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A case series of congenital nevus and their various manifestations

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ABSTRACT

A nevus is characterized by collection of partially differentiated or well-differentiated cells normally found in the skin. Some nevi are associated with disorders such as autism, epilepsy, ophthalmogical disorders, intracranial abnormalities, and others. In this case series, we aim to analyze six cases with congenital nevus, matched our findings with case reports published and reviewed the literature, to come to a conclusion that would help the clinician to do focused clinical examination and investigations when they come across such nevi. Furthermore, as these sort of skin lesions cause psychological morbidity to both parents and patients, proper counseling is required along with dermatological therapy and treatment of comorbid conditions. As well as regular follow-up with monitoring of the lesions. The following are the cases: Case-1, is a case of congenital melanocytic nevi who presented with delayed milestone, epilepsy and neuroimaging revealed intracranial melanosis. Case-2 nevus of Ota on face with scleral nevus and glaucoma in the left eye. In Case-3: Nevus achromicus was present over the abdomen and scalp in a child who presented with status epilepticus and there was focal cortical dysplasia of left frontal cortex on imaging. Nevus sebaceous was present in case-4 who had seizure disorder but neuroimaging was normal. Case-5 child had nevus spilus over left frontal area with melanocytic satellite nevi who presented with febrile convulsion but normal neuroimaging. The sixth case is a 5-year-old male child with linear nevus without any other association.

Key words: Congenial nevus; Melanocytic nevi; Nevus of Ota; Nevus achromicus; Nevus spilus; Nevus sebaceous; Melanocytic satellite nevus; Linear nevi; Facial nevus; Neurocutaneous melanosis; Nevus depigmentosus

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INTRODUCTION

A nevus is characterized by collection of partially differentiated or well differentiated cells normally found in the skin. There are two categories of melanocytic nevi, Acquired nevi (those that appear after birth) and congenital nevi (present at birth). A nevus can be hypopigmented, whitish, or hyperpigmented with various shades of brown.[1] Happle proposed a definition of nevus as "Nevi are visible, circumscribed, and long-lasting lesions of the skin or the neighboring mucosa, reflecting genetic mosaicism. With the exception of melanocytic nevi, they do not show neoplastic growth."[2] Sometimes, nevus are associated with various underlying systemic diseases like in congenital melanocytic nevus.[3,4] In our series leptomeningeal and parenchymal satellite nevus, autistic spectrum disease was associated with the nevi found superficially.

We report six cases of congenital nevi with various types of manifestation along with systemic manifestation in some cases, which will be very much helpful for a clinician to predict conditions associated with these congenital nevi.

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Case 1 (Melanocytic nevi)

A 2-year-old male child presented with recurrent convulsions for 6 months of age. On examination, multiple

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medium and small melanocytic nevus were present on the face, hands and few similar lesions were found on the trunk, size of which varied from medium nevi (1.5–20 cm) to small nevi (<1.5 cm) in diameter (Figure 1a and b).[1] The baby had autistic traits and delayed motor component of development. T1-weighted images of magnetic resonance imaging (MRI) brain had focal high intensity signals at multiple areas of the brain including the temporal lobes, pons, and medulla, highly suggestive of melanosis. There was no evidence of hydrocephalus. Ultrasonography (USG) of abdomen and echocardiography with Doppler was normal. The child was kept under follow-up with antiepileptic medication and behavior modification therapy for autism.

Case 2 (Nevus of Ota)

A 5-year-old male child presented with bluish discoloration of sclera of left eye noticed for 3 months of age and multiple speckled hyper pigmented macules along the ophthalmic (V1), and maxillary (V2) divisions of the left trigeminal cranial nerve suggestive of nevus of Ota which were gradually increasing in size with age (Figure 2). He had no other systemic involvement. Oral mucosa was normal. On ophthalmic examination, intraocular pressure (IOP) of the left eye was raised (15 mmHg) and that of the right eye was normal (10 mmHg), Antiglaucoma medication was started. Hearing assessment was normal. The child was advised to avoid direct exposure to sunlight and to apply sunscreen routinely. He was referred to ophthalmologist and dermatologist for further care. Parent was counseled for regular follow-up.

