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Case Series

Paediatrics Section

Giant Congenital Melanocytic Naevi in Newborns: A Case Series

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ABSTRACT

Giant Congenital Melanocytic Naevi (GCMN) is a very rare condition that mostly occurs due to an oncogenic mutation involving the NRAS (neuroblastoma RAS viral oncogene homologue) gene. GCMNs can be clinically diagnosed due to their typical features, but histopathology confirms the diagnosis. GCMN has a high propensity for transforming into malignant melanoma and leptomeningeal melanocytosis, leading to neurological deficits such as epilepsy and neurofibromatosis. As it is associated with Central Nervous System (CNS) melanosis, Magnetic Resonance Imaging (MRI) of the brain and spine is crucial. Here, three cases are reported of the babies born with GCMN from August 2022 to July 2023 in a tertiary care hospital among a total of 11,915 live births, where the incidence is much higher than found in the literature. Present series describes three cases with GCMN, including clinical features, MRI findings, short-term outcomes, risk factors, and modalities of the management. All three cases showed extensive blackish pigmented patches involving most of the body surface and MRI evidence of Neurocutaneous Melanosis (NCM). The third baby succumbed to death due to fulminant sepsis on day 2 of life. Management of GCMN requires a multimodal approach, including medical, surgical, chemotherapeutic, palliative, and psychological support for patients as well as parents, and follow-up is necessary for the early detection of malignant transformation. Detailed knowledge of this very rare condition may enable us to develop newer treatment modalities to achieve better outcomes in the near future.

Keywords: Leptomeningeal melanocytosis, Malignant melanoma, Multimodal approach, Pigmentation, Skin patch

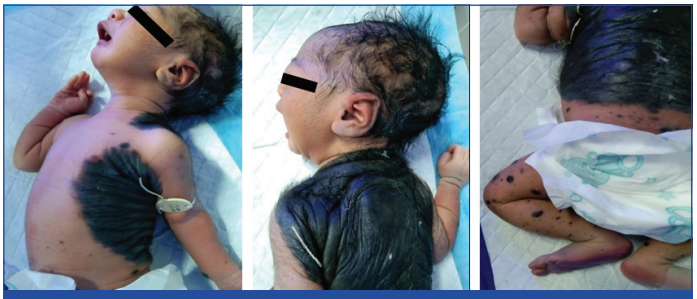
INTRODUCTION

Congenital Melanocytic Naevi (CMN) are benign melanocytic proliferations, present at birth or becoming clinically evident within the first year of life [1]. CMN with a size >20 cm in largest diameter in adulthood is called GCMN, and it is very rare, affecting 1:200,000 live births [2,3]. GCMNs with a size >40 cm in largest diameter in adulthood and involving the trunk are called "garment" naevi and are extremely rare, affecting 1:500,000 live births [4-6]. GCMNs are also called bathing trunk, coat sleeve, or stocking naevi according to the anatomical area of involvement [7]. Apart from cosmetic issues, giant melanocytic naevi have an increased risk of malignant melanoma and NCM [8,9]. The incidence of GCMN in the last year at the study institution was 1:3972, which is much higher than what is found in the literature. Therefore, three cases of GCMN in a case series form are reported.

