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Case Report

Paediatrics Section

Importance of Family History and Clinical Examination in Evaluation of Paediatric Brain Tumours- A Unique Case Report of Tuberous Sclerosis

ALHAD MULKALWAR[1], SHRUTI MONDKAR[2], MUKESH AGRAWAL[3]

ABSTRACT

Tuberous sclerosis complex is an autosomal dominant neurocutaneous disorder characterised by the development of hamartomas in various tissues. The present report describes the case of a 4-year-old male child who was admitted to the Paediatrics Ward with a history of headache and vomiting since two months and weakness in the right upper limb and right lower limb since 15 days. Examination revealed right-sided hemiparaesis with facial involvement and signs of raised intracranial tension (papilloedema and hypertension). General examination revealed neurocutaneous markers such as multiple ash leaf macules over forehead, chest, abdomen and dental pits, which were suggestive of tuberous sclerosis. The child's mother was a known case of focal seizures since childhood, had adenoma sebaceum and Magnetic Resonance Imaging (MRI) brain showed subependymal nodules-suggestive of tuberous sclerosis. Based on neuroimaging {Computed Tomography (CT) and MRI} the child was diagnosed to be suffering from tuberous sclerosis with Subependymal Giant cell Astrocytoma (SEGA) with secondary hydrocephalus. The child underwent resection of the intraventricular tumour (SEGA) with good neurological recovery and is currently asymptomatic. Histopathology confirmed the diagnosis of SEGA. The present case emphasises on the significance of a detailed clinical examination and family history which aided neuroimaging in making a diagnosis of tuberous sclerosis in a child who would otherwise be diagnosed only as a case of astrocytoma.

Keywords: Astrocytoma, Hydrocephalus, Neuroimaging, Subependymal calcification

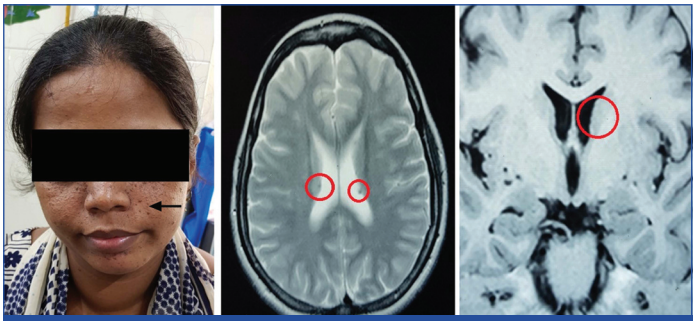
CASE REPORT

A 4-year-old male child was admitted to the Paediatrics Ward with a history of headache and vomiting since two months and weakness in the right upper limb and right lower limb since 15 days. The headache was bilateral, frontal and occipital in location. It was initially intermittent but later became continuous five days prior to admission. Vomiting was non bilious, projectile and initially once per week. Two days before admission, vomiting increased in frequency to twice a day. The headache was found to temporarily decrease in intensity following an episode of vomiting. Weakness of the right side of the body was progressive, first noticed by the school teacher due to the child's inability to lift his arm above the head. This gradually progressed over the next 15 days to limping while walking, difficulty in getting up from squatting position, dragging of right foot while walking and finally inability to sit up from sleeping position.

There was no history suggestive of speech, sensory, cerebellar, bladder or bowel deficits. The child had no history of convulsions, blurring of vision or worsening of sensorium. There was neither history of tuberculosis in the child or family members, nor any history of trauma or fever. The child's mother had history of occasional focal seizures since childhood and was on tablet carbamazepine for the same, with seizures being well controlled. She also had history of two spontaneous abortions, both in the third month of gestation. The child's perinatal history was uneventful and he was developmentally appropriate for his age.

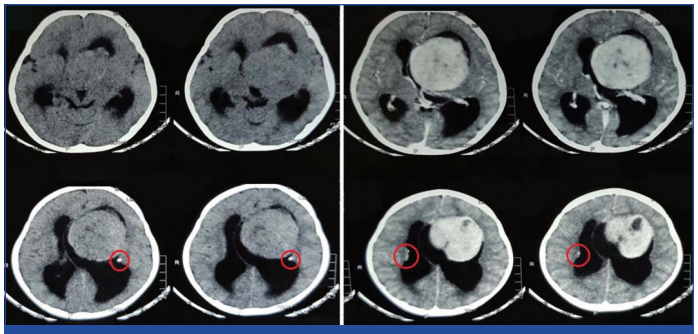
Physical examination revealed right-sided hemiparaesis with right-sided facial palsy (upper motor neuron type) and signs of raised intracranial tension (papilloedema and hypertension). Neurocutaneous markers were suggestive of tuberous sclerosis- multiple ash leaf macules over the trunk [Table/Fig-1] and dental pits [Table/Fig-2]. The child's mother who was a case of focal seizures since childhood, had adenoma sebaceum over the face [Table/Fig-3] and her Magnetic Resonance Imaging (MRI) brain suggested tuberous sclerosis [Table/Fig-4]. Preoperative haematological investigations of the child were normal.