Case 3 (Nevus depigmentosus)

A 15-year-old boy presented to emergency with status epilepticus which required multiple antiepileptic medications, ventilatory care, and other supportive measures. Convulsion was focal to start with and was left-sided progressing to a secondarily generalized one. On examination, there were macular hypopigmented patches or streaks with bizarre irregular borders over right chest, stopping abruptly at the midline, without surrounding hyperpigmentation (Figure 3a). A hypopigmented non-progressive horizontal patch over right lower abdomen, triangular in shape measuring 25 cm by 8 cm, starting from midline and tapering laterally was seen, which was present since birth and progressively increasing in size. There was no sensory deficit over the patch. There was a similar hypopigmented patch of size 1.5 cm × 2 cm found over right anterior scalp. On woods lamp examination by dermatologist, the patch appeared off-white, without fluorescence (versus chalk-white accentuation which is seen in vitiligo). Diascopy was found to be negative. Dermoscopy of achromic naevus revealed serrated border, pallor, and faint pigmented network. No other neurocutaneous stigmata was seen in the child. On examination, the child was afebrile. There were no apparent neurological deficits. Examination of respiratory, cardiac, and gastrointestinal systems did not reveal any significant abnormality. The MRI brain showed focal cortical dysplasia of left frontal cortex (Figure 3b and c). The nevus lesion fulfilled the criteria given by Coup (1976) for clinically diagnosing Nevus depigmentosus.[5] In literature review, we found extracutaneous manifestations with nevus achromicus are seizures, mental retardation, unilateral limb hypertrophy, atopic dermatitis, and abnormal systemic features.[5] This emphasizes the need for screening for underlying problems in cases of nevus achromicus found superficially. The child was kept on antiepileptic medication and follow-up by dermatologist with counseling.

Case 4 (Nevus sebaceous)

A 1-month-old male baby presented with subtle seizure in the form of intermittent staring look lasting for 2–3 min occurring several times in a day. Biochemical parameters such as blood sugar, serum calcium, and electrolytes were

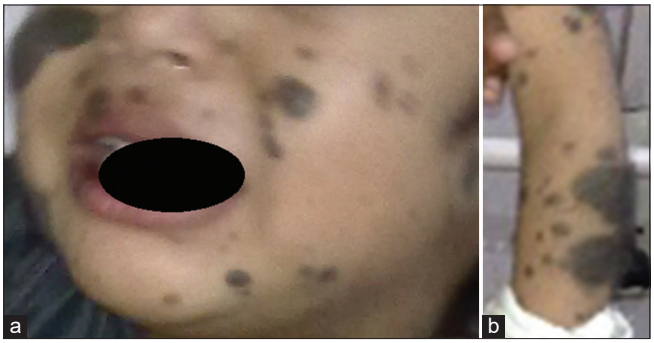

Figure 1: (a) Clinical photograph of a 2-year-old boy (Case 1) with multiple medium and small melanocytic nevus present on the face. (b) Clinical photograph of a child (Case 1) with multiple medium and small melanocytic nevus present on the hand

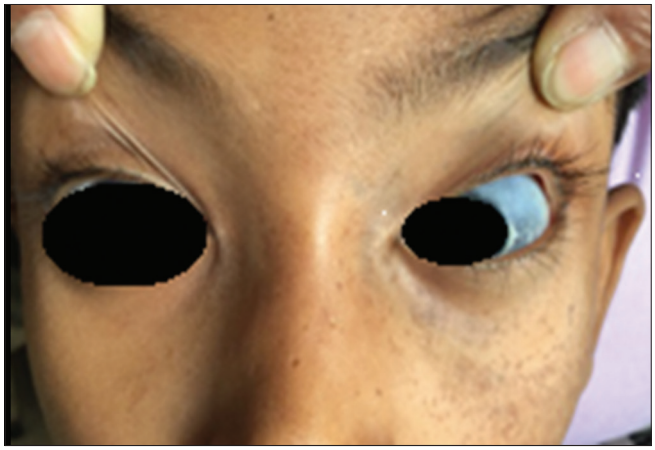

Figure 2: Clinical photograph of Case-2 showing bluish discoloration of sclera of the left eye and multiple speckled hyper pigmented macules along ophthalmic (V1), and maxillary (V2) divisions area of face innervated by the left trigeminal cranial nerve (nevus of Ota)

