Case Report

A complex craniovertebral junction malformation in a patient with late onset glycogenosis 2

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Abstract

Glycogenosis II (GSDII) is an autosomal recessive lysosomal storage disorder resulting from deﬁciency of acid alpha-glucosidase and subsequent lysosomal accumulation of glycogen in skeletal, cardiac and smooth muscles. The late-onset form is characterized by wide variability of the phenotypical spectrum. Clinical ﬁndings may include muscle weakness, respiratory insufﬁciency, vascular abnormalities, low bone mineral density and higher risk of developing osteoporosis. Craniovertebral junction (CVJ) malformations have never been described so far. We here report on a GSDII 43-year-old woman who harbored the mutations IVS1-13T>G and c.2237G>A in the acid alpha-glucosidase gene. She recurrently suffered from headache, neck pain and dizziness. Brain MRI and CT scan showed the presence of a very rare complex CVJ malformation composed of basilar invagination, basiocciput hypoplasia, partial C1 assimilation, C1 posterior arch aplasia and C1 lateral mass hypoplasia and offset. Although we cannot rule out their coincidental occurrence, the rarity of multiple CVJ malformations in the general population as well as the well-known GSDII multisystem involvement should suggest to study the CVJ in the diagnostic process of GSDII patients in order to assess the CVJ malformation frequency in GSDII population and verify a possible relationship between these two conditions.

Key words: Craniovertebral junction malformation, CVJ, GSDII, late — onset glycogenosis

INTRODUCTION

Glycogenosis II [Glycogen storage Disease type II (GSDII); Pompe disease] is an autosomal recessive lysosomal storage disorder due to deﬁciency of acid alpha-glucosidase resulting in lysosomal accumulation of glycogen in skeletal, cardiac and smooth muscle, with progressive motor, cardiac and respiratory failure.¹ Although the pathological process mainly affects muscles, several other tissues may be involved in the course of the disease; therefore GSD II should be regarded as a multisystem disorder also involving liver, spleen, salivary glands, kidney, bone and blood vessels.²,³ Craniovertebral junction (CVJ) malformations have never been reported so far in GSDII patients.

We here report a GSDII patient who recurrently suffered from headache, neck pain and dizziness which were likely related to a very rare complex CVJ malformation.

CASE DESCRIPTION

We describe the case of a 43-year-old woman affected with GSDII who harbored the mutations IVS1-13T>G and c.2237G>A in the acid alpha-glucosidase gene. The onset of symptoms was at the age of 16 with diﬃculty in climbing stairs and standing up from the floor. Her neurological examination
showed anserine gait, proximal muscle weakness especially of lower limbs, and mild eyelid ptosis.

Since several years she suffered from persistent neck pain, dizziness and headache that greatly affect her quality of life. In order to investigate these symptoms, she was submitted to brain MRI and cervical spine CT scan with selective study of skull occipital junction.

Neuroimaging showed a rare complex CVJ malformation composed of basilar invagination, basiocciput hypoplasia, partial C1 assimilation, C1 posterior arch hypoplasia, C1 lateral mass hypoplasia and offset [Figure 1]. Measurement tools used to assess the diagnosis were Chamberlain line, Wackenheimclivus baseline and atlanto-occipital joint axis angle.[4]

**DISCUSSION**

The bony CVJ is an articulation point capable of complex motions distinct from the remainder of the vertebral column. It can be conceptually divided into two components with respect to the governance of intersegmental movements.[5]

The first component mainly consists of a central pivot made up of the dens and the C2 vertebral body. However, the basiocciput, though anatomically part of the foramen magnum, is embryologically and functionally in vertical linearity with the dens and is thus part of the central pillar. The second component consists of two ringed structures surrounding the central pivot, albeit eccentrically. They are the foramen magnum ring (comprising the lateral portion of the basiocciput and the exocciput including the occipital condyles and the opisthion) and the atlantal ring with its anterior and posterior arches and lateral masses.

*Hox* and *Pax* genes are involved in the regulation of CVJ development.[6] *Hox* genes control the body plan of the embryo along the anterior-posterior axis. Following primary segmentation, they determine the positional identity of the pre-vertebral segments and the vertebral phenotypes (types of vertebrae that will form on different segments). *Pax* gene family is important in early development for the specification of specific tissues and is implicated in sclerotomal resegmentation.

The malformation found in our patient involves both the components of CVJ, including basiocciput and atlantal ring, and it is likely to give rise to neck pain, dizziness and headache by altering the complex motion function of this region.

The correlation between CVJ malformation, *Hox* and *Pax* gene families and GSDII in this patient remains unknown and we cannot reasonably rule out the incidental co-occurrence of the two conditions. However, the rarity of this malformation as well as the well-known GSDII propensity to multisystem involvement (i.e. brain abnormalities, bone mineral density alterations, rigid spine, large vessel malformations, hemangiomas) makes intriguing the idea of a possible relationship, thus suggesting to study the CVJ in the diagnostic process of GSDII patients in order to assess the CVJ malformation frequency in GSDII population.

**REFERENCES**

1. Filosto M, Scarpelli M, Torin P et al. Muscle glycogenoses: an overview. In: Filosto M, Toscano A, Padovani A, editors. Advances in Diagnosis and Management of Glycogenosis II. New York: Nova Science Publisher; 2012. p. 51-67.
2. Filosto M, Todeschini A, Cotelli M, Vielmi V, Rinaldi F, Rota S, et al. Non-muscle involvement in late-onset glycogenosis II. Acta Myol 2013;32:91-4.
3. Hagemans ML, Winkel LP, Van Doorn PA, Hop WJ, Looen MC, Reuser AJ, et al. Clinical manifestation and natural course of late-onset Pompe’s disease in 54 Dutch patients. Brain 2005;128:671-7.
4. Smoker WR. Craniovertebral junction: Normal anatomy, craniometry and congenital anomalies. Radiographics 1994;14:255-77.
5. Pang D, Thompson DN. Embryology and bony malformations of the craniovertebral junction. Childs Nerv Syst 2011;27:523-64.
6. Laforêt P, Doppler V, Caillaud C, Laloui K, Claeyss KG, Richard P, et al. Rigid spine syndrome revealing late-onset Pompe disease. Neuromuscul Disord 2010;20:128-30.
7. van den Berg LE, Zandbergen AA, van Capelle CI, de Vries JM, Hop WC, van den Hout JM, et al. Low bone mass in Pompe disease: A predictor of bone mineral density. Bone 2010;47:643-9.
8. Sacconi S, Bocquet JD, Chanalet S, Tanant V, Salviati L, Desnuelle C. Abnormalities of cerebral arteries are frequent in patients with late-onset Pompe disease. J Neurol 2010;257:1730-3.
9. Toda G, Yoshimuta T, Kawano H, Yano K. Glycogen storage disease associated with left ventricular aneurysm in an elderly patient. Jpn Circ J 2001;65:462-4.
10. Cotelli M, Todeschini A, Vielmi V, Seddio C, Padovani A, Filosto M. Hemangioma of the semimembranosus muscle in a patient with late-onset Glycogenosis II. Muscle Nerve 2013;47:142-3.

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