CASE SERIES

Case 1

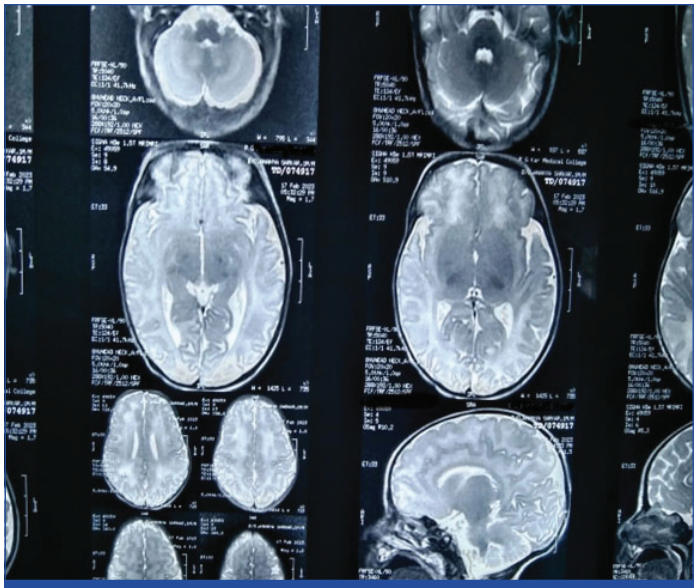
A male baby, born at 38 weeks and weighing 2.8 kg, to a 25-year-old P1, G1 mother from a non consanguineous marriage, presented in the Neonatology department with an extensive blackish pigmented patch with excessive hair. There was no history of a similar lesion in family members or relatives, and the antenatal period was uneventful. The extensive patch (largest diameter 30 cm) was concentrated on the back, trunk, left axilla, and below the left side of the neck, with irregular surface margins and areas of excessive hair growth [Table/Fig-1-3]. Multiple satellite lesions were also scattered over the body and extremities with hypertrichosis [Table/Fig-3]. Apart from the congenital giant naevus, the physical examination was otherwise normal. The baby cried at birth, with a heart rate of 140/min, a respiratory rate of 42/min, and SpO_2 of 96% at room air, with no pallor or cyanosis noted. The baby was feeding well, haemodynamically stable, and no episodes of convulsions, irritability, high-pitched cry, or lethargy were noted.



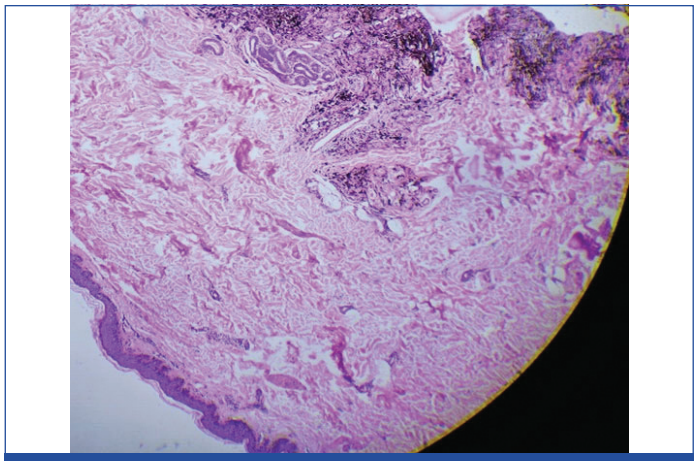
[Table/Fig-1]: Figure shows hyperpigmented lesion in the region above the left clavicle and along the left axilla and extending to chest.
[Table/Fig-2]: Figure shows hyperpigmented lesion along the back along with areas of hypertrichosis in a 'coat-like' manner.
[Table/Fig-3]: Figure shows area of hyperpigmentation along with regions of hypertrichosis on the back along with scattered nevi concentrated on the lower limbs on the back. (Images from left to right)

A contrast-enhanced MRI of the brain revealed diffuse leptomeningeal enhancement in the bilateral cerebral hemispheres suggestive of NCM [Table/Fig-4]. Hyperintensity was also noted along the bilateral cerebellar hemisphere, bilateral frontal and occipital horn of lateral ventricles. The baby was clinically diagnosed with a case of congenital giant melanocytic naevus, confirmed by histopathology which showed involvement of subcutaneous tissue, dermal collagen bundles, skin adnexa, and blood vessels by melanocytic proliferation [Table/Fig-5].