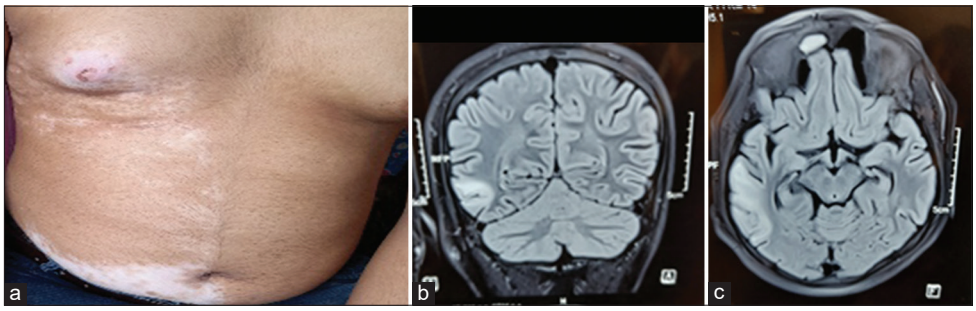

Figure 3: (a) Clinical photograph of 15-year-boy (Case 3) having nevus achromicus in right trunk. (b) Magnetic resonance imaging (MRI) brain of Case 3 showing focal cortical dysplasia of the right frontal cortex. (c) MRI brain of Case 3 showing right temporal focal cortical dysplasia.

normal. On examination, a well-defined greasy yellowish localized patch was found over the Left forehead adjacent to the hairline with loss of hair suggestive of sebaceous nevus (Figure 4). Neurological examination was normal. No significant abnormalities in any other system were noted. The child was delivered at term to non-consanguinous parents by normal vaginal delivery, cried at birth. No family history of convulsion was reported. MRI brain, ophthalmological examination, and skeletal survey was normal. Electro encephalography (EEG) revealed seizure disorder and child was started on anticonvulsant therapy with regular follow-up for neurological and ophthalmological examination.

Case 5 (Nevus spilus)

A 9-month-old male child presented with febrile convulsion. The child was born at term, out of non-consanguinous marriage. There were no significant antenatal and postnatal issues and the child was developing normally. On examination, a large light brown macular patch was found over left frontal area and forehead within which multiple darker flat or raised brown melanocytic satellite nevi, some being hairy, were present (Figure 5). The lesion was there since birth involving a small area but as baby grew, size and number both increased proportionately. The baby was evaluated with MRI brain, EEG, and USG abdomen but no abnormality was detected. The above skin lesion was suggestive of nevus spilus. The child was advised to be under close follow-up of dermatologist and serial photography of the lesions to be kept to detect any changes at the earliest.

Case 6 (Linear nevus)

A 5-year-old male child presented with brown colored raised linear lesion over forehead and base of the nose extending up to the tip of the nose. This linear mark was present since birth and progressively increased in size and became more prominent as the child grew (Figure 6). Clinical examination of central nervous system, eye examination, and other systemic examination including musculoskeletal system was normal. The child had normal developmental milestones. The skin lesion was suggestive of linear nevus. MRI brain did not reveal any abnormaly. Parents were counseled and the child has been kept under regular follow-up under dermatologist.

