Personalized Psychiatry and Neurology

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Phenocopy of Amyotrophic Lateral Sclerosis in Patients with Chiari 1 Malformation Associated Syringomyelia: Brief Literature Review

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Abstract: Arnold-Chiari malformation or Chiari malformation (CM1) is the name of a group of deformities of the posterior fossa and hindbrain (cerebellum, pons and medulla oblongata). The pathogenetic basis of this disease is associated with herniation of the cerebellar tonsils through the foramen magnum. CM1 is classified as a rare disease. CM1 can present with a wide variety of symptoms, also non-specific, with consequent controversies on diagnosis and surgical decision-making, particularly in asymptomatic or minimally symptomatic. Syringomyelia (Syr), hydrocephalus, craniocervical instability, encephalocele, scoliosis, spina bifida and spinal dysraphism are the most common comorbidities that may present at the time of diagnosis or develop secondarily. Most attention has been paid to syringomyelia complicated by CM1 (CM1-related Syr). Formation of single or multiple fluid-filled cavities in the spinal cord and/or bulb as a result of pulse changes in intracranial pressure associated with disruption of normal cerebrospinal fluid circulation due to morphological abnormalities of the brain at the magnum level. This condition can be complicated by a rarer disease caused by the development of damage to the anterior horns of the spinal cord - amyotrophic sclerosis (ALS syndrome). In this brief literature review we are trying to demonstrate the mean pathogenic basis of amyotrophic lateral sclerosis in patients with chiari 1 malformation associated syringomyelia.

Keywords: *amyotrophic lateral sclerosis; syringomyelia; Chiari 1 malformation; cerebrospinal fluid; related disorder; differential diagnosis; adult.*

Introduction

Chiari malformation type 1 (CM1) is characterized by the caudal descent of the cerebellar tonsils through the foramen magnum at least 5 mm in adults, measured by McRae Line which drawn from the basion to the opisthion [1, 2, 3]. According to Bogdanov's statistics, 33% of patients with typical symptoms of CM1 had tonsillar ectopia from 2 to 4 mm [4]. According to the definition of the Chiari Consensus Conference held in Milan in 2019, CM1 was considered herniation of one or both cerebellar tonsils ≥ 5 mm below McRae's line or even 3 to 5 mm but with syringomyelia or peg-like appearance of the tonsils [5]. Despite that CM1 is classified as a rare disease (ORPHA268882) prevalence study showed that CM1 diagnosed in up to 1%−3.6% of magnetic resonance imaging (MRI) and symptomatically affects 0,1% of general population [6].

CM1 can present with a wide variety of abnormalities such as hydrocephalus [7], spina bifida [8], spinal deformity [9], tethered cord syndrome [10], craniosynostosis [11], Ehlers-Danlos syndromes [12], Klippel-Feil syndrome [13] and syringomyelia (Syr) [3, 4,

14]. Association CM1 and Syr according to literature data varies from 20 to 74% [15, 16, 17]. In this regard, the International Classification of Diseases 11 revision (ICD-11, 2018), classifies CM1 as follows: Arnold-Chiari syndrome without spina bifida or hydrocephalus (Q07.00); Arnold-Chiari syndrome with spina bifida (Q07.01); Arnold-Chiari syndrome with hydrocephalus (Q07.02); and Arnold-Chiari syndrome with spina bifida and hydrocephalus (07.03) [18]. According to the diagnostic recommendations of the Interregional Chiari and Syringomyelia Consortium, CM1 is classified into CMI-A (in the presence of Syr in MRI) and CMI-B (in the absence of Syr in MRI) [16].

