Megalencephaly-Capillary Malformation-Polymicrogyria Syndrome (MCAP): A Rare Dynamic Genetic Disorder

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Abstract
Megalencephaly-capillary malformation-polymicrogyria syndrome (MCAP) is an uncommon malformation syndrome, characterized by primary megalencephaly, capillary malformations of the midline face and body, or distal limb anomalies such as syndactyly and polymicrogyria. Herein, we report a young male child, who presented with complaints of increasing head size, delay in speech, and one episode of focal seizure with distinctive morphological and neuroradiological manifestations which led to the diagnosis of MCAP. We have also reviewed recently published literature and the various diagnostic criteria proposed by authors to achieve the early clinical diagnosis of these patients in the outpatient department.

Categories: Genetics, Neurology, Radiology
Keywords: phosphatidylinositol 3-kinase (pi3k)-akt pathway, megalencephaly, brain vascular malformation, mcap syndrome, megalencephaly-capillary malformation-polymicrogyria syndrome

Introduction
Megalencephaly-capillary malformation-polymicrogyria syndrome (MCAP) is an uncommon genetic syndrome characterized by primary megalencephaly, cutaneous vascular malformations, polymicrogyria, and other anomalies [1]. This condition was first described in 1997 as macrocephaly-cutis marmorata telangiectasia congenita (M-CMTC) by Clayton-Smith et al. [2] and Moore et al. [3]. After diagnosis in 1997, around 300 cases have been reported in the literature [4]. In 2007, this condition was renamed macrocephaly-capillary malformation syndrome (MCM) by Toriello and Mulliken et al. [5] and Conway et al. [6] Finally, in 2012 Mirzaa et al. renamed MCM to megalencephaly-capillary malformation-polymicrogyria syndrome (MCAP) to reflect the abnormally large size of the brain and to highlight the importance of perisylvian polymicrogyria [1]. Current studies have found its genetic cause to be linked with the PI3K- AKT pathway [7]. Herein, we describe a case, that presented to us with both intracranial and cutaneous manifestations of MCAP. Clinicians should have a high degree of suspicion with regular follow-up as the entity has highly dynamic clinical manifestations.

Case Presentation
A three-and-a-half-year-old male child presented with complaints of increasing head size (>2 Standard Deviation (2SD)), delay in speech, and one episode of focal seizure at three years of age. His perinatal history was uneventful. There was no family history of similar illnesses in the family. Examination revealed macrocephaly with frontal bossing (Figure 1a) with numerous cutaneous capillary malformations on the face and bilateral lower limbs (Figures 1a, 1b). Multiple thick doughy subcutaneous tissues were also present over the back (Figure 1c), which was confirmed as fibrofatty tissue on USG. No evidence of facial, body asymmetry, syndactyly, or polydactyly was found.
FIGURE 1: shows features seen on clinical examination of the patient

Figure 1 shows the features found on general examination of the patient, macrocephaly with frontal bossing with cutaneous capillary malformations above the upper lip of face (1a), multiple cutaneous capillary malformations over bilateral lower limbs (1b), multiple thick doughy subcutaneous tissues over the back (1c).

Magnetic resonance imaging (MRI) of the brain showed ventricular asymmetry with prominent left lateral ventricle (Figure 2a), left-sided incomplete opercularization with widened left Sylvian fissure and cavum septum pellucidum (Figure 2b), bilateral perisylvian polymicrogyria (Figure 2c), abnormally thickened mega corpus callosum (Figure 2d), multiple foci of T2/FLAIR hyperintensities in bilateral deep and periventricular white matter (Figure 2e), prominent bilateral optic nerve sheaths (Figure 2f, 2h) and enlarged venous sinuses (Figure 2f, 2g).

FIGURE 2: showing MRI Brain Imaging performed on this patient

Figure 2 shows MRI Brain imaging performed on this patient. Axial T1W image reveals ventricular asymmetry with prominent left lateral ventricle (white arrow, Fig. 2a). Coronal T1W image reveals left-sided incomplete opercularization with widened left Sylvian fissure (white arrow, Fig. 2b), cavum septum pellucidum with prominent left lateral ventricle is also seen (black arrowhead Fig. 2b). T1W parasagittal image reveals perisylvian polymicrogyria (black arrowheads, Fig. 2c). T1W mid-sagittal image reveals abnormally thickened mega corpus callosum (white arrow, Fig. 2d). Axial FLAIR image demonstrates multiple foci of abnormally increased signals in bilateral deep and periventricular white matter (white arrowheads, Fig. 2e). Axial T2W image reveals prominent bilateral optic nerve sheaths (white arrows, Fig. 2f) and enlarged left transverse sinus flow void (white arrowhead, Fig. 2f). T2W mid-sagittal image reveals an enlarged straight sinus flow void (white arrow, Fig. 2g). Coronal T2W image reveals prominent bilateral optic nerve sheaths (white arrows, Fig. 2h).

Based on the clinical and neuroimaging findings, the diagnosis of a megalencephaly-capillary malformation-polymicrogyria syndrome (MCAP) was made as per the proposed criteria by Mirzaa et al. with...
MCAP is a rare genetic syndrome characterized by a wide range of abnormalities like primary megalencephaly, cutaneous vascular malformations, prenatal overgrowth, connective tissue dysplasia, digital anomalies, body asymmetry with distinctive brain imaging features like polymicrogyria, asymmetry of the lateral ventricles, hydrocephalus, polymicrogyria, large cerebellum resulting in the crowded posterior fossa, cerebellar tonsillar herniation or ectopia, thick corpus callosum, and other features [1]. Other simulating brain overgrowth syndrome includes megalencephaly-polydactyly-polymicrogyria-hydrocephalus (MPPH) syndrome, where megalencephaly is seen associated with distal limb anomalies like postaxial polydactyly and hydrocephalus [1]. Other diseases associated with megalencephaly and skin manifestations are congenital lipomatous overgrowth, vascular malformations, epidermal nevi (CLOVE) syndrome, and Bannayan-Riley-Ruvalcaba syndrome (BRRS) [19].

Even though imaging features like hydrocephalus and cerebellar tonsillar ectopia were absent at present in the present case, he is planned for regular follow-up with imaging at one year.

Conclusions

Being a rare condition, MCAP requires careful clinical evaluation and neuroimaging for its diagnosis. Moreover, clinicians should be aware of its dynamic nature and so follow-up with MRI is required for cerebellar tonsillar ectopia and brainstem compression which may be life-threatening.
Disclosures

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