As MRI findings suggested diffuse involvement of the bilateral brain hemispheres, it can act as foci for abnormal electrical discharge in the brain at any time and thus can initiate life-threatening active convulsions. To combat this, prophylactic anticonvulsants were added. The baby was discharged with prophylactic antiepileptics (phenobarbitone @5 mg/kg/day, once a day, to continue until further review), parental counselling, and was advised for a follow-up visit after one week. A dedicated team consisting of dermatologists, plastic surgeons, paediatric surgeons, paediatricians, neonatologists, neurologists, neurosurgeons, radiologists, specialists of radio and chemotherapy, psychiatrists, and counsellors of our institution was formed to make a treatment plan and tackle various issues. In this



[Table/Fig-4]: Contrast enhanced MRI of the brain gave the impression of diffuse leptomeningeal enhancement along bilateral cerebral hemispheres-likely due to neurocutaneous melanosis.

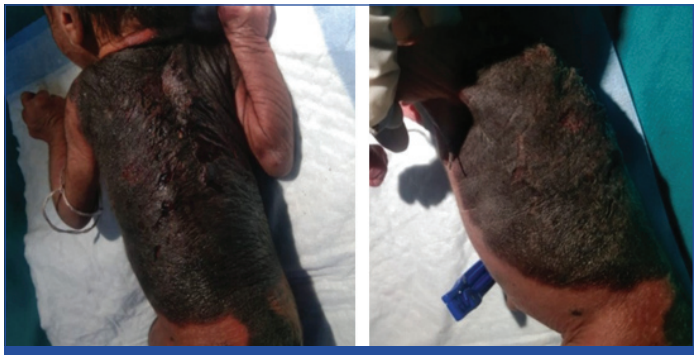


[Table/Fig-5]: Involvement of subcutaneous tissue, dermal collagen bundles, skin adnexa, blood vessels by melanocytic proliferation (H&E, 100x).

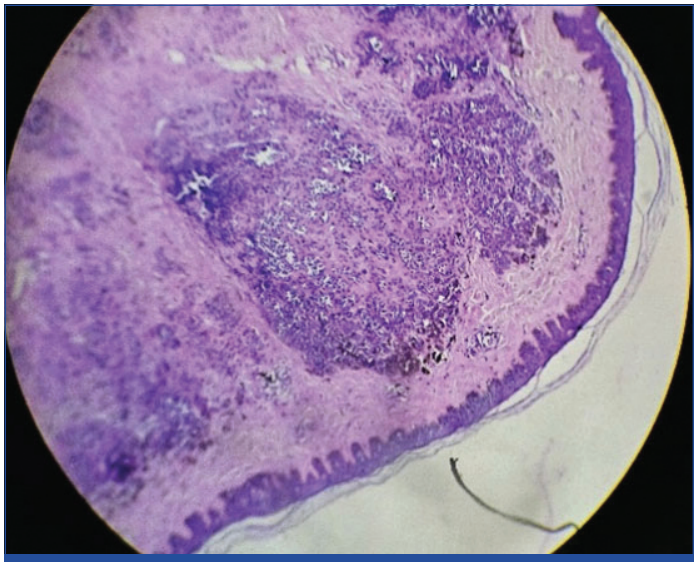
case with Central Nervous System (CNS) involvement evident from MRI, prophylactic anticonvulsants to prevent seizures was planned. During the follow-up visit, the baby was doing well, and breastfeeding was established. The parents were counselled to attend Outpatient Department (OPD) every week for follow-up and to attend the paediatric emergency if needed. The team had planned a staged excision with grafting starting from one month of age.