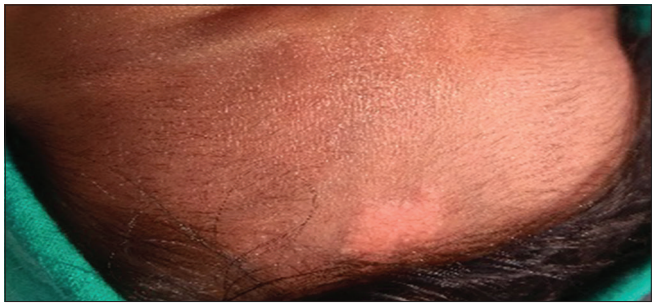

Figure 4: Clinical photograph of 1 month boy with sebaceous nevus over left forehead

DISCUSSION

Facial nevus are isolated and restricted to the face or it can be distributed to other body parts. Nevus may be melanocytic or non-melanocytic. Melanocytic nevi are benign clusters of nevus cells at the dermoepidermal junctions having various alterations and proliferations throughout the life up to fourth decade. Repeated sun exposure and photo injury make them prone to surface changes and future malignancy. The non-melanocytic nevus such as nevus achromicus is characterized by presence of nevus cell of neuroectodermal origin of neural crest lineage. Nevus cells have their embryonic origin from neural crest cells irrespective of their melanocytic or non-melanocytic types. Various problems arising out of non-uniform and abnormal migration of neural crest cell such as Hirsh sprung disease and various aganglionosis may be associated. Up to 30% cases of cutaneous nevus is associated with central nervous system and other anomalies.[1] In our series, two cases have central nervous system presentation with refractory seizures and MRI brain showed high intensity signal areas at multiple areas of the brain (Case 1) and focal cortical dysplasia in nevus achromicus (Case 2). Hence, when a clinician finds a congenital nevus, should be able to identify it and try to look for the underlying associations.

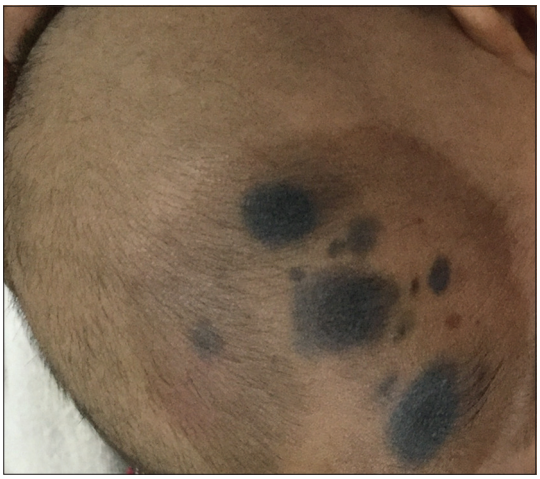

Figure 5: Clinical photograph of a 9-month-old baby with Nevus spilus over left frontal area and forehead

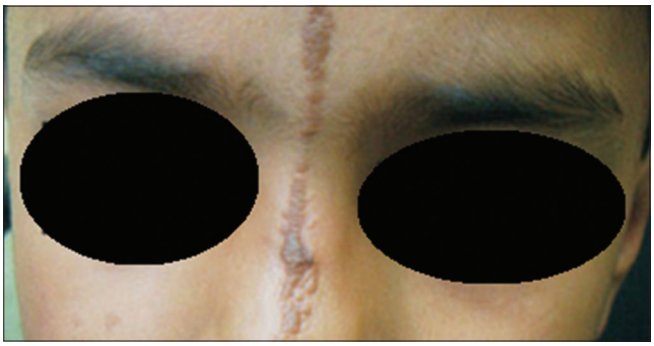

Figure 6: Clinical photograph of a 5-year-old male with linear nevus over forehead and nose

Case 1 (Melanocytic nevi)

