Medico Research Chronicles

ISSN No. 2394-3971

Case Report

# ARNOLD-CHIARI MALFORMATION TYPE 1 WITH SYRINGOMYELIA, KYPHOSCOLIOSIS, AND CAFÉ-AU-LAIT SPOTS

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Submitted on: December 2016
Accepted on: January 2017
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**Abstract**

We present a case report of a 39-year old woman with Arnold-Chiari malformation type 1 with syringomyelia, kyphoscoliosis, and café-au-lait spots. The first complaints started 2 years ago and included paresthesias/numbness and diminished temperature sensation of the right arm, followed by muscle weakness. There has also been a remitting-relapsing pain in the right arm recently. The neurologic examination revealed a syndrome of cervical intumescence impairment with $C_8$ dermatome hypesthesia, temperature anesthesia for the right arm, a lower motor neuron paresis in the distal part of the upper extremities (predominantly for the right arm), spastic muscle tone of the lower extremities, mild right leg weakness, positive Babinski sign bilaterally. Several café-au-lait spots in the trunk were found. MRI visualized kyphoscoliotic deformation of the cervicothoracic spine, a homogenous intraspinal lesion from $C_2$ to $Th_9$ level, hypointense on $T_1$ and hyperintense on $T_2$ (syrinx), and a prolapsed left cerebellar tonsil through the foramen magnum. The patient was unsuccessfully treated with medications. The case is of interest with the extremely rare combination of the abovementioned clinical and neuroimaging manifestations, the late onset of sensory complaints, lack of family history, headache, and other congenital abnormalities, as well as the late diagnosis confirmation. We consider this combination to be more than coincidental and a rare variant of Chiari type 1 malformation. The relevant literature has been reviewed.

**Keywords: Arnold-Chiari, syringomyelia, kyphoscoliosis, café-au-lait**

## Introduction

The debut of predominantly congenital central nervous system abnormalities is in childhood. Our case is of special interest with the late onset of clinical manifestations and the presence of several abnormalities of different germ layers: mesodermal (kyphoscoliosis, spina bifida and Arnold-Chiari malformation type 1) and neuroectodermal abnormalities (syringomyelia, café-au-lait spots).

## Case report

### 1. Disease history

We present a 40-year old woman, who was admitted to the Clinic of Neurology at the

University hospital "St. George" in Plovdiv with the following disease history:

- Symptoms with onset 2 years ago:

- paresthesias and diminished temperature sensation in the right arm,
- the weakness of the right hand,
- the difficulty with right leg walking.

- Symptoms with onset at birth:

- kyphoscoliosis,
- café-au-lait spots.

No dynamics in symptoms was registered. There is no disease history about traumatic injuries, tumors, pre-, peri- and postnatal diseases, as well as heredity of the described abnormalities. The patient was treated for these complaints and their cause was accepted as vertebral/dipsogenic radiculopathy/myelopathy. MRI of the cervicothoracic region of the spine was performed before the hospitalization. It visualized degenerative pathology, a disc protrusion on the $C_{5-6}$ level and a large intramedullary cystic formation from $C_2$ to $Th_2$ level, hyperintense and non-homogenous on $T_2$ and hypointense on $T_1$ sequences. A syrinx distal to the formation up to $Th_{10}$ level was also described. The pathological finding was interpreted as ganglioglioma.

**Clinical manifestations**

1. Left convex scoliosis of the thoracic spine.
2. Five abdominal café-au-lait spots, the largest of which with a size of up to 4 cm in diameter; small multiple café-au-lait spots all over the body (< 0.5 cm) - freckles (Fig.1).
3. Neurological status examination – a syndrome of cervical intumescence impairment was found, that consisted of:

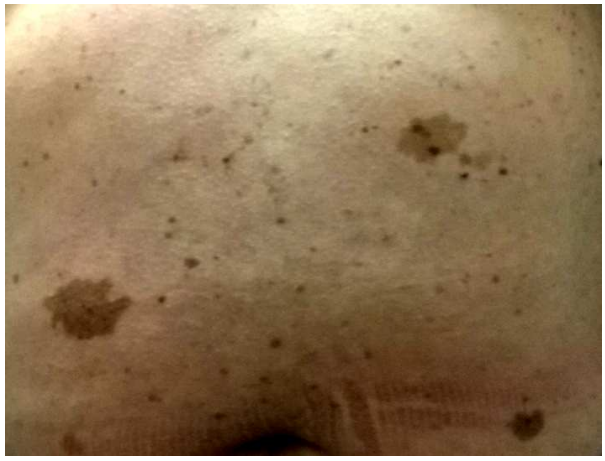
- Spinal cord segmental impairment:

1. Motor symptoms: lower motor neuron paresis of the distal parts of upper extremities, more expressed for the right arm; deep tendon hyporeflexia of upper extremities with anis areflexia and increased reflex responses for the left arm (with the exception of symmetrical triceps reflex response); initial hypotrophy of the right thenar, hypothenar, and interossei muscles;
2. Sensory symptoms: bilateral $C_8$-dermatome hypesthesia, left $Th_8$-$L_{3-4}$ dermatomes hypesthesia, temperature anesthesia for the right arm.

- Impairment of spinal cord tracts:

1. Motor symptoms: latent inferior right mono paresis, mild muscle spasticity, spastic-paretic gait, pathological deep tendon hyperreflexia of lower extremities with anis areflexia and increased reflex response for the right leg, bilaterally positive Babinski sign.
2. Sensory symptoms – organic right hemihypesthesia.

**Fig. 1.** Café-au-lait spots and freckles of the anterior abdominal wall



**Investigations**

1. Laboratory investigations – full blood count, biochemistry, and urine – in referent limits.

2. Neuroimaging: MRI of the brain, craniospinal region and the spinal column visualizing the following pathological findings:

- Arnold-Chiari malformation type 1: prolapsed cerebellar tonsils below foramen magnum with a vertebra $C_2$-level stenosis of the posterior and lateral epidural space by the left tonsil and the caudal contour of the vertebra by both tonsils (Fig. 2).
- Syringomyelia from $C_2$ to $Th_9$ vertebra: a homogenous intramedullary lesion (syrinx) – hypointense on $T_1$ and hyperintense on $T_2$, which dilates the spinal cord cross-section, mostly on the level of the $C_7$-$Th_{1-2}$ vertebra (maximal sagittal plane size at this level of 1.05 cm) (Fig. 2 and Fig. 3). The suggestion about ganglioglioma was rejected by this MRI.
- Spina bifida oculta of $C_2$ vertebra: non-accretion of the right arch of a $C_2$ vertebra in the dorsal part (Fig. 4).
- S-type left convex scoliosis of the thoracic spine with signs of intraarticular spondylolisthesis and severe later Oli thesis, cervical lordosis, degenerative osteochondrosis and spondylosis (Fig. 5).

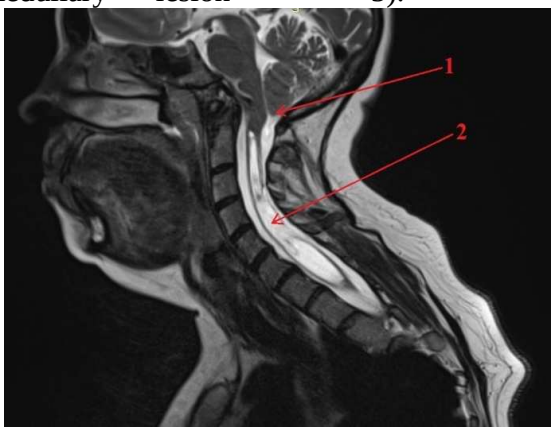



**Fig. 2.** MRT sagittal $T_2$ sequence image
1 - left cerebellar tonsil protrusion below foramen magnum 2 - syrinx in the cervicothoracic spine