Case 2

A preterm, 36-week-old, female baby, with low birth weight (2.2 kg), born out of a non consanguineous marriage from a 32-year-old P5G5 mother, by normal vaginal delivery, presented with patches of blackish pigmentation concentrated on the back (largest diameter 21 cm) and some areas of the buttocks with no regions of hair growth [Table/Fig-6,7]. There was no history of a similar lesion in family members and relatives, and the antenatal period was uneventful. On physical examination, one ulcerative lesion (2×1.5 cm) on the back was noted, which eventually showed minute bleeding. Apart from those lesions, the rest of the physical examination findings were within the normal limit. The baby cried at birth, HR-140/min, RR- 44/min, and SpO_2 of 95% at room air, with no pallor or cyanosis noted. It was clinically diagnosed as a case of CMN with haemorrhagic ecchymosis and confirmed by histopathology, which showed involvement of subcutaneous tissue, dermal collagen bundle, skin, adnexa, blood vessels by melanocytic proliferation by Haematoxylin and Eosin stain [Table/Fig-8]. The baby developed feed intolerance on day 3, but there were no episodes of convulsions, irritability, high-pitched cry, or lethargy. The sepsis screen was positive (total leukocyte count 3300/mm^3, Absolute neutrophil count-1400/mm^3, immature; total neutrophil >0.3, C-reactive protein-10 mg/dL), but the Cerebrospinal Fluid (CSF) study was normal, and blood culture was negative. The patient was started on empirical i.v. antibiotics (Inj. cefotaxime @50 mg/kg/dose×8 hrly and Inj. Amikacin @15 mg/kg/dose×24 hourly) for seven days as per the current recommendation by the institutional infection control committee. Both plain and contrast-enhanced MRI of the brain and spinal cord were normal. The baby was discharged after parental counselling and advised to follow-up after one week. On the follow-up visit, the treatment team planned to defer surgical intervention until two months of age, as this was a preterm, low birth weight baby and also suffered from blood-culture-negative sepsis. Till then, symptomatic treatment was planned along with parental counselling. As the initial MRI was normal, the next follow-up MRI was planned after six months.



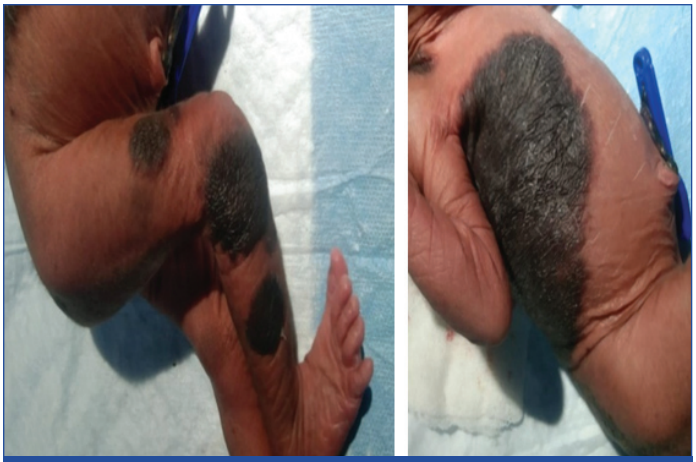
[Table/Fig-6]: Figure shows hyperpigmented patches along back extending over buttocks in a garment like fashion.
[Table/Fig-7]: Figure shows hyperpigmented patch over the region of left axilla and areas below it. (Images from left to right)



[Table/Fig-8]: Nest's of melanocytes in the reticular dermis (H&E,40x).

Case 3

A preterm 33-week-old male child, with low birth weight (2.4 kg), delivered by normal vaginal delivery, born out of a non consanguineous marriage from a 35-year-old P1G1 mother presented with a few scattered hyperpigmented patches of satellite naevi on the right lower limb and a patch of extensive blackish pigmentation (largest diameter 14 cm) on the region below the right axilla and the right side of the chest [Table/Fig-9,10] with no areas of hypertrichosis. A history of maternal gestational diabetes and eclampsia was present during the antenatal period. The baby did not cry at birth and needed resuscitation by positive pressure ventilation with a bag and mask for two minutes, after which spontaneous breathing started, and then the baby was shifted to the Sick Newborn Care Unit (SNCU). At SNCU, the vital parameters were: HR-120/min, SpO_2-90% with O_2, capillary refill time >3 sec, Capillary Blood Glucose (CBG)- 48 mg/dL.