Neurocutaneous melanosis is a rare congenital syndrome characterized by the association of large or multiple congenital melanocytic nevi associated with or without benign or malignant melanotic tumors in the central nervous system. Large and giant congenital nevi often harbor NRAS mutations, while BRAF mutations typically seen in regular melanocytic nevi are most common in small or medium congenital nevi. Development of melanoma in a small congenital nevus is rare before puberty, hence removal of all small congenital nevi is not warranted. Leptomeningeal involvement occurs most often when the nevus is located on the head or midline on the trunk, particularly when associated with multiple "satellite" melanocytic nevi (>20 lesions).[6,7] Nevus cells within the leptomeninges and brain parenchyma may cause increased intracranial pressure, hydrocephalus, seizures, intellectual disability, and motor deficits or may undergo transformation into melanomas. MRI demonstrates asymptomatic leptomeningeal melanosis in 30% of individuals with giant congenital nevus.[8] The overall incidence of malignant melanoma arising in a giant congenital nevus is 1–2% with high mortality. The risk of melanoma is greater when the predicted adult size of the nevus is >40 cm, lesions on trunk, presence of satellite lesions, and the nevus over the head or spine. MRI may detect neural melanosis, the presence of which makes gross removal of a nevus from the skin a futile effort. MRI of the brain and spine should be performed in any high-risk patient exhibiting neurologic symptoms. However, we also suggest that asymptomatic and high-risk patients be screened for neurocutaneous melanosis with gadolinium-enhanced MRI of the brain and spine (ideally during the first 6 months of life) before myelination is complete, as myelination may obscure the evidence of melanosis. Asymptomatic neurocutaneous melanosis is detected by MRI in 5–25% of infants and children with high-risk. In a 5-year follow-up study, only one of 10 patients with MRI findings suggestive of central nervous system melanosis progressed to develop neurologic symptoms.[8] Other malignancies, such as rhabdomyosarcoma, liposarcoma, and malignant peripheral nerve sheath tumors, also have been reported.

In Case-1 of this case series, the 2-year-old male child had multiple medium and small melanocytic nevus over face and trunk. He was epileptic and on anticonvulsant medication. He had global developmetal delay with autistic traits. T1-weighted images of MRI brain revealed focal high intensity signal areas at multiple sites of the brain including the temporal lobes, pons, and medulla which was highly suggestive of melanosis, There was no evidence of hydrocephalus; however, USG abdomen and echocardiography were normal. It is recommended that these children should be followed up every 6 monthly for 5 years and yearly thereafter. Serial photographs of the nevus taken by the parents may aid in detecting early changes.

Case 2 (Nevus of Ota)

Nevus of Ota (also known as nevus fuscoceruleus ophthalmomaxillaris or oculodermal melanocytosis) was first reported by Hulke in 1860 before Ota's description in 1939. It is characterised by unilateral, patchy, irregular, and grey discoloration of skin supplied by ophthalmic and maxillary divisions of trigeminal nerve, especially the regions of periorbital areas, temples, malar prominence, forehead, and nose. It results from an abnormal migration of melanoblastic cells of the primitive neural tube along the first and second divisions of the trigeminal nerve during embryogenesis.[9] Nevus of Ota differs from a more common dermal melanotic patch, by having a speckled pattern rather than a uniform appearance. The etiology of nevus of Ota is presumed to be similar to that of mongolian spots, involving errors in melanocyte migration from the neural crest to the epidermis. Unlike mongolian spots, nevus of Ota does not become fade or resolve with time, and may rather increase in size and colour intensity. Lesions are present at birth in 50% of affected individuals, with a second peak of onset around puberty.[10,11]

There may be patchy involvement of the conjunctiva, retina, hard palate, pharynx, nasal mucosa, buccal mucosa, or tympanic membrane and leptomeninges. Malignant change is extremely rare. The most serious complications include glaucoma and transformation to malignant melanoma and associated deafness. Successful treatment of the nevus has been achieved with Q-switched ruby and Q-switched YAG laser surgery. CNS melanocytosis has been reported in association with nevus of Ota. Progressive ipsilateral sensorineural deafness has also been reported with nevus of Ota. Different disorders such as Sturge–Weber syndrome, Klippel–Trenaunay syndrome, neurofibromatosis, multiple hemangioma, spinocerebellar degeneration, ipsilateral deafness, and cataract have been associated with nevi of Ota.[12]

