A case report of a patient with McCune-Albright Syndrome, type I Chiari Malformation and spontaneously resolved syringomyelia

Zespół McCune-Albright’a, zespół Arnolda-Chiariego typu I i samoistnie wycofująca się jamistość rdzenia – opis przypadku

Keywords: McCune-Albright syndrome, cranial fibrous dysplasia, type I Chiari Malformation, spontaneous resolution of syringomyelia

Hasła Kluczowe: zespół McCune-Albright’a, dysplazja włóknista kości czaszki, zespół Arnolda-Chiariego typu I, samoistne wycofanie się jamistości rdzenia.

CASE REPORT

The patient, woman aged 49, first sought physician’s help in 2006 because of increasing pain in her left palm. A X-ray was performed followed by 99mTc-MDP scintigraphy. The latter revealed multiple lesions in: IV and V metacarpal bones of the left palm, occipital bone, Th4 and Th5 vertebrae, 5th rib, left humerus and ulna. The picture was characteristic for a primary multifocal bone disease, rather than metastatic lesions, but required histopathological confirmation.

In November 2006 the lesion from the left metacarpal bones was excised and histopathological examination confirmed the diagnosis of fibrous dysplasia.

Although the patient had a history of premature puberty and has a big café-au-lait macule on her back, the diagnosis of McCune-Albright syndrome was never articulated. Although no written documentation has been preserved from that period, the patient claims to had had her menarche at the age of 2 and had been menstruating ever since, although irregularly. In her childhood, she had been under endocrinologist’s care for her premature puberty and growth retardation.
Despite her irregular menstruation, the patient had no difficulties becoming pregnant and is mother to three healthy children. Her height is 158cm and she shows no signs of scoliosis.

In 2009 the patient first consulted neurosurgeon for her increasing headaches and vertigo. A head MRI was performed revealing fibrous dysplasia lesions in the occipital bone and clivus. The cerebellar tonsils were dislocated 12mm below the plane of the foramen magnum, typically for Chiari Malformation type 1.

A follow-up MRI was performed in July 2012: at the level of C2 through C4 of the cervical spine, a syrinx within the medulla measuring 28x10x8 mm was visible.

At the MRI performed in November 2013 there is no syrinx.

Throughout the history of her complaints, the patient showed the following clinical symptoms: intermittent numbness in her left upper limb, headaches exacerbated by straining, vertigo and rarely tinnitus. Stress fractures, cognitive or memory deficits, epilepsy, diplopia or blurred vision never occurred. At the occipital region of the skull the patient has a painless bony bulge.

As of yet, the patient is under neurosurgical control; due to the mild intensity of the symptoms the suboccipital decompression surgery has not been necessary. The fibrous dysplasia lesions were treated with vitamin D3 and calcium, with no effect. Currently she takes diclofenac, tramadol and pracetamol as pain medication.

Figure 1. 99mTc-MDP bone scintigraphy demonstrating tracer enhancement in IV and V metacarpal bones of the left palm, occipital bone, Th4 and Th5 vertebrae, 5th rib, left humerus and ulna.
There are several reports of cases in which syringomyelia symptoms resolve spontaneously or stop progressing. Chiari malformation Type I is a developmental abnormality of the craniovertebral junction, often associated with spinal cord abnormalities such as syringomyelia and scoliosis.
Ground-glass appearance of fibrous dysplasia lesions in the occipital bone and clivus. Syrinx inside the spinal cord visible at the level of Th2-Th4. Date of examination: July 2012.

The syrinx has disappeared.
**DISCUSSION**

Syringomyelia is a dilatation caused by excessive cerebrospinal fluid accumulation inside the central canal. The theory of craniospinal CSF pressure dissociation has been suggested to explain syringomyelia[21]. The common causes of this phenomenon are: type 1 and 2 Chiari malformation, Dandy-Walker syndrome, cerebellar ectopia, basilar impression, basilar arachnoiditis, posterior fossa tumors and arachnoid cysts, medulla spinalis tumors, spinal trauma and infections [10]. Syringomyelia may cause sensory and motor deficit, urinary and fecal incontinence, painless arthropathy, pain in the neck, back and occipital region. Milhorat et al. have classified syringomyelia into 3 groups according to autopsy findings, clinical and neuropathological features in their study where they evaluated 105 postmortem cases with syringomyelia not due to tumor. They found central canal dilation associated with the 4th ventricle (communicating) in 47, central canal dilation (isolated non-communicating) not associated with the 4th ventricle in 23, and a syrinx that was extracanalicular within the parenchyma in 35 of the 105 patients [18].

Syringomyelia associated with Chiari Malformation type 1 presents clinically as a slowly progressive central cervical myelopathy distinct from other myelopathies and polyneuropathies.

Before the syrinx is visible on MR images, longitudinal, intramedullary edema and swelling associated with clinical manifestations of syringomyelia denote the “presyrinx” state in CM1 patients [8,15]. In general, neurologic deficits progress rapidly in the initial period of the spinal cord “presyrinx” edema and syrinx formation. Neurologic function stabilizes later in about one-third to one-half of patients with syringomyelia for 10 or more years [1,4,12].

In the literature there are descriptions of several cases in which spontaneous radiological resolution of syringomyelia in children and adults, with or without clinical restoration [13]. In some of these cases the collapse of the syrinx was associated with spontaneous upward displacement of the cerebellar tonsils [2]. In a nation-wide epidemiological survey in Japan among 1243 patients with syringomyelia, one-half of them with CM1, 39 patients (2.3%) had spontaneous resolution of symptoms and 202 patients (16.2%) had a stable course of disease [19].