[Table/Fig-9]: Figure shows scattered areas of hyperpigmentation over the right thigh and around the right shin.
[Table/Fig-10]: Figure shows area of hyperpigmentation over the right axilla and areas below it extending over to right chest wall. (Images from left to right)

Arterial blood gas analysis showed metabolic acidosis (pH-7.25, HCO_3-19 mEq/litre). The baby was on O_2, intravenous fluid, nothing per oral, inj. Cefotaxim @50 mg/kg/dose×8 hourly i.v. and inj. Amikacin @15 mg/kg/dose in once a day dosages i.v. was started. At six hours, the baby developed features of shock and hypoglycaemia. Treatment was started as per protocol with intravenous fluid bolus @10 mL/kg/dose with an increasing glucose infusion rate of 10 mg/kg/minute, Epinephrine infusion rate of 0.05 µg/kg/minute, and antibiotics were escalated to inj. meropenem @40 mg/kg/dose 8 hourly along with inj. Amikacin as per institutional antibiotic policy. USG brain on day 1 revealed no abnormality. The baby developed abdominal distension at 22 hours, and gastrointestinal bleeding started at 26 hours, which was treated with inj. vit K @1 mg i.v., Fresh frozen plasma @10 mL/kg/dose, platelet transfusion @10 mL/kg/dose. The baby developed sclerema and convulsions at 28 hours, followed by cardiac arrest and unfortunately succumbed to death on day 2. Sepsis screen was positive, and blood culture revealed the growth of *Klebsiella pneumoniae* later. As the baby succumbed to death on day 2 of life, histopathology of the skin lesion and MRI of the brain and spine could not be done. The baby was clinically diagnosed as a case of giant congenital melanocytic naevus due to its characteristic features. Clinical findings for all the three cases are tabulated in [Table/Fig-11].

DISCUSSION

The CMN are pigmented cutaneous lesions that occur in about 1% of newborns [10]. They are due to a post-zygotic c-met proto-oncogene linked morphogenic error in the neuroectoderm occurring between the 5th and 24th weeks of gestation, causing altered growth, differentiation, and migration of melanoblasts [11,12]. Large and giant CMN mostly involve a mutation in NRAS, while small or medium CMN involve a mutation in the BRAF proto-oncogene [1]. The naevi are larger and deeper if the process starts in the embryonic or early foetal period [11].

Females have a higher prevalence of GCMN with female-to-male ratios ranging from 1.17:1 to 1.46:1 [8], but in present case series, the female-to-male ratio is 1:2. GCMNs are often hairy [13], as seen in 1st and 2nd cases. Among the risk factors, the number of moles in either parent, maternal smoking and ill health during pregnancy, and a history of a similar illness among first-degree relatives contribute to the development of CMN [14-16], but in present case series, only maternal ill health as a risk factor was present in the 3rd case. Thus, no specific risk factor could be identified for the cases. As the incidence rate was much higher, it motivated us to record those cases and report them in a case series form.

CMNs are divided according to their largest diameter in adulthood, as small (<1.5 cm), medium (1.5-19.9 cm), and large/giant (>20 cm), and if >40 cm and involves the trunk, it is called a giant "garment" CMN [2,4]. The adult projected size of CMN can be calculated by multiplying the at-birth value by a numeric value according to the location of the naevus (head-1.7; arm, forearm, hand, feet, hips, torso-2.8; legs-3.3; thigh-3.4) [13]. The three cases met the criteria of giant CMN, being 30 cm, 21 cm, and 14 cm in largest diameter at birth, respectively, with a propensity to increase in size in adulthood [2,13].

