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**Authors:**

Santosh Rai (dr santosh_win@yahoo.com)
Satish Sonawane (surgeonsonawane@gmail.com)
Piyush Kalakoti (drpiyushkalakoti@gmail.com)
M. M. Aarif Syed (smmaarif@yahoo.com)
Gaurav Kalra (residentkalra@gmail.com)
Rishi Jain (doctorrishijain@gmail.com)
Gurmeet Singh (drgsingh99@gmail.com)

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An unusual case of congenital melanocytic nevus presenting as neurocutaneous melanoma coexisting with Tuberous Sclerosis complex: a rare association or a new syndrome?

Santosh Rai¹, Piyush Kalakoti², M. M. Aarif Syed³, Rishi Jain⁴, Sankalp Yadav⁵, Gaurav Singh Parhar⁶, Gaurav Kalra⁷, Puneeta Kaur Arora⁸, Gurmit Singh⁹, Deepak Singh¹⁰, Shikha Shrivastava¹¹

¹ MBBS, MS, FMIS, Assistant Professor, Department of Surgery, Rural Medical College, Loni, Maharashtra, India
² MBBS Intern, Rural Medical College, Loni, Maharashtra, India
³ MBBS Intern, Rural Medical College, Loni, Maharashtra, India
⁴ Surgery Resident, Rural Medical College, Loni, Maharashtra, India
⁵ MBBS, Rural Medical College, Loni, Maharashtra, India
⁶ Medical Intern, Rural Medical College, Loni, Maharashtra, India
⁷ Surgery Resident, Rural Medical College, Loni, Maharashtra, India
⁸ MBBS Intern, Rural Medical College, Loni, Maharashtra, India
⁹ MBBS, MD, Assistant Professor, Department of Paediatrics, Rural Medical College, Loni, Maharashtra, India
¹⁰ Medical Student, Rural Medical College, Loni, Maharashtra, India
¹¹ Medical Student, Rural Medical College, Loni, Maharashtra, India

SR- drsantosh_win@yahoo.com
PK- drpiyushkalakoti@gmail.com
MMAS- smmaarif@yahoo.com
RJ- doctorrishijain@gmail.com
SY-sankalpy@yahoo.com
GSP-gaurav.parhar@gmail.com
GK- residentkalra@gmail.com
PKA-pooja_frenz2000@yahoo.com
GS- drgsingh99@gmail.com
DS- drdeepaksingh88@gmail.com
SS- drshikhashrivastava27@gmail.com

Corresponding Author

Piyush Kalakoti
Final Year Medical Student,
Rural Medical College,
Loni- 413736, Maharashtra, India.
Email- drpiyushkalakoti@gmail.com
Contact- +91-9970951036
Abstract

Congenital melanocytic nevi (CMN) are found in approximately 1% of newborn infants and represent a special group of melanocytic lesions that covers large areas of the body and have a potential risk for developing malignant melanoma. Neurocutaneous melanosis (NCM) is a rare, congenital, nonhereditary disorder characterized by the presence of multiple and/or giant congenital melanocytic nevi. Tuberous sclerosis complex (TSC) is a form of the neurocutaneous syndrome (NCS), however its concurrence with NCM is an unusual finding which to the best of our knowledge has not been documented in the literature so far. We herein present such an unusual association of NCM with TSC in a 16 year old post pubertal Indian female that presented to our hospital with a scalp mass.

Key words

Neurocutaneous melanoma, Tuberous Sclerosis Complex, Congenital Melanocytic Nevus
Background

Congenital melanocytic nevi (CMN) are found in approximately 1% of newborn infants, but 90% of them are very small. A giant congenital nevus (GCN), giant hairy nevus or nevocellular nevus represents a special group of melanocytic lesions that generally covers large areas of the body and have a potential risk for developing malignant melanoma [1]. Congenital nevi are one of several known risk factors for the eventual development of melanoma. Fortunately, melanoma remains an uncommon malignancy in prepubertal children, with an annual incidence of 0.7 cases per million children aged 0-9 years. Patient concerns regarding changing or worrisome-looking nevi are, nonetheless, very common. Moreover, by the time a child reaches adolescence, the incidence of melanoma increases substantially, with a rate of 13.2 cases per million children aged 15-19 years [2].

Neurocutaneous melanosis (NCM) is a congenital, nonhereditary disorder defined by the presence of multiple and/or giant congenital melanocytic nevi associated with abnormal melanin deposits in the brain and/or leptomeninges documented by Magnetic Resonance Imaging (MRI) or autopsy [3-6]. It is a rare condition, with fewer than 200 cases reported in the literature. Although there is proliferation of melanocytes in the skin and arachnoid mater, there is currently no embryological explanation for the genesis of this disorder. Approximately half of all patients with NCM eventually develop melanoma of the central nervous system [7]. However, presence of tuberous sclerosis complex (TSC), a form of the neurocutaneous syndrome (NCS) concurrent with NCM is an unusual and rare finding which to the best of our knowledge has not been documented in the literature so far. We herein present such an association in an 11 year old girl.

