Posterior fossa arachnoid cyst, tonsillar herniation, and syringomyelia in trichorhinophalangeal syndrome Type I

Case report

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The authors report the case of a patient with Chiari malformation Type I (CM-I) and syringomyelia probably caused by a retrocerebellar arachnoid cyst. The patient’s phenotype corresponded to trichorhinophalangeal syndrome Type I. The authors attributed the origin of both the retrocerebellar cyst and the abnormal posterior fossa to endochondral ossification anomalies that occur in this syndrome. The patient’s spinal pain was most likely a result of the combination of CM-I and syringomyelia. To the best of the authors’ knowledge, this is the first report on the association of CM-I and syringomyelia with a retrocerebellar arachnoid cyst occurring in a patient with trichorhinophalangeal syndrome Type I. The authors discuss the pathogenetic mechanisms involved in the production of tonsillar descent and syringomyelia in this patient, and review the current literature on related conditions that can result in this association. (DOI: 10.3171/JNS/2008/109/10/0746)

Key Words • arachnoid cyst • Chiari malformation Type I • posterior fossa anomaly • syringomyelia • trichorhinophalangeal syndrome Type I

Chiari malformation Type I is classically defined as a downward displacement of the cerebellar tonsils through the foramen magnum.12,17 Its structure involves a small posterior fossa with subsequent herniation of the cerebellar tonsils.9 Authors of recent studies have demonstrated that displacement of the cerebellar tonsils can originate from a variety of conditions, including anomalies of the skull base, diverse bone diseases, craniocerebral disproportion, and supra- or infratentorial tumors.6,13–16,17 Several authors have documented the association of posterior fossa arachnoid cysts with syringomyelia. In these cases, the arachnoid pouch itself constituted the obstacle to CSF circulation.1 A different mechanism consists of the development of tonsillar descent and accompanying syringomyelia due to the pressure produced by the posterior fossa cyst.1,10 This last scenario constitutes a much rarer occurrence, with only 3 previous cases documented in the current literature.

Trichorhinophalangeal syndrome Type I is a rare autosomal dominant disorder characterized by sparse thin hair, a pear-shaped nose, and bone deformities, particularly cone-shaped epiphyses of the phalanges.3,4,7 The putative TRPS1 gene has been mapped to band 8q24.7,8 Cone-shaped epiphyses result from an endochondral anomaly of ossification in which the epiphyses are invaginated into the metaphyses of the small tubular bones of the hands and feet.7 The skull base develops by a similar process of endochondral ossification. In TRPS-I, the defective ossification of the skull base probably leads to the development of an abnormal posterior fossa, tonsillar descent, and arachnoid cyst formation.3,7,8

We describe a patient with TRPS-I and an abnormal posterior fossa in whom CM-I and syringomyelia developed, likely due to the pressure exerted by an associated retrocerebellar arachnoid cyst. To our knowledge, this is the first report on the triad of arachnoid cyst, CM-I, and syringomyelia occurring in a patient with TRPS-I. We discuss the pathogenetic mechanisms involved in this patient’s condition and briefly review similar cases reported in the current literature.
Chiari malformation Type I in trichorhinophalangeal syndrome

Case Report

History and Presentation. This 36-year-old man presented with headaches, back pain, dizziness, and a 2-year history of evolving gait instability. He also reported clumsiness in both hands and 2 episodes of sudden falls. He had been seen at the age of 12 years for a Legg-Calvé-Perthes disease–like condition in his right hip. His 3 siblings and nonconsanguineous parents were normal.

 Examination. The results of a neurological examination revealed mild weakness in both upper limbs, predominantly distally. The deep tendon reflexes were decreased in both arms and hyperactive in the legs, but the upper-right cutaneous abdominal reflex could not be elicited. His position sensation was decreased in both legs, but there was no impairment of temperature or pain perception. The patient’s height was in the normal range (170 cm). His face was elongated and micrognathic, he had a horizontal groove on his chin, a bulbous “pear-shaped” nose together with a prominent long philtrum, his hair was fine and sparse, and his eyebrows were thin laterally (Fig. 1). His hands were broad and short (Fig. 2 upper). The patient had left-sided thoracic scoliosis. Plain skull radiographs showed hyperostosis frontalis interna, enlarged paranasal sinuses, and a marked external occipital protuberance. Radiographs of the patient’s hands demonstrated short metacarpals of the third, fourth, and fifth fingers and cone-shaped epiphyses at the phalanges (Fig. 2 lower). There was an exostosis on the right femoral head. Magnetic resonance imaging of the head demonstrated a 6-mm descent of the cerebellar tonsils, a retrocerebellar arachnoid cyst, and a small posterior fossa (Fig. 3 left) but ruled out the presence of hydrocephalus. Spinal MR imaging demonstrated a syringomyelic cavity extending from C-2 to T-2 (Fig. 3 right) together with an L5–S1 Tarlov cyst. The patient’s karyotype was 46,XY. The results of a molecular genetic study showed a TRPS1 gene missense mutation in exon 7 (R952H), already reported in the literature.