The reported lifetime risk for developing melanoma is between 0-4.9% in patients with CMN <20 cm in diameter and between 4.5-10% in patients with giant CMN [13,15]. The risk of malignancy is also increased in the case of larger naevi (>50 cm), axial locations, multiple satellite lesions, the presence of nodules, dark patches, junctional activity, deep dermal neurogenic elements, or a blue naevus component, and solar radiation [9,17]. Axial location and satellite naevi are important risk factors for NCM, as in our first case, and primary CNS melanomas may arise from degeneration of these

	Case 1	Case 2	Case 3
Gestation	**Term**	**Preterm**	**Preterm**
Birth weight	Normal	Low birth weight	Low birth weight
Sex	Male	Female	Male
Antenatal history	Uneventful	Uneventful	Mother had gestational diabetes, eclampsia
Intranatal history	Uneventful	Uneventful	Bag mask ventilation for two minutes
Family history of similar nevus	Absent	Absent	Absent
Location of naevi	Back, trunk, left axilla, left neck	Back, buttocks	Right axilla, right lower limb
Size (Largest diameter)	Largest diameter was 30 cm	Largest diameter was 21 cm	Largest diameter was 14 cm
Satellite lesions	Present	Present	Present
Hypertrichosis	Present	Absent	Absent
Ulcer, bleeding at local site	Absent	Present	Absent
Neurological sign and symptoms	Present	Absent	Present
Blood investigations	Normal	Sepsis screen positive	Sepsis screen positive and blood culture positive for *Klebsiella pneumoniae*
MRI	MRI brain suggestive of neurocutaneous melanosis	Normal	-
Histopathology	Involvement of subcutaneous tissue, dermal collagen bundles, skin adnexa, blood vessels by melanocytic proliferation	Nests of melanocytes in the reticular dermis	-
Treatment	Anticonvulsants prophylactically	Antibiotics	Antibiotics, anticonvulsants , dextrose, ionotropes
Outcome	Discharged with advice for follow-up	Discharged with advice for follow-up	Death

[Table/Fig-11]: Table shows comparison of characteristic features of the three cases in the series.

melanocytes [8,9,18]. Fifty percent of patients with GCMN with NCM become symptomatic before the age of five years [19]. The prognosis is poor, as >50% of patients succumb to death within 3 years and 70% within 10 years [18].

The diagnosis of CMN is primarily clinical. Histological study confirms the diagnosis and rules out malignant transformations [16]. In the histopathology of GCMN, there is often diffuse pandermal, subcutaneous involvement, with nodular proliferations of high cellularity or nuclear atypia [20]. Most CMN lack p16 mutations and show lower p21 and p53 expression compared to malignant melanoma [21], so these markers may help in early detection. MRI of the brain and spine helps in detecting NCM and is also a very important tool for follow-up [9]. In present first case, CNS involvement was evident from MRI before any CNS symptoms appear, so we were able to plan prophylactic oral phenobarbitone syrup (@5 mg/kg/day, once a day). The cerebellum, temporal lobe, amygdala, pons, and medulla are usually involved [9], but in present first case, bilateral cerebellar hemisphere, bilateral frontal and occipital horn of lateral ventricles were involved.

The management of GCMN is multidisciplinary, and a consensus guideline is yet to be formed, as it is a very rare entity with high mortality and morbidity. Medical treatment is mostly symptomatic, but a few cases in the literature have shown a response with BRAF and MEK inhibitors in melanoma with a mutation in the NRAS gene [22]. For surgical treatment, some schools of thought promote curettage within the first two weeks after birth to achieve better cosmetic results and decrease the risk of malignant melanoma [18]. Others state that as one third of malignant lesions do not develop at the base of the naevus [4], so the benefit of early curettage is controversial. Some promote excisional surgery within the first month of life in 2 to 3 sessions with skin grafting [18]. Scalp lesions need tissue expansion [18]. Laser treatment of GCMN is still controversial [18].