Case Presentation

History and Presentation: A 16 year old girl presented to our hospital with swelling on the scalp. She was born with a black pigmented triangular patch over the scalp covered with hair with multiple black hairy patches on her extremities, back and most of the anterior trunk. The patch on the scalp increased in size over a period of 8 years since birth. In the past 3 months, the swelling progressed from the hairline to just above the left brow leading to unilateral mechanical ptosis. On pressure, there was scanty, yellowish, non foul smelling discharge, occasionally blood stained and was associated with intense itching without any pain. Her sleep, appetite, bowel and bladder were unaltered. She had attained menarche at the age of 15 years and her menstrual cycles were normal and regular. Her birth and developmental history were normal. The family history was negative for congenital nevi or melanoma.

Examination: Clinical examination revealed the patient to be afebrile, with pulse rate of 64 per minute, respiratory rate of 16 per minute and blood pressure of 120/70 mm Hg. Examination of cardiovascular system was normal. Cranial nerve functions were normal and no neurological deficit was found in the limbs. The plantar responses were flexor. There was no evidence of meningeal irritation.

Local examination revealed a single swelling of size 10 cm X 8 cm on the left side of the scalp. The swelling extended antero-posteriorly from 3 cm in front of the left parietal eminence to just above the lateral part of the left supraorbital ridge while transverse extension was from the line passing through the left parietal eminence to the right of the midline (Figure 1). The local temperature was not raised and tenderness was absent. The surface was irregular, rough with multiple pits; margins were irregular with rounded edges and firm in
consistency. The swelling was mobile and the anterior part of the swelling overlying the forehead could be lifted. The underlying skin appeared normal. It was non pulsatile with no evidence of impulse on coughing. Regional lymph nodes were not palpable. Numerous hairy naevi were present over the scalp, trunk and limbs.

**Patient** was referred to the departments of neuro-ophtalmology and otolaryngology for further assessment. Fundoscopy and visual evoked potentials were normal. Otorhinolaryngological evaluations were normal.

Routine blood investigation showed haemoglobin 11.6%, total leucocyte count 4200/mm³ with relative neutrophilia (80%). Serum urea and electrolytes levels were normal. Lumbar puncture revealed clear cerebrospinal fluid (CSF) with normal cell count and biochemistry, and no growth on culture, and no growth on culture. Liver and kidney function tests were within normal limits. ECG did not show any abnormal features.

**Radiological Findings:** X Ray of skull (Posteroanterior view) revealed a soft tissue swelling in the left temporo-fronto-parietal region. Ultrasonography (USG) of the swelling showed a large, homogenous, hypoechoeic solid lesion of size 9.4 cm x 6.8 cm x 1 cm in the scalp on the left frontal region and partially extending into the parietal region on the left side. The underlying outer table of the skull and diploic spaces were normal with few hyper reflective areas scattered throughout the lesion with distal shadowing suspicious of tiny calcific foci. The interface between the lesion and the scalp was obscured. On Colour Doppler, no significant colour flow noticed. These findings were highly suggestive of a possible angiofibroma. Power Doppler showed highly vascularised lesion.

MRI of brain (both plain and contrast) was done by taking multiecho, multiplanar technique which showed the presence of 8.99cm x 2.26cm sized abnormal signal intensity involving the scalp (subcutaneous plane within fat) in the left fronto-parietal region appearing iso to hyperintense on T1 W images with few small tubers with cortical dysplasia in the left fronto-parietal region with asymmetric dilatation of the left ventricle, hypointense on T2W and FLAIR images. There were few foci seen within the lesions appearing hyperintense on T2W and FLAIR images. The MRI impression revealed multiple intracranial lesions; these included a benign homogenously enhancing subcutaneous scalp lesion in left fronto-parietal region suggesting angiofibroma, few calcified subependymal nodules within the body of the lateral ventricles on right side, few small tubers with cortical dysplasia in the left fronto-parietal region and left maxillary sinusitis (Figure 2). These radiological findings were highly suggestive of Tuberous Sclerosis. MR angiography revealed the absence of involvement of any underlying blood vessels.

**Histopathological Findings:** Microscopic examination of the scalp swelling revealed the presence of lining keratinised stratified squamous epithelium and underlying dermis. Epidermis was thinned out with loss of rete pegs. Dermis showed lobules and nests of nevi cells, hair follicles, sweat glands and sebaceous glands. There was diffuse deposition of melanin pigment and presence of melanocytes around and within hair follicles and sebaceous glands extending up to deep subcutis and infiltrating the fat (Figure 3). All these findings were suggestive of congenital melanocytic nevi.

**Operation and Postoperative Course:** On the basis of the correlation of these imaging findings with the patient’s clinical symptoms, surgery was considered. Excision with primary
skin grafting was done (Figure 4). Graft was taken from the medial aspect of the right thigh. The postoperative result was satisfactory with what the patient could afford.