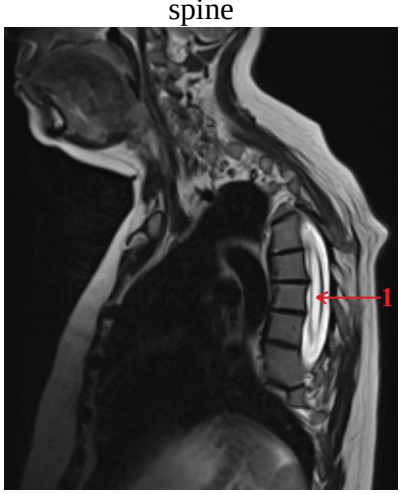



**Fig. 3.** MRT sagittal $T_2$ sequence image
1 – syrinx spreading to the middle and the lower thoracic spine

**Fig. 4.** MRT coronal $T_2$ sequence image
1 - non-accretion of the right arch of $C_2$ vertebra in the dorsal part (spina bifida oculta)

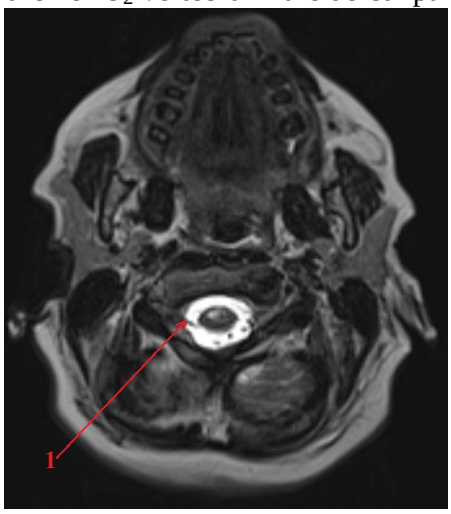
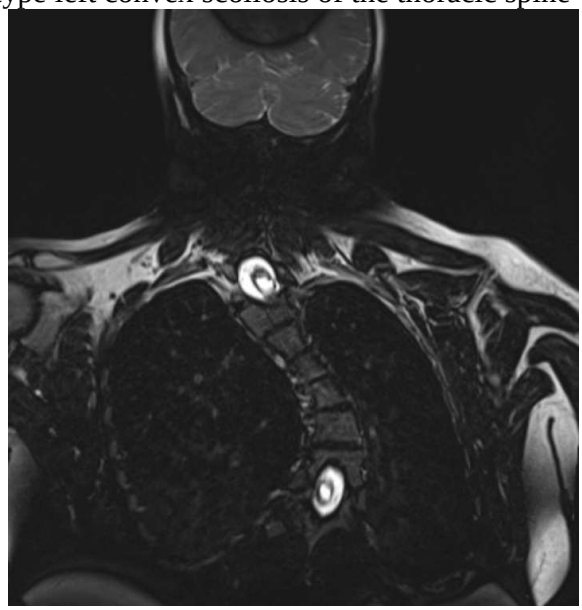



**Fig. 5.** MRT axial T2 sequence image
1 - S-type left convex scoliosis of the thoracic spine



**Therapy**

The patient was treated with vasodilator drugs, vitamins from group B, non-steroid anti-inflammatory drugs and anticonvulsants for the neuropathic pain without clinically significant improvement. Surgical treatment has not been discussed.

**Discussion**

There has been no case report in literature presenting with a combination of Arnold-Chiari malformation type I, syringomyelia, spina bifida of the $C_2$ vertebra and café-au-lait spots. In our case report, we accept Arnold-Chiari malformation type I as being congenital. This Arnold-Chiari malformation is usually complicated with syringomyelia [1], because of disturbances in cerebrospinal fluid dynamics and circulation, but not with spina bifida which is more typical as spina bifida aperta in association with Arnold-Chiari malformation type II. Therefore our patient

presents with a concomitant abnormality that is typical for another type of Arnold-Chiari malformation, although manifested with untypical severity [2, 3].

Regarding the other main symptom – scoliosis, according to the study results of Strahle et al. (2015) it is not an obligatory sign of cerebellar tonsils prolapse in patients without a syrinx [4]. On the other hand, the prevalence of scoliosis in patients with RAS/MAPK (mitogen-activated protein kinase)-associated diseases is high [5]. Despite the typical phenotype and many similar clinical signs in these cases, differential diagnosis may be difficult, especially in neurofibromatosis type 1, Noonan syndrome, Leopard syndrome, when there are some features in common with the presented case (Table 1), but the typical for RASopathies craniofacial abnormalities, congenital cardiac valvular disease, low height, cognitive deficit and predisposition to cancer, are lacking [6].