[Table/Fig-1]: Multiple hypomelanotic ash leaf macules on child's trunk.
[Table/Fig-2]: Multiple dental pits. (Images from left to right)

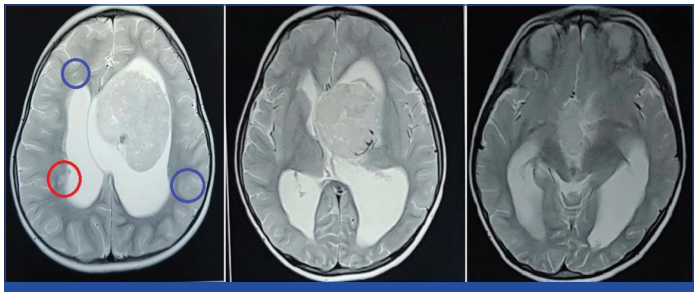


[Table/Fig-3]: Child's mother depicting adenoma sebaceum on the face (arrow).
[Table/Fig-4]: MRI brain of the child's mother showing subependymal nodules (marked with red circles). (Images from left to right)

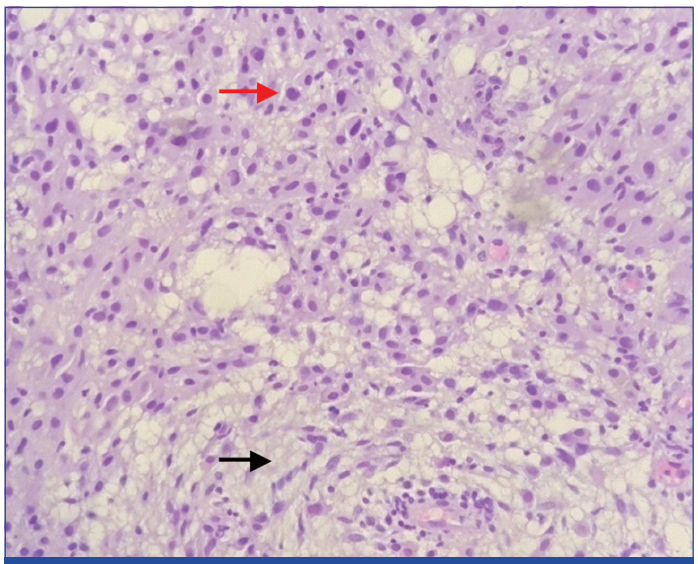
Neuroimaging {Computed Tomography (CT) scan and MRI} revealed an 8×5.5×7 cm sized tumour arising from the third ventricle and extending into the left lateral ventricle, distending both lateral ventricles (left>right) with deviation of septum pellucidum to the right by 1.5 cm; the child was diagnosed to have tuberous sclerosis with Subependymal Giant cell Astrocytoma (SEGA) with secondary hydrocephalus [Table/Fig-5,6]. The child underwent resection of the intraventricular tumour on day 8 of admission. Histopathology of the excised tumour confirmed the diagnosis of SEGA [Table/Fig-7].



[Table/Fig-5]: Preoperative CT scan brain (Plain and Contrast)- Intensely enhancing heterodense lesion 60×56×65 mm in the third ventricle, extending superiorly into the body and frontal horn of left lateral ventricle with midline shift of 2 cm to the right, suggestive of a space-occupying lesion with decompensated hydrocephalus. Foci of subependymal calcification can also be appreciated (marked in red circles).

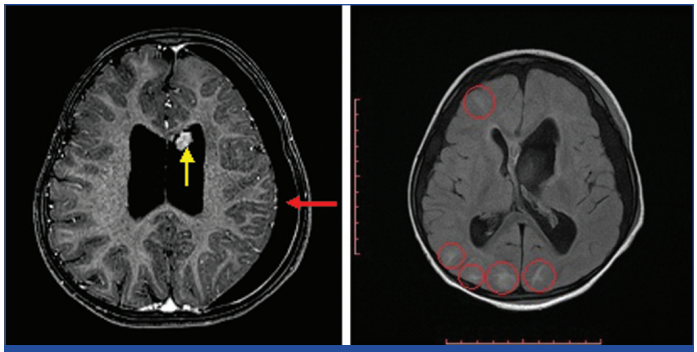


[Table/Fig-6]: Preoperative MRI brain- An 8×5.5×7 cm sized T2 isointense mass with heterogenous post-contrast enhancement at foramen of Monro with areas of calcification, distending both lateral ventricles (left>right) and deviation of septum pellucidum to the right by 1.5 cm, with mild periventricular ooze. Subependymal nodules are seen around the temporal horn (red circle). Temporal and frontal cortex are showing cortical tubers (blue circles), few extending into the ventricular margins- confirming tuberous sclerosis with subependymal astrocytoma causing obstructive hydrocephalus.



