryn, Alina Ivaniuk, and Yuliia Solodovnikova; analysis and interpretation of the patient's data, Yuliia Solodovnikova, Alina Ivaniuk, and Anastasiia Kobryn; writing (original draft preparation), Anastasiia Kobryn and Alina Ivaniuk; writing (review and editing), Yuliia Solodovnikova and Anatoliy Son; supervision, Yuliia Solodovnikova and Anatoliy Son.

Declarations

Ethics approval Ethical approval was waived by the local Ethics Committee in view of the nature of the study.

Consent to participate Not applicable.

Consent for publication Relatives of the deceased patient have consented to the submission of the case report to the journal.

Conflict of interest The authors declare no competing interests.

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