Syr is considered as a chronic progressive disorder which characterized by the development of fluid-filled longitudinal cavitation (syrinxes) inside the spinal cord. The spinal cord cavities filled with cerebrospinal fluid (CSF) or a fluid similar in composition to it [19]. Syr classified as a neurological rare disease (ORPHA3280), with a prevalence of 1.9-8.4 per 100,000 population [20,21]. Widespread MRI use in medicine increase prevalence of Syr several times [22, 23, 24]. For example, diagnosed cases of Syr increased by 9.78 times between 1971 and 2003 years in New Zealand [20]. This increase of Syr prevalence is largely due to the accidental detection of Syr signs in the study of patients with spinal pain using MRI [25]. In most cases, Syr is diagnosed 2 times more often in adults, especially in the 3rd decade, than in children. In this regard, symptomatic Syr is higher than 40% in adults and does not exceed 23% in children [26]. This fact is explained precipitating factors that contributes to an increase in CSF pulse pressure at the craniovertebral junction as microtrauma and physical activity which accumulate changes in spinal cord with age [27]. Female are affected more often than males by 17-27% [28]. Sensory dis-orders are diagnosed in 48% of cases, and motor disorders in 32% patients with CM1-related Syr [16]. At the same time, the frequency of asymptomatic CM1-related Syr varies from 7% to 40% [15, 16].

There are several classifications of Syr, but the most famous of them is the classification of Milhorat, published in 2000 (Figure 1) [29]. Communicating Syr accounts for about 10% of cases from all forms of Syr. It is characterized by the presence of a pathological communication between the syrinx in the spinal cord and the fourth ventricle of the brain, which is caused by diseases leading to the obstruction of Magendie's and Luschka's foramen. This pathology may be congenital (as a result of plumbing stenosis and Magendie's and Luschka's foramen atresia) or acquired (as a result of obstruction of plumbing by neoplasms or colloidal cysts) [30]. However, uncommunicating Syr is more common with the formation of central and paracentral syringes, as a result of CM1, basilar invagination, spinal arachnoiditis, extramedullary compression by a tumor or herniated intervertebral disc (Figure 2), fixation of the spinal cord due to a rigid terminal thread and acquired dislocation of the tonsils of the cerebellum [31].

In CM1, ectopia of the cerebellar tonsils into the large occipital foramen causes partial occlusion of the cerebrospinal tract in the subarachnoid space and serves as a piston that creates increased pulse pressure, which excessively compresses the spinal cord from the outside, not from the inside. At the same time, the expansion of the CSF spaces of the brain during cardiac systole creates a pressure wave of CSF with each heartbeat that propagates caudally [32]. Increased CSF pressure in the spinal canal prevents the process of normal attenuation of the pulsating pressure of CSF. As a result of excessive CSF pulsation around the spinal cord, CSF is directed to the Virchow-Robin spaces, which are forced into the spinal cord parenchyma to form microcysts. These microcysts gradually merge with each other into syrinxes. Subsequently, the pulsating waves raise the CSF pressure within the syrinx, which causes the CSF to move caudally within the syrinx, and eventually to a gradual increase in cavity size (Figure 3).