A dedicated team consisting of dermatologists, plastic surgeons, paediatric surgeons, paediatricians, neonatologists, neurologists, neurosurgeons, radiologists, specialists of radio and chemotherapy, psychiatrists, and counsellors was formed in present institution to make a treatment plan and tackle various issues of the two surviving neonates. In present first case with CNS involvement evident from MRI, prophylactic anticonvulsants was planned to prevent seizures. As the baby was doing well and breastfeeding was established, we counselled the parents to attend OPD every week for follow-up visits and to attend the paediatric emergency if needed. The team had planned staged excision with grafting starting from one month of age. As the baby had extensive involvement and features of CNS melanosis, the prognosis, as evidenced from available literature, was also explained. The second baby was a preterm, low birth weight baby and also suffered from blood-culture negative sepsis, so the treatment team planned to defer surgical intervention until two months of age. Till then, symptomatic treatment was planned along with parental counselling. As the initial MRI was normal, the next follow-up MRI was planned after six months.

Follow-up every six months for the first five years of life and yearly thereafter is advocated [1]. It can be done by clinical examinations, by matching with serial photographs to detect changes, and MRI of the brain and spine [1]. Due to severe physical disfigurement and stigmata of the lesion, the psychological implications of the patients, parents, and family must be thoroughly addressed and managed with medical therapy, behavioural therapy, counselling as per need to achieve a better outcome [12,18]. Comparison of the findings in the present study with contrast studies is shown in [Table/Fig-12] [7,14,15,17,19].

Author name	Place and Publication year	Age of presentation	Type	Outcome
Present study	India, 2024	Birth	GCMN	One died. Two on follow-up. One of them has leptomeningeal melanosis but clinically no neurological abnormality detected.
van Houten AH et al., [7]	Singapore, 2010	Birth	GCMN	No neurological abnormality/malignant transformation.
Wiecker TS et al., [14]	Germany, 2003	2-7 years	Congenital nevus	Nevi development in children has an association with parental moles.
Kinsler VA et al., [15]	London, 2009	Birth	GCMN	Abnormal neurodevelopment, malignant melanoma.
Rivers JK et al., [17]	Australia, 1995	6-15 years	Atypical nevi, nevi >5 mm	Increased risk of freckling on solar exposure.
Tyagi S et al., [19]	India, 2020	Birth	GCMN	No neurological abnormality/malignant transformation.

[Table/Fig-12]: Comparison of present study with other studies [7,14,15,17,19].
GCMN: Giant congenital melanocytic naevi

CONCLUSION(S)

In this case series of GCMN, no definitive or common risk factor could be identified. Despite the high mortality and morbidity and limited management options, was created step-wise management plan with a multimodal approach involving specialists from various streams of medicine and surgery was created. In the background of a lesser-explored entity and as the consensus guideline is yet to be formed, our message to researchers is that there is a need for more reporting of such cases, formulating a registry of such cases, sharing the experience of treating such cases, adapting a multimodal approach on a case-by-case basis, and long-term follow-up with clinical examinations, serial photographs, and MRI of the brain and spine, so that a better prognosis can be achieved in the near future.

Author's contribution: SM: Contributed to the conception and design of this study, collected the data, performed analysis of facts, interpreted the facts and drafted the manuscript. PB and DH: Contributed to the conception and design of this study, performed analysis of facts, interpreted the informations and facts, drafted and critically reviewed the manuscript. NK: Contributed to the design of this study, performed analysis of facts and critically reviewed the manuscript. AB: Contributed to design of this study, performed analysis of histopathological slides and critically reviewed the manuscript.