Spontaneous resolution of the syrinx has also been seen in the pediatric age group. Clinical and MRI examinations were performed serially over many years in 27 children and adolescents with scoliosis and syringomyelia; the syrinx resolved spontaneously and completely in 9 and was reduced in size in another 5 of them [22]. The authors attributed this phenomenon to growth of the posterior fossa bones and normalization of CSF dynamics at the foramen magnum. Spontaneous syrinx collapse can also result from spontaneous rupture of an arachnoid membrane at the foramen magnum, which opens the CSF pathways, or from spontaneous syringe-subarachnoid drainage [3].
Type 1 Chiari malformation is in general a congenital condition characterized by an anatomic defect of the base of the skull, in which the cerebellum and brain stem herniate through the foramen magnum into the cervical spinal canal. The onset of Chiari syndrome symptoms usually occurs in the second or third decade. The diagnosis is established with neuroimaging techniques.

Chiari malformation Type I is often associated with spinal cord abnormalities such as syringomyelia and scoliosis. The rate of scoliosis in pediatric patients with CM-I has been reported to be as high as 80% [7]. Some authors have speculated that the etiology of scoliosis in such patients is the related to the expanding spinal cord syrinx on the function of medially located motor neurons; the resulting imbalance in the paraspinal musculature is thought to predispose the individual to spinal deformity [11].

Fibrous dysplasia of the cranium is a well-described entity of unknown etiology in which normal bone is replaced by abnormal fibro-connective tissue proliferation[16,17]. Cases of hindbrain herniation and syringobulbia due to fibrous dysplasia of skull base have been previously reported [5]. Studies report that the most commonly FD affected bones of the skull is the frontal bone followed by the sphenoid, ethmoid, parietal, temporal and occipital bones [20, 23].

The onset of craniofacial involvement is usually insidious, characterized by a barely noticeable, gradually increasing, painless swelling in the neurocranium. Radiation therapy is ineffective and contraindicated because of possibility of malignant transformation[9,20].

Fibrous dysplasia/McCune-Albright syndrome (FD/MAS), the result of an early embryonic postzygotic somatic activating mutation of GNAS (encoding the cAMP pathway-associated G-protein, Gsα), is characterized by involvement of the skin, skeleton, and certain endocrine organs. However, because Gsα signaling is ubiquitous additional tissues may be affected [24].

The diagnosis of fibrous dysplasia/McCune-Albright syndrome (FD/MAS) can be established in individuals who have two or more typical clinical features of MAS. In individuals whose only clinical finding is monostotic fibrous dysplasia, identification of a GNAS somatic activating mutation is required to establish the diagnosis.

FD/MAS is rare, prevalence estimates range between 1:100,000 and 1:1,000,000 [6].

The diagnosis is established in individuals with two or more of the following features:

- Café-au-lait skin macules with characteristic features, including:
  - Irregular borders, often referred to as resembling the ‘coast of Maine’
  - Distribution showing an association with (“respecting”) the midline of the body and following the developmental lines of Blaschko, which reflect patterns of embryonic cell migration.

- Polyostotic fibrous dysplasia (i.e., involvement of >1 bone) or GNAS mutation-proven monostotic fibrous dysplasia (i.e., involvement of a single bone).
- Any of the following primary endocrinopathies:
  - Gonadotropin-independent precocious puberty resulting from recurrent ovarian cysts in girls and autonomous testosterone production in boys
  - Testicular lesions including Leydig and/or Sertoli cell hyperplasia with characteristic ultrasonographic features, with or without associated gonadotropin-independent precocious puberty
  - Thyroid lesions with characteristic ultrasonographic features, with or without non-autoimmune hyperthyroidism
  - Growth hormone excess
  - FGF23-mediated phosphate wasting with or without hypophosphatemia in association with fibrous dysplasia
  - Neonatal hypercortisolism

The phenotypic spectrum of FD/MAS ranges from asymptomatic incidental findings to neonatal lethality. There is a high degree of variability between individuals, both in the number of affected tissues and the degree to which they are affected. Disease manifestations depend on the time during embryogenesis that the somatic mutation occurred, the tissue involved, and the role of Gs\textsubscript{a} in the affected tissue. Mutations occurring early in development lead to widespread disease, while those occurring later in development lead to limited disease.

The effects of autonomous sex steroid production on pituitary-gonadal function and fertility in adults are not well-characterized. Women with FD/MAS may have recurrent cysts leading to irregular menses in adulthood. While many women achieve successful pregnancies, it is possible that interruption of ovulatory cycles could decrease fertility and increase the time to conception [14].

Differential diagnosis of FD/MAS includes: neurofibromatosis type 1, cutaneous-skeletal hypophosphatemia syndrome, giant cell tumors of bone, ossifying fibromas, osteofibrous dysplasia.

REFERENCES
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ABSTRACT

Arnold Chiari Malformation is a rare congenital condition affecting the cerebellar tonsils, which are displaced through the foramen magnum causing various neurological symptoms. Syringomyelia is an acquired dilatation of central canal of the spine resulting from a disturbance of cerebro-spinal fluid circulation. McCune-Albright Syndrome is a complex genetic disorder affecting bone, skin and hormones. We present a case study of a female patient affected with type I Arnold Chiari malformation, syringomyelia and mild form of McCune-Albright Syndrome, with fibrous dysplasia in the peripheral bones as well as skull base.

STRESZCZENIE


Artykuł zawiera 21460 znaków ze spacjami + grafika (17164 znaków + 322,27 cm²)