In Case-2 in this series, the 5-year-old male child is having Nevus of Ota along the ophthalmic (V1) and maxillary (V2) divisions area of the left trigeminal nerve (Tanino Type II) and also over sclera of the left eye (Figure 2). Based on the extent and distribution, Tanino has classified nevi of Ota as: Type I: Mild, Type II: Moderate (as seen in our patient's case), Type III: Intensive, and Type IV: Bilateral.[13]

Ophthalmic examination was normal for both eyes except for the left ocular nevus. Hearing was normal. The child was advised to avoid direct exposure to sunlight, routinely to apply sunscreen. He was referred to dermatologist for dermatological care and the parents have been counseled for regular follow-up.

Case 3 (Nevus achromicus)

Nevus achromicus (also called nevus depigmentosus or achromic nevus) is a benign, congenital, non-familial, and non-progressive hypopigmented macule or patch present from birth. It is commonly found on the trunk, but may also present on the limbs or elsewhere. It is solitary in 50% of cases and may follow Blaschko lines. These nevi are usually light colored spots often solitary or may be present as multiple whorls or streaks. They are usually stable in their shape but the size gradually increases in proportion to the growth of the child. Coupe identified diagnostic criteria for achromic naevus in 1976:

1. The patch of pale skin is present at birth or early in life
2. It remains in the same site throughout lifetime
3. There is no alteration in texture or change in sensation in the lesions
4. There is no dark border around the affected skin.

This nevus needs to be differentiated from vitiligo and Ash leaf macules clinically.

Achromic nevus (naevus depigmentosus) is not completely white, unlike vitiligo which completely lacks melanocytes. Achromic nevi are usually solitary, whereas ash-leaf spots found in tuberous sclerosis have characteristic leaf like appearance and may be multiple. The pathology behind this nevus is that it is caused by an altered clone of melanocytes (pigment cells) with a decreased ability to make melanin (brown pigment). Melanocyte numbers are normal or reduced in number or it may be that melanosomes are reduced within the melanocytes and/or keratinocytes suggesting impaired transfer. Wood lamp examination: Achromic naevus appears off-white, compared to the chalk-white accentuation seen in vitiligo.[14,15] Dermoscopy of achromic naevus: Serrated border, pallor, and faint pigment network. Skin biopsy: Normal or slightly reduced melanocyte numbers with decreased melanin. Treatment of achromic naevus is often unnecessary. Cosmetic camouflage may be helpful. Extra-cutaneous manifestations in the form of seizures, mental retardation, and unilateral limb hypertrophy have been rarely reported.[16] Care should be taken with sun exposure since these area can sunburns easily.

The 15-year-old boy (Case 3 in this series) with nevus achromicus over trunk, limbs, and face from birth had cortical dysplasia of left frontal cortex in MRI brain and refractory convulsion which required antiepileptic drugs (Figure 3a and b).

Case 4 (Nevus sebaceous)

Nevus sebaceous, also called nevus sebaceous of Jadassohn or organoid nevus, is a benign hamartoma of the skin, characterized by hyperplasia of the epidermis, immature hair follicles, sebaceous, and apocrine glands. Lesions are usually present at birth and appear as waxy, yellow-orange or tan, and hairless plaques. They have a tendency to thicken and become more verrucous over time, especially around the time of puberty. Nevus Sebaceous and Nevus Sebaceous syndrome (Schimmel Penning syndrome) are thought to be caused by post zygotic mutation in the HRAS and KRAS genes although isolated cases due to mosaic mutation NRAS mutation and FGFR2 have also been reported which are mosaic RASopathies.[17] RAS promotes cell growth through activation of mitogen activated protein kinase (MAPK). Several inherited malformation syndromes (for example Costello syndrome, Noonan syndrome, Neurofibromatosis 1, Legius syndrome) are caused by activation of germ line mutations in this gene, some of which are associated with increased risk of cancer.[18] Schimmelpenning syndrome is caused by extensive mosaicism for activating mutations involving the skin, skeletal, ocular, and central nervous systems.

