Case Report

Chiari I Malformation Associated with Turner Syndrome

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Abstract

Turner syndrome (TS) is a rare genetic disease due to the absence of one X chromosome. Patients with TS have more subtle neurological/neuropsychiatric problems, while headache is an uncommon clinical presentation which needs attention. We report a 12-year-old child presenting with typical cough headache. Her magnetic resonance imaging revealed Chiari I malformation associated with TS. To the best of our knowledge, Chiari I malformation associated with TS is not described in literature. We report the first case of TS associated with Chiari I malformation. Interestingly, Chiari I malformation is also associated with Noonan's syndrome, which is a close morphological mimicker of TS, raising the possibility of sharing similar pathogenesis in both conditions.

Keywords: *Chiari I malformation, headache, magnetic resonance imaging, Turner syndrome*

Introduction

Turner syndrome (TS) is a rare genetic disease due to the absence of one X chromosome. Neurological manifestations in TS are less frequent. Epilepsy and central nervous system (CNS) tumors account for most of the cases. While neuropsychological abnormalities are more common, they need extensive battery of tests for the identification of specific conditions. Conventional imaging techniques identify gross structural abnormalities, while subtle structural, chemical, and functional abnormalities in the brain are explored by recent advanced techniques in neuroimaging, namely, Voxel-based morphometry (VBM), surface-based morphometry, magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), tractography, and functional magnetic resonance imaging (fMRI). Gross congenital abnormalities are rare and only a few cases are reported in the literature. We describe a first case of Chiari I malformation associated with TS and review about gross and subtle structural, functional, and chemical abnormalities of CNS reported in literature.

Case Report

A 12-year-old female presented with a history of headache of 2 months duration. The headache was in bifrontal region and vertex, more in the early morning, and aggravated with coughing. It started with a bout of respiratory tract infection 2 months back; headache persisted even after the remission of respiratory tract infection. She is only child born to nonconsanguinous parents. There was no history of perinatal insult, cried immediately after delivery. After 2 weeks of birth, she developed respiratory distress. Webbing of the neck was noticed. On evaluation, echocardiogram revealed ventricular septal defect and persistent ductus arteriosus. Her karyotyping disclosed a chromosomal abnormality 46, XO suggestive of TS. She had a history of recurrent respiratory infections and features of cardiac failure during her childhood.

At the time of presentation to our hospital, she had no signs/symptoms of respiratory infection. Recent echo showed pulmonary hypertension. Her oxygen saturation was maintained. On examination, she has short stature, hypertelorism, microcephaly, flat chest, webbing of the neck. She had not attained puberty. She is average in studies.

She underwent MRI of the brain and cervical region, which showed tonsillar herniation, elongation of medulla [Figure 1a], crowding of structures at foramen magnum [Figure 1b], dilated bilateral lateral ventricles, and enlarged third ventricle [Figure 1a and c]. Excessive fat deposition was noted at the nape of neck [Figure 1a]. Focal FLAIR hyperintensity was seen in vermian region, the possible significance of which is not known [Figure 1d]. Cervical vertebral bodies, posterior elements, and spinal cord were normal.

Discussion

The possibility of CNS abnormalities being part of TS was raised by Brun and Skold in 1968.[1] Neurological symptoms as initial presentation are rare as most of the patients had already diagnosed as TS. Since 1968, multiple structural, functional, and chemical abnormalities of CNS are studied in TS, summarized as follows.

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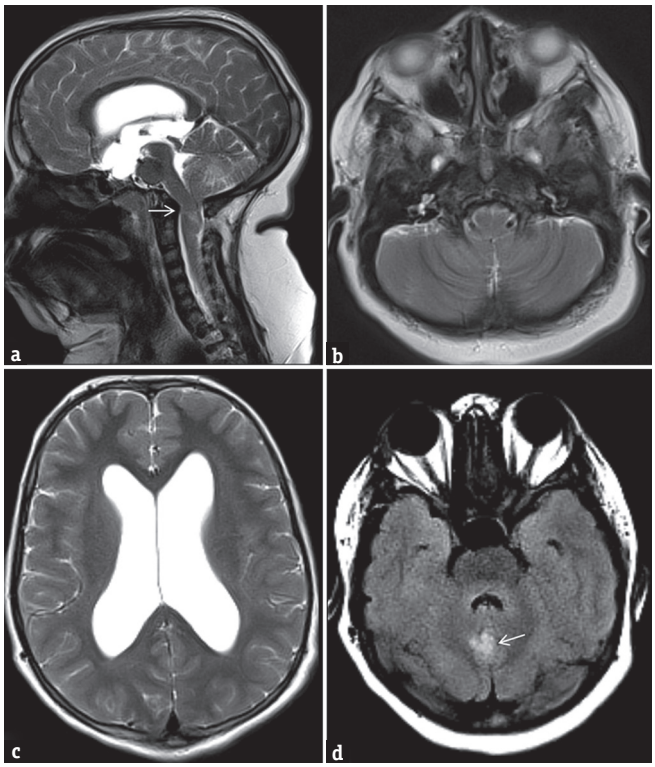

Figure 1: (a) Sagittal T2-weighted magnetic resonance image showing tonsillar herniation (arrow), elongation of medulla, crowding of structures at foramen magnum, dilated third ventricle. (b) Axial FLAIR magnetic resonance image showing crowding of structures at foramen magnum with effaced cerebrospinal fluid spaces. (c) Axial T2-weighted image showing dilatation of bilateral lateral ventricles. (d) Axial FLAIR image of posterior fossa showing abnormal hyperintense focus in vermian region (arrow)