Operation. The patient underwent a 3-cm suboccipital craniectomy and laminectomy of the atlas. The operation was remarkable for the presence of thickened bone with a concave inverted occipital squama. The dura mater was opened and the retrocerebellar arachnoid cyst was widely excised, allowing ample communication with the basal cisterns. The fourth ventricle appeared normal. Dural closure was achieved with an autologous graft obtained from the cervical fascia. Results of the histopathological analysis of excised tissues were consistent with the diagnosis of an arachnoid cyst.

Postoperative Course. The patient’s postoperative course was unremarkable. At the 1-year follow-up, he reported continued back pain, but the headaches and dizziness had disappeared. No objective changes in his neurological examination were noted. A repeated MR imaging study showed resolution of the tonsillar herniation and a marked reduction in the size of both the cervicothoracic

Fig. 1. Photograph of the patient showing a pear-shaped nose, sparse fine hair, and thinned eyebrows.

Fig. 2. Photograph (upper) of the patient’s hands demonstrating brachydactyly, and radiograph (lower) showing misshapen fingers.
syringomyelic cavity and the retrocerebellar arachnoid cyst (Fig. 4).

**Discussion**

*Trichorhinophalangeal Syndrome*

Trichorhinophalangeal syndrome Type I is characterized by the presence of 3 striking features: sparse thin hair, a prominent nose with a bulbous tip, and peripheral dysostosis with cone-shaped epiphyses in the hands and feet. Individuals with TRPS-I usually have normal intelligence. The Type II form of this syndrome—also known as Langer–Giedion syndrome—shares the phenotype of TRPS-I but includes mental retardation, microcephaly, and multiple exostoses. Patients with TRPS-III have the facial appearance typical of that in TRPS-I and are usually of normal intelligence, but they have more severe brachydactyly and growth retardation. The established pattern of inheritance in TRPS is autosomal dominant, but autosomal recessive inheritance has also been documented. The TRPS1 gene maps to band 8q24.1 and appears to encode a zinc-finger transcription factor. Patients with TRPS-II present with multiple exostoses in addition to the features of TRPS-I. The deletion of TRPS1 and EXT1 leads to TRPS-II. An extensive study on mutation analysis has indicated that TRPS1 is the major locus for TRPS-I and -III. Trichorhinophalangeal syndrome Type III is at the severe end of the TRPS spectrum and is most often due to a specific series of mutations in TRPS1. The phenotypic and genotypic variations in TRPS have been recently described but are beyond the scope of our paper.

**Skeletal Abnormalities in TRPS**

There are noticeable variations in the skeletal manifestations of TRPS. The most typical radiographic findings in the syndrome are cone-shaped epiphyses, predominantly of the middle phalanges. Hip malformations—such as coxa vara, coxa magna, or coxa plana—are present in ~70% of patients. Some patients affected with TRPS may also have scoliosis, lordosis, pectus carinatum, or genu recurvatum. Short stature and brachydactyly are also common. All these features result from generalized and progressive shortening of all phalanges and metacarpals as well as some long bones. Growth retardation in TRPS is considered to be a postnatal event and constitutes a progressive process. Some authors have hypothesized that TRPS is the result of a general disorder of bone development. The formation of cone-shaped epiphyses has been attributed to an endochondral ossification anomaly in which the epiphyses are invaginated into the metaphyses of the small tubular bones of the hands and feet. King and Frias performed a cephalometric study of the craniofacial skeleton in patients with TRPS and have documented a shortened posterior face height, a short mandibular ramus, and a reduced and superiorly deflected posterior cranial base. Fernández et al. have reported a patient with TRPS-I with syringomyelia, attributing its formation to basilar impression related to an endochondral anomaly in the development of the skull base. Abnormalities in the cranial posterior fossa development that occur in TRPS-I can be the consequence of impaired endochondral ossification of the cartilaginous scaffold that forms the skull base, and the first 4 embryonic somites that take part in the formation of the occipital bone. However, many of these bone anomalies can remain undetected if they are not actively sought.

**Neurological Involvement in TRPS**

Apart from mental retardation, which is a frequent feature of TRPS-II, neurological involvement in TRPS has been rarely documented. Ramírez Balza et al. have reported 7 patients with TRPS-I and -III. Trichorhinophalangeal syndrome Type III is at the severe end of the TRPS spectrum and is most often due to a specific series of mutations in TRPS1. The phenotypic and genotypic variations in TRPS have been recently described but are beyond the scope of our paper.