REFERENCES

[1] Kliegman E. Congenital Melanocytic Nevus, Nelson Textbook of Pediatrics, 21st ed. Philadelphia: Elsevier:2020;2:3470.
[2] Callen JP, Kopf AW, Bart RS, Hennessey P. Congenital melanocytic nevi and malignant melanomas. J Am Acad Dermatol. 1979;1(2):123-30.
[3] Castilla EE, da Graça Dutra M, Orioli-Parreiras IM. Epidemiology of congenital pigmented naevi: I Incidence rates and relative frequencies. Br J Dermatol. 1981;104(3):307-15.
[4] Krengel SA, Hauschild, TS. Melanoma risk in congenital melanocytic naevi: A systematic review. Br J Dermatol. 2006;155(1):01-08.
[5] Rhodes AR. Melanocytic precursors of cutaneous melanoma. Estimated risks and guidelines for management. Med Clin North Am. 1986;70(1):03-37.
[6] Rhodes AR, Weinstock MA, Fitzpatrick TB. Risk factors for cutaneous melanoma: A practical method of recognising predisposed individuals. JAMA. 1987;258(21):3146-54.
[7] van Houten AH, van Dijk MC, Schuttelaar ML. Proliferative nodules in a giant congenital melanocytic nevus-case report and review of the literature. J Cutan Pathol. 2010;37(7):764-76.
[8] Bittencourt FV, Marghoob AA, Kopf AW, Koenig KL, Bart RS. Large congenital melanocytic nevi and the risk for development of malignant melanoma and neurocutaneous melanocytosis. Pediatrics. 2000;106(4):736-41.
[9] Foster RD, Williams ML, Barkovich AJ, Hoffman WY, Mathes SJ, Frieden IJ. Giant congenital melanocytic nevi: The significance of neurocutaneous melanosis in neurologically asymptomatic children. Plast Reconstr Surg. 2001;107(4):933-41.
[10] Rhodes AR. Benign neoplasias and hyperplasias of melanocytes. In: Fitz Patricks Dermatology in General medicine year. (5th) 1999:1026-32.

[11] Viana AC, Gontijo B, Bittencourt FV. Giant congenital melanocytic nevus. Anais Brasileiros De Dermatologia. 2013;88(6):863-78.
[12] Takayama H, Nagashima Y, Hara M. Immunohistochemical detection of the c-met proto-oncogene product in the congenital melanocytic nevus of an infant with neurocutaneous melanosis. J Am Acad Dermatol. 2001;44(3):538-40.
[13] Marghoob AA, Schoenbach SP, Kopf AW, Orlow SJ, Nossa R, Bart RS. Large congenital melanocyte nevi and the risk for the development of malignant melanoma. A prospective study. Arch Dermatol. 1996;132(2):170-75.
[14] Wiecker TS, Luther H, Buettner P, Bauer J, Garbe C. Moderate sun exposure and nevus counts in parents are associated with development of melanocytic nevi in childhood. Cancer. 2003;97(3):628-38.
[15] Kinsler VA, Birley J, Atherton DJ. Great ormond street hospital for children registry for congenital melanocytic naevi: Prospective study 1988-2007. Br J Dermatol. 2009;160(1):143-50.
[16] Endomba FT, Mbega CR, Tochie JN, Petnga SN. Giant congenital melanocytic nevus in a Cameroonian child: A case report. J Med Case Rep. 2018;12(1):175.
[17] Rivers JK, MacLennan R, Kelly JW, Lewis AE, Tate BJ, Harrison S, et al. The Eastern Australian childhood nevus study: Prevalence of atypical nevi, congenital nevus-like nevi, and other pigmented lesions. J Am Acad Dermatol. 1995;32(6):957-63.
[18] Oranje AP. Practical Pediatric Dermatology. 1st ed. Switzerland: Springer; 2016:91-97.
[19] Tyagi S, Kumar B, Kumar MK. Giant congenital melanocytic nevus: A rare case report. Int J Contemp Pediatr. 2020;7(11):2236-38.
[20] Barnhill RL, Fleischli M. Histologic features of congenital melanocytic nevi in infants 1 year of age or younger. J Am Acad Dermatol. 1995;33(5 Pt 1):780-85.
[21] Herron MD, Vanderhooft SL, Smock K, Zhou H, Leachman SA, Coffin C. Proliferative nodules in congenital melanocytic nevi: A clinicopathologic and immunohistochemical analysis. Am J Surg Pathol. 2004;28(8):1017-25.
[22] Salgado CM, Basu D, Nikiforova M, Bauer S, Johnson D, Rundell V, et al. BRAF mutations are also associated with neurocutaneous melanocytosis and large/giant congenital melanocytic nevi. Pediatr Develop Pathol. 2015;18(1):01-09.

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