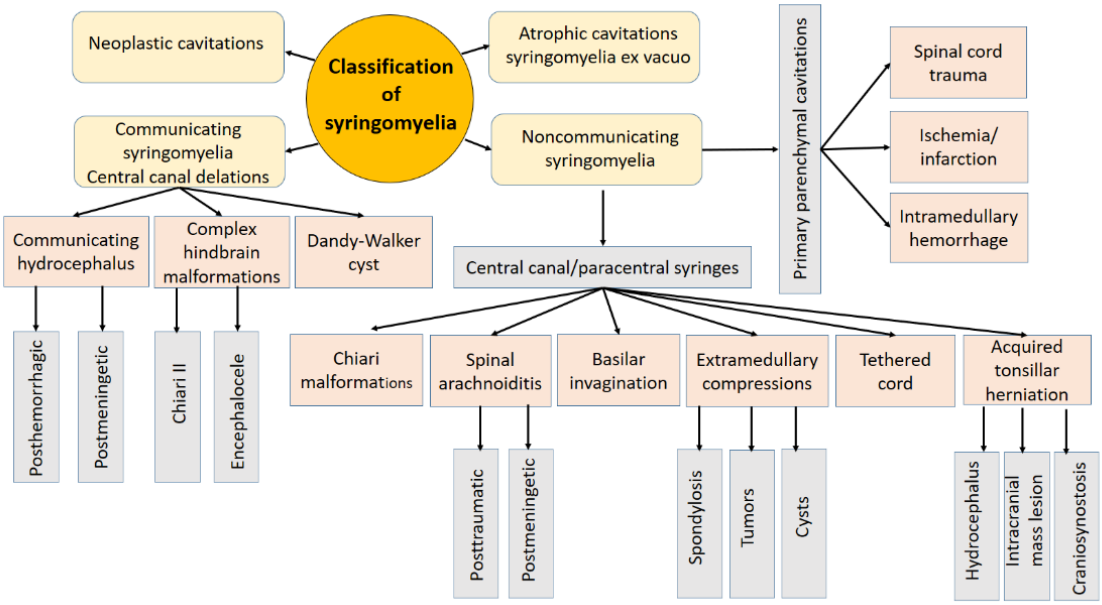


Figure 1. Milhorat Classification of Syringomyelia (modification by authors from [29]).

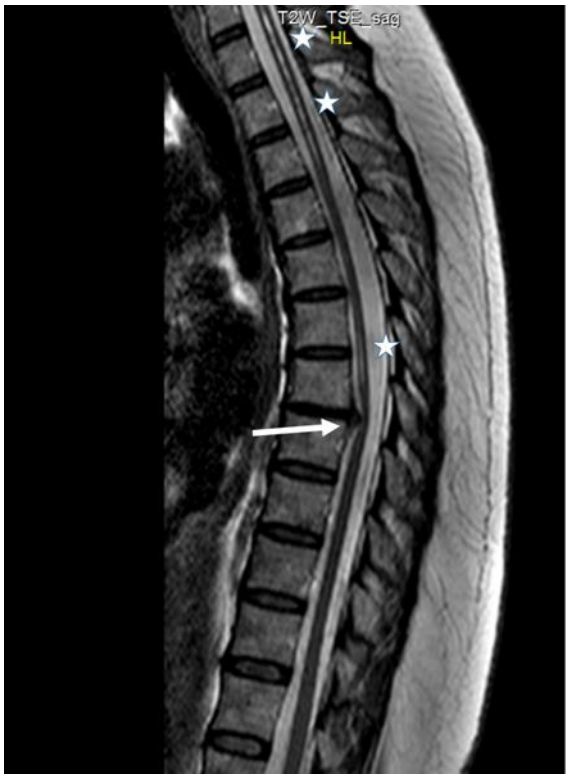
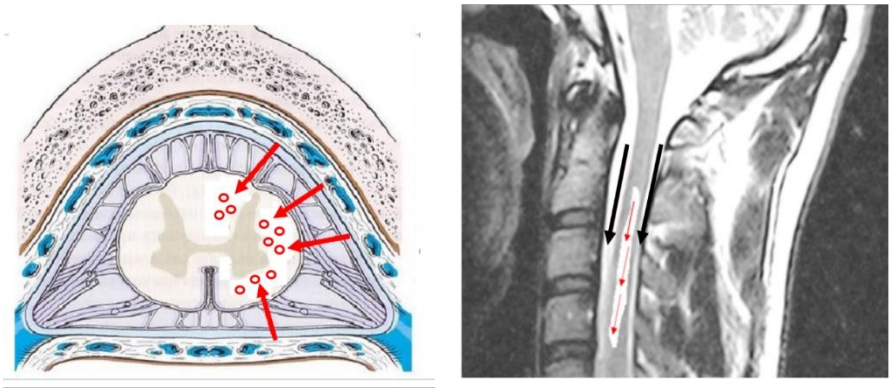


Figure 2. Sagittal T2-weighted MRI of spinal cord of 54-years old woman with hernia related Syr. Note: white arrow - extramedullary compression of the spinal cord by a herniated intervertebral disc between Th7 and Th8 thoracic vertebrae; white asterisk – hernia-related Syr.