![Fig. 3. Preoperative MR images demonstrating the posterior fossa arachnoid cyst with tonsillar herniation (left) and cervicothoracic syringomyelia (right).](image1)

![Fig. 4. Postoperative MR images showing disappearance of the tonsillar descent (left) and marked regression of the syringomyelic cavity (right).](image2)
Chiari Malformation Type I and Syringomyelia in TRPS-I

Chiari malformation consists of a spectrum of hindbrain anomalies characterized by downward herniation of the cerebellar tonsils.12,16,17 Chiari malformation Type I is identified as a tonsillar descent of at least 3–5 mm below the foramen magnum.12 Milhorat et al.12 have reviewed a series of 364 symptomatic patients with CM-I, and reported associated anomalies included syringomyelia (65%), scoliosis (42%), and basilar invagination (12%). Forty-three patients had a familial history of CM-I or syringomyelia, which suggests a genetic transmission. The clinical presentation of patients in that series consisted of headaches, pseudotumor-like episodes, Meniere disease—like syndrome, and lower cranial nerve and spinal cord signs. Magnetic resonance imaging findings comprised obliteration of the retrocerebellar CSF spaces, tonsillar herniation of at least 5 mm, and cranial base dysplasia. Magnetic resonance imaging also showed a significant decrease in the volume of both the posterior fossa and of the CSF together with a normal hindbrain size. Clinical manifestations of CM-I—headaches, syringomyelia, hydrocephalus, pseudotumor-like episodes, and endolymphatic hydrops—best explained by the disturbances in CSF flow and compression of neural structures. For most authors, CM-I is a disorder of the paraxial mesoderm characterized by underdevelopment of the posterior cranial fossa and overcrowding of the normally developed hindbrain.8,11 An increase in cranio cervical osseous anomalies among patients with CM-I has been documented, supporting the view that CM-I might be due mainly to occipital dysplasia.9,11,16 Congenital and acquired conditions involving bone development and metabolism are also apt to result in skull base changes and in the development of CM-I. Chiari malformation has been described in idiopathic growth hormone deficiency, hypophosphatemic rickets, achondroplasia, some forms of syndromic craniosynostosis, neurofibromatosis Type I, Paget disease of bone, cleidocranial dysplasia, cystic fibrosis, and in some complex syndromes such as Goldenhar, William, and velocardiofacial.5,11,16,17 Chiari malformation Type I has also been found in association with conditions that increase the intracranial volume, such as hydrocephalus, pseudotumor cerebri, and supra- and infratentorial tumors.13,16 A family with a dominant inheritance syndrome (craniofacial conodysplasia) whose clinical features include craniofacial dysplasia and cone-shaped epiphyses of the hands and feet has been reported by Beals et al.2 This syndrome may be associated with neurological complications arising from hydrocephalus and spinal cord compression at the craniocervical junction.

Syringomyelia has also been documented in patients with posterior fossa cysts. Spinal cord cavitation in the majority of these cases has been attributed to obstruction of CSF flow caused by the downward invagination of the cyst itself within the foramen magnum.1,10 Most interesting is the development of CM-I and syringomyelia due to the direct pressure exerted by a retrocerebellar cyst, as occurred in our patient. Arachnoid cysts are thought to represent congenital malformations in the normal development of the arachnoid.13 The arachnoid forms as an expansion of the extracellular space in the mesenchyme that surrounds the neural tube. Most embryologists consider both the arachnoid and pia mater as derivatives of the primitive mesenchyme surrounding the neural tube. The neural crest ectoderm forms the inner layers of pia mater, and the mesoderm forms the outer pia-arachnoid membrane. The formation of the subarachnoid space is dependent on the opening of the rhombic roof. The flow of CSF pumped by the pulsations of the choroid plexus constitutes the force that carves up the subarachnoid space. We hypothesize that the origin of the posterior fossa arachnoid cyst in our patient was related to the abnormal development of the occipital bone in relation with anomalous endochondral ossification that characterizes TRPS-I. The development of tonsillar descent and syringomyelia in our patient seems to have originated from the pressure exerted by the retrocerebellar cyst on the posterior fossa content in the presence of an already malformed cranial posterior fossa. This association has been reported by Bauer et al.1 in a patient with achondroplasia and by Martínez-Lage et al.30 in another individual without obvious bone abnormalities. The association of the retrocerebellar arachnoid cyst with CM-I and syringomyelia in our patient supports the view that surgical treatment should consist of a thorough exploration of the posterior fossa and excision of the cyst walls, in addition to osseous and dural decompression.

Conclusions

We have reported the case of a patient with TRPS-I and CM-I—syringomyelia complex probably caused by the pressure exerted by a posterior fossa arachnoid cyst. We briefly reviewed possible mechanisms to explain the formation of CM-I with syringomyelia in the context of TRPS-I and other bone dysplasias. As in other cases of CM-I and syringomyelia, we suggest that the surgical approach should be aimed to correct the hypothetical causative factor.

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Disclaimer

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