**Table 1.** Overlapping typical symptoms of RASopathies and our case

| **RASopathies** | **Neurofibromatosis type 1** | **Noonan syndrome** | **Legius syndrome** | **LEOPARD syndrome** |
|---|---|---|---|---|
| **Clinical manifestations** | multiple café-au-lait spots | - | multiple café-au-lait spots | café-au-lait spots |
| | freckles | - | freckles in the axillary and/or genital area | freckles in the axillary area |
| | (kypho) scoliosis | scoliosis | - | - |
| | - | Arnold-Chiari malformation type 1 | - | - |

Our patient has not 2 of the 7 clinical criteria which are obligatory for the diagnosis neurofibromatosis type 1 – 6 or more café-au-lait spots and freckles in the axillary and genital area. The number of café-au-lait spots is not sufficient. Apart from that, the other 5 criteria (neurofibromas, heredity, Lisch nodules, optic glioma and typical bone lesions) are also lacking [6]. There are also some very rare associations between the typical and untypical clinical findings which overlap the presented case to some extent. Three cases with LEOPARD syndrome and Arnold-Chiari malformation type 1 and two cases with cervical syringomyelia have been reported in the literature [7, 8]. Single patients and a series of cases with Arnold-Chiari malformation type 1 and neurofibromatosis type 1 have been documented, the most probable explanation being the similar early dysgenesis of the mesoderm [9]. The frequent manifestation of spina bifida and scoliosis in patients with neurofibromatosis suggest that this association may not be accidental.

The presence of heterogeneity in the overlapping of various RAS-opathies and also in the group of Arnold-Chiari malformation has been accepted. A single 8-year-old case with a combination of Arnold-Chiari malformation type 0, spina bifida and multiple café-au-lait spots has been reported in the literature [10].

The clinical course, diagnostic problems and ineffective treatment in our case report, prove the necessity of a neuroimaging investigation of the brain, craniospinal area and spinal cord in patients with syringomyelia with the purpose of confirmation/rejection of other

abnormalities. Differential diagnosis with ganglioglioma is also important, moreover, our case demonstrated many typical for ganglioglioma imaging findings including long segment solid enhancing tumor, T2 hyperintensity, scoliosis, and syrinx formation [2].

Other features of interest, in this case, are also the mild complaints with a very late onset. The typical symptoms of Arnold-Chiari malformation type 1 in children older than 3 years of age are a headache, scoliosis [11], muscle weakness, gait disturbance, sensory impairment [12], in 16% there are no neurological complaints, in 56% there is no neurological deficit [13]. Eighty-one percent of adult patients complain from a sub-occipital headache that worsens during physical efforts and position changes [14]. The reported case presents with a combination of symptoms typical for different ages, and the most typical symptom – a headache, is absent.

**Conclusion**

Because of the multiple abnormalities, in this case, the differential diagnosis includes 1. A variant of neurofibromatosis type 1 or another RASopathy; 2. A rare variant of Arnold-Chiari malformation type 1; 3. A variant of a new syndrome that has not been reported by now. Therefore a detailed neuroimaging investigation of the central nervous system and the associated skeletal structures is needed for the purpose of confirmation/rejection of concomitant abnormalities as a part of other syndromes. The genetic investigation is also recommended, although, in RAS-opathies, genotype does not necessarily correlate with phenotype in all cases. That is why the constant correction and filling out of clinical and neuroimaging diagnostic criteria are useful for the precise diagnosis and diagnostic problems solving in clinical practice.

We confirm that: 1) no part of this manuscript is currently under consideration for publication elsewhere; 2) this manuscript does not contain the same information in whole or in part as manuscripts that have been published, accepted, or are under review elsewhere, except in the form of an abstract, a letter to the editor, or part of a published lecture or academic thesis; 3) authorization for publication has been obtained from the authors' employer or institution; and 4) all contributing authors have agreed to submit this manuscript.

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