(a) (b)

Figure 3. Chiari malformation type 1 related microsyrenx (a) and macrosyrenx (b) formation. Note: thick red arrows demonstrate microsyrinx formation; thin red arrows demonstrate the formation of macrosyrinxes; thick black arrows demonstrate extramedullary movement of cerebrospinal fluid.

CM1-related ALS syndrome is of the greatest clinical interest among all Syr-related disorders in patients with CM1 [33, 34, 6, 13], because it requires a differential diagnosis with idiopathic ALS (also known as Lou Gehrig's disease) [35]. ALS is characterized by damage to the motor neurons of the anterior horns of the spinal cord with the formation of progressive muscle atrophies and fasciculations, which can outpace the development of motor deficit [36]. Syr-related ALS syndrome is caused by mechanical compression of the anterior horns of the spinal cord by the syrinx, in contrast to idiopathic ALS [37]. In this regard, the treatment tactics and prognosis of the disease in Syr-related ALS syndrome differ significantly from idiopathic ALS. At the same time, early diagnosis of this disorder can help stop its progression and thus improve the prognosis. For unknown reasons, some patients with CM1-related Syr develop anterior horn lesions without degenerative changes in other neural structures adjacent to the syrinx. As a result, damage to the lower motor neuron (LMN) develops without damage to the upper motor neuron (UMN). This form of the Syr-associated ALS syndrome may be associated with a reduced resistance of spinal motoneurons to hypoxia and compression compared to the fibers of the pyramidal tracts in the lateral and anterior cortical-spinal tracts (Figure 4) [38].

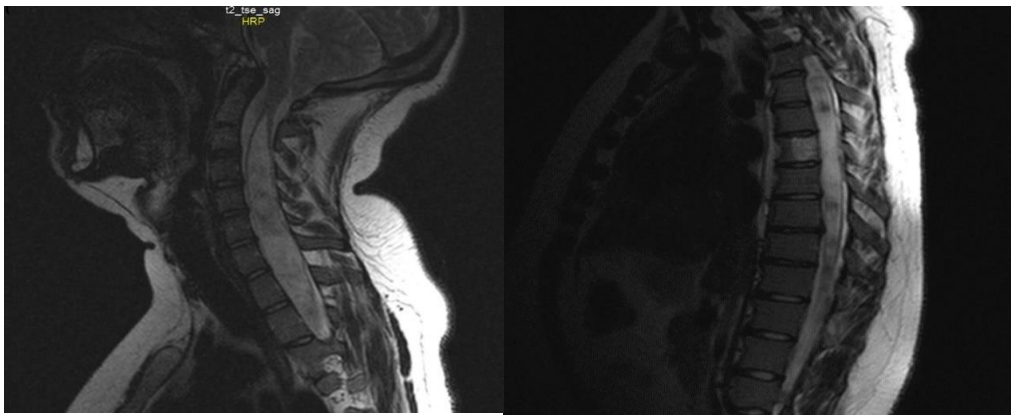


Figure 4. Sagittal T2-weighted MRI of spinal cord of 24-Year-Old Man with Chiari 1 Malformation and Syringomyelia: huge single syringomyelic cyst with a length from segment C2 to Th12. Upper flaccid paraparesis of muscle and atrophy in hands was developed with the absence of motor disorders in the lower extremities A peculiarity of this case is the absence of clinical manifestations characteristic of syringomyelia in the form of loss of pain and temperature sensitivity with preserved tactile and vibration sensitivity (segmentally dissociated loss of sensitivity).

Conflicts of Interest: The authors declare no conflict of interest.

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