Gross structural abnormalities

Congenital gross structural abnormalities of the CNS in TS detected on conventional imaging modalities are less frequent compared to subtle abnormalities. Five cases of corpus callosum agenesis in association with TS are reported.[2-6] A necropsy study from a 45-year-old patient showed an aberrant intracallosal longitudinal fiber bundle that was not detected by conventional MRI.[7] The different MRI abnormalities in patients with epilepsy include bilateral perisylvian hypoplasia,[8] bilateral frontal polymicrogyria,[9] bizarre cortical dysgenesis of the cerebrum – a mixture of relatively normal gyri and structures resembling pachygyria and lissencephaly,[10] diffuse periventricular and subcortical white matter FLAIR hyperintensities.[11] Based on these findings, possible dysgenetic role of X-chromosome was attributed in cortical morphogenesis.

Rare case reports of pseudotumor cerebri,[12] Dandy-Walker malformation, and cerebral venous sinus thrombosis are described.[13] To the best of our knowledge, Chiari I malformation associated with TS is not described in literature. We report the first case of TS associated with Chiari I malformation. Interestingly, Chiari I malformation is also associated with Noonan's syndrome, which is a close morphological mimicker of TS, raising the possibility of sharing similar pathogenesis in both conditions.

Tumors

CNS and non-CNS tumors are seen with increased frequency as compared to general population, suggesting a possible tendency of oncogenesis in TS. Thirteen cases of meningioma associated with TS are described in literature with various neurological presentations including asymptomatic incidental detection.[14] Few cases of meningioma are attributed to estrogen replacement therapy in patients with TS. Few cases of glioblastoma multiforme are seen in associated with TS,[15,16] and few cases of craniopharyngioma are reported.[17]

Subtle morphological abnormalities

The subtle neurological deficits in spatial-numerical processing and social cognition seen in patients with TS were attributed to specific alterations of white matter fiber tracts connecting various parts of the brain.[18] Subtle alterations in neurodevelopmental trajectories in some regions of brain were attributed to estrogen deficiency during pre- and post-natal period.[19] Few authors used advanced imaging techniques such as DTI and volumetric imaging techniques to demonstrate extensive aberrant white matter and volume changes in TS.[20,21]

Reduced amygdala and hippocampal volumes are also seen which are attributed to social cognition and memory deficits in TS patients.[22,23] Reduced volume of corpus callosum, pons, vermis lobules VI–VII and increased fourth ventricle region are reported in TS, suggestive of morphometric abnormalities in posterior fossa structures apart from supratentorial structures.[24] VBM studies showed spatial patterns of altered brain morphometry in TS.[18,25] Apart from white matter abnormalities, abnormalities in gray matter (differential decrease/increase in volume of different regions of brain) are also seen using volumetric studies in TS, also contributing to neuropathological basis of cognitive deficiencies.[26-29] Study of surface area of parietal lobe using structural MRI showed an aberrant growth of white matter volume and surface area of the left superior parietal regions in TS.[30] Brain volume analysis using high-resolution MRI also demonstrated decrease in bilateral parietal gray and occipital white matter associated with increased cerebellar gray matter.[31] Studies particularly evaluating superior temporal gyrus abnormalities using volumetric MRI study demonstrated larger volumes of both gray and white matter of right superior temporal gyrus in TS.[32,33] Subregional abnormalities within bilateral parietal lobes specifically involving superior parietal and postcentral gyri were seen in TS.[34]

Proton MRS technique was also used to demonstrate abnormalities in chemical composition of the brain parenchyma (lower concentration of N-acetyl aspartate in the lower parietal lobe and higher hippocampal choline).[27,35]

TS patients not only have age-independent congenital defect but also have altered brain development, more specifically, age-dependent maturational defect.[36]

Functional abnormalities

Atypical functional activation of the brain was demonstrated during multiple object tracking task,[37] judgment of line orientation task,[38] and Go/NoGo task[39] in patients with TS

using fMRI. Visuospatial working memory abnormalities were demonstrated in TS using fMRI studies.[40-42]

Cerebrovascular diseases

Several cases of stroke in TS are described, possibly due to vasculopathy/premature atherosclerosis.[43-46] A case of TS presenting with ischemic stroke showed interesting finding of pulvinar sign on T1-weighted imaging of MRI.[47] A rare case of stroke associated with features of fibromuscular dysplasia of the right internal carotid and vertebral arteries was reported.[44]

While dissection of aorta in TS is frequently reported, dissection of carotid-vertebral artery dissection is rare. Few cases of single vessel/multiple cerebral arterial stenosis presenting with stroke are reported.[43,45,48] Few cases of moyamoya syndrome are reported presenting as SAH and intracerebral hemorrhage[49] and stroke-like symptoms.[50] A case of vertebral artery dissection in TS presenting as cervical radiculopathy is reported.[51]

Although few cases of cerebral hemorrhage are reported, hypertension was associated with and possible etiology of such hemorrhages; nevertheless, cerebral vascular abnormalities are also reported in some cases.[52-55]

Conclusion

Gross congenital CNS abnormalities are rare, while subtle structural and functional abnormalities are common. Magnetic resonance imaging is useful in identification of abnormalities associated with TS. Conventional MRI needs to be considered in patients with headache to rule out underlying gross structural abnormalities.

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Conflicts of interest

There are no conflicts of interest.

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