**Discussion**

Rokitansky in 1961 first described neurocutaneous melanosis in a 14 year female child [8]. CMN are one of several known risk factors for the eventual development of melanoma. CMN are classified into large (≥ 20 cm), medium (1.5 to 19.9 cm) and small (≤1.5cm) nevi according to their size [9]. The term "multiple" is used when more than three lesions are present. NCM is the result of neuroectodermal dysplasia [1]. The exact pathogenesis of NCM is unclear. It is thought to be a result of an error occurring during morphogenesis in the neuroectoderm [10]. NCM is currently diagnosed by the following criteria put forth by Kadonaga and Frieden [10] in 1991: 1) large and/or multiple CMN in association with meningeal melanosis or melanoma; 2) no evidence of cutaneous melanoma, except in patients with histologically benign meningeal lesions; or 3) no evidence of meningeal melanoma, except in patients with histologically benign cutaneous lesions. They also found that 66% of NCM patients had large nevi, and the remaining 34% had numerous pigmented lesions in the absence of a single large congenital melanocytic nevus. In their study, all NCM patients had either posterior midline nevi or head and neck lesions, which suggest that the axial distribution is an important risk factor for developing NCM. Our patient also had a single large-sized CMN with an axial distribution over the scalp with no evidence of meningeal melanoma but had histologically benign cutaneous scalp lesions pointing towards the diagnosis of NCM.

Clinically, patients may present with a mass lesion or increased intracranial pressure due to hydrocephalus, cranial nerve paralysis, myelopathy, convulsive seizures, etc [14]. Most cases of melanoma arising within the GCN occur before puberty [15], with a reported incidence of melanoma of 8.52%, the life-risk is in the range of 2.3% [16-20]. GCMN (Giant congenital melanocytic nevi) occurs approximately in one per twenty thousand people and about a hundred cases had been reported prior to the year 2000 worldwide [21-23]. It is recommended that GCMN be removed soon after the diagnosis due to cosmetic problems and its propensity for malignant change [10, 21, 24-27]. The neurological manifestations of NCM vary with age [10]. Before the age of 2 years, the most common initial clinical signs and symptoms of NCM are related to increased intracranial pressure, including headache (35%), vomiting (42%), generalized seizures (48%), increased head circumference (23%), cranial nerve palsies (26%; in particular VI), papilledema (10%), and meningeal signs (3%) [28]. The subset of patients with a discrete intracranial mass becomes symptomatic when older (mean age, 12.8 years; range, from birth to 65 years) and is more likely to develop focal seizures, localized sensorimotor deficits, difficulties with speech, or psychiatric symptoms [28]. The prognosis of symptomatic NCM is poor. Our patient was asymptomatic at the time of presentation and reported to us only due to aesthetic reasons.

Definite tuberous sclerosis complex is diagnosed by the presence of 2 major features, or 1 major feature plus 2 minor features. Probable tuberous sclerosis complex is indicated by 1 major feature plus 1 minor feature. Possible tuberous sclerosis complex is indicated by either 1 major feature, or 2 or more minor features. The present case pointed towards a definite diagnosis of tuberous sclerosis complex due to the presence of 2 major features i.e. calcified subependymal nodules within the body of the lateral ventricles and cortical tubers, confirmed on MRI. However, there was no history suggestive of TSC in her parents or siblings.
Our patient had congenital giant hairy melanotic nevi of the skin (scalp) which gradually progressed to present as a cutaneous scalp tumour depicting melanoma. NCM is known to be associated with the other neurocutaneous syndromes such as Sturge-Weber, von Recklinghausen’s disease. Associations were also reported with Dandy-Walker complex, spinal lipoma and arachnoid cyst [12,13]. About 100 cases of neurocutaneous melanosis have been reported. However coexistence of tuberous sclerosis with NCM is an unusual finding which to the best of the knowledge of the authors has not been documented so far.

Conclusion

This case warrants further research to provide concrete evidence of such an association. Research should be conducted to prove whether NCM with TSC is an unusual association or a new syndrome. Also, similar cases occurring in other parts of the globe should be documented as it would provide substantial support to such an association. Genetic and molecular investigations with specific tumor markers should be sought for. However due to paucity of facilities in the institution and economic constraints of the patient, detail investigations could not be materialized.

Consent

Written informed consent was obtained from the patient and her father for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SR, PK, MMAS, RJ participated in the clinical diagnosis, sequence alignment, drafting the manuscript and made useful contribution in the revision of the literature. SR, GK and RJ were the operating team of surgeons. PK & RJ participated in writing discussion. PK, SY, GSP, PKA, DS and SS helped in the revision of the manuscript. All authors read and approved the final manuscript.

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References


Legends

Figure 1
Gross appearance of the lesion

Figure 2
Thin White Arrow- The Benign Tumour
Thin Black Arrow- Subependymal nodule with dilated left ventricle
Thick White Arrow- Cortical Dyslasia

Figure 3
Thin White Arrow- Melanin
Thin Black Arrow- Melanocytes
Thick White Arrow- Epidermodermal Junction
Thick Black Arrow-Stratified Squamous Epithelium

Figure 4
Postoperative photograph of the scalp with grafting