[Table/Fig-7]: Photomicrograph (H&E, 40X) depicting a uniform population of astrocytic cells with thin, delicate hair-like processes (black arrow) imparting a fibrillar appearance to the background. The nuclei are round to oval with bland chromatin (red arrow); suggestive of a pilocytic (WHO grade 1) astrocytoma.
* WHO: World Health Organisation

Postoperative MRI brain depicted most of the tumour to be successfully excised with a small, clinically insignificant residual lesion in the left lateral ventricle [Table/Fig-8]. It also revealed multiple hyperintense subcortical areas suggestive of cortical tubers, [Table/Fig-9] due to which the child may develop focal seizures in the future, similar to his mother. The parents were advised to revisit the hospital in the event of the same. The child was discharged and regular follow-up examinations were scheduled. During the follow-up visit two weeks after discharge, physical neurological examination revealed good postoperative clinical outcome with complete recovery of the right-sided hemiparaesis and facial palsy. The signs of raised intracranial tension-papilloedema and hypertension had also resolved.



[Table/Fig-8]: Postoperative MRI brain showing small residual lesion measuring 7×11 mm, seen anterior to the body of left lateral ventricle (yellow arrow) with left subdural collection of maximum thickness of 14 mm (red arrow).
[Table/Fig-9]: Postoperative MRI brain - multiple subcortical areas (marked with red circles) showing hyperintensity on T2-flair suggestive of cortical tubers. (Images from left to right)

DISCUSSION

Tuberous Sclerosis Complex (TSC) is an autosomal dominant neurocutaneous disorder characterised by the development of benign tumours (hamartomas) in various tissues (mainly the brain, skin, heart, kidneys, and liver) [1]. The incidence of this disorder has been estimated to be around 1 in 6000 live births [2]. Inactivating mutations in either of two genes: TSC1 (15-20% cases) or TSC2 (65-75% cases), causing hyperactivation of mammalian target of rapamycin (mTOR) pathway leads to TSC [3]. About one third of individuals diagnosed with TSC have an affected parent [1].

A detailed family history in the present case revealed that the child's mother had a history of occasional focal seizures since childhood, one of the commonest neurologic symptoms associated with TSC-prevalence ranging from 62-93% [4-6]. Cortical tubers and subependymal nodules (which were seen on MRI brain of the mother as well as the child) are what cause these neurological manifestations like epilepsy [7]. The patient also had a history of two spontaneous abortions, which are associated with both foetal and maternal TSC [8,9]. This prompted a detailed clinical and radiological examination of the mother which revealed presence of two major features (facial angiofibromas/adenoma sebaceum and subependymal nodules), thus confirming the diagnosis of TSC in the mother which passed onto the child. The patient should have been adequately evaluated and ideally been diagnosed with TSC when she first developed seizures. Although two-thirds of cases of TSC are due to spontaneous mutations, there are no known risk factors, other than having a parent with tuberous sclerosis, in which case, each child has a 50% chance of inheriting the disease [10]. Therefore, appropriate genetic counselling was provided to the parents, if they wished to conceive another child in the future.

Subependymal giant cell astrocytoma (SEGA), which develops in up to 20% of individuals with tuberous sclerosis, is a rare benign tumour [11]. They are usually located near the foramen of Monro and are typically asymptomatic until they reach a size large enough to cause ventricular obstruction and hydrocephalus, as seen in the present case [12]. Surgical resection remains the recommended treatment for SEGA producing clinical symptoms while drugs like everolimus (mTOR inhibitors) could be used for growing but asymptomatic tumors [13]. Surgical resection leads to rapid resolution of the symptoms, which was also noticed in this child.

Comprehensive diagnostic criteria for TSC were first published by Dr. Manuel R. Gomez; they currently exist in a revised form as outlined in a consensus statement from the United States' Diagnostic Criteria Committee of the National Tuberous Sclerosis Association [14]. These diagnostic criteria comprise of eleven major and nine minor features. Presence of two major features or one major feature plus two or more minor features is diagnostic of TSC [14]. In the present case, a thorough clinical evaluation and Neuroimaging of the child revealed the presence of four major (cortical tubers,

subependymal nodules, SEGA and more than three hypomelanotic macules) and one minor (multiple randomly distributed pits in dental enamel) feature of TSC.

CONCLUSION(S)

The present case emphasises the fact, that, the apple does not fall far from the tree. A detailed clinical examination and family history supplemented Neuroimaging in making a diagnosis of tuberous sclerosis in this child. The case was managed with resection of the intraventricular tumour and revealed good postoperative clinical outcome and neurological recovery.

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PARTICULARS OF CONTRIBUTORS:
1. Intern, Department of Paediatrics, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Mumbai, Maharashtra, India.
2. Assistant Professor, Department of Paediatrics, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Mumbai, Maharashtra, India.
3. Professor and Head, Department of Paediatrics, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Alhad Mulkalwar,
Intern, Department of Paediatrics, King Edward Memorial Hospital and Seth Gordhandas Sunderdas Medical College, Parel, Mumbai-400012, Maharashtra, India.
E-mail: alhad.mulkalwar@gmail.com

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