The risk of malignancy increases with age, but basal cell carcinomas have also been reported in children. No additional evaluation is needed for children presenting with a small and

solitary nevus sebaceous. However, in patients with large or extensive lesions and suspected nevus sebaceous syndrome, a thorough neurologic and ophthalmologic examination should be performed. Additional evaluation is based on clinical findings and may include electroencephalography, neuroimaging studies with MRI, skeletal radiography, and analysis of liver and renal function, including urine calcium and phosphate levels. Affected individuals may also have abnormalities affecting the brain such as seizures or intellectual impairment, the eyes such as clouding (opacity) of the cornea or coloboma of the iris or retina (coloboma), and the skeleton such as spinal malformations, craniofacial defects, and deformities of the hands and legs.

In our Case 4 of this series, a 1-month-old male baby presented with subtle seizure who had a well-defined greasy over the left forehead (Figure 4). EEG revealed seizure disorder however neuroimaging, ophthalmological examination and skeletal survey were normal and the child was put on anticonvulsant therapy with neurological and ophthalmological follow-up.

Case 5 (Nevus spilus)

Nevus spilus is a pigmented skin lesion, either congenital or acquired, consisting of a large light tan patch, containing macules or papules. Usually, these superimposed lesions are numerous, small circumscribed, dark brown in color, flat, or slightly raised. Clinically, it is distinguished into small or medium-size (≤20 cm) and giant or segmental/zosteriform Nevus spilus.[19,20] It can be seen most commonly on the chest and upper limbs. Nevus spilus was first described by Burkley in 1842 as evenly pigmented patches and Ito and Hamado in 1952 were the first to apply the term Nevus spilus to speckled lesions. Although it is a benign lesion, cases of melanoma arising in Nevus spilus have been published. The development of Nevus spilus starts at birth as a hyper-pigmented patch (cafè-au-lait spot), and, according to River, reaches its peak in number between the ages of five and nine, and it has its characteristic speckled appearance between the ages of 6 and 39. As many lesions disappear between the ages of 31 and 60, Kopf suggested that some forms of Nevus spilus may regress or completely disappear in time, similar to acquired nevi.

In Case-5 of this series, the 9-month-old boy had nevus spilus over left frontal area without any neurocutaneous manifestation. The child has been kept under regular follow-up and regular dermatological examination with dermoscopy for the progress of the melanocytic satellite nevus. The malignant transformation of Nevus spilus is a very rare and low absolute risk.

Case 6 (Epidermal nevi)

Epidermal nevi are usually present since birth or appear during the 1st year of life.[2] Initially, they appear as mild linear patches or thin brown plaques which may be verrucous. Gradually around puberty, they become darker and thicker. These lesions can be solitary or multiple, large, or small and usually located on the trunk or extremities.[2] Rarely they may involve the oral mucosa. Lesions tend to have sharp midline demarcation and follow linear patterns on the skin known as "lines of Blaschko".[21,22]

Linear nevus sebaceous syndrome result from genetic mosaicism occurs in 1 in 1000 live births.[21] The mutations occurring very early in embryonic development tend to give rise to more extensive epidermal nevi and may potentially affect additional organ system. The children usually present with seizures and mental retardation. Abnormalities in cardiovascular system (coarctation aorta and ventricular septal defect) and ophthalmology (lipodermoid scleral tumor, microphthalmia, corneal opacities, and coloboma) may be associated. Hence, physicians need to be aware of the possible underlying features when a linear nevus is found especially in the midline.[3,22,23]

In Case no 6, the 5-year-old male child had linear nevus over the midline in the forehead extending up to the tip of the nose present since birth and progressively increasing in size (Figure 6). No intracranial, ophthalmologic cardiovascular, or musculoskeletal abnormalities were detected on screening. Parents were counseled regarding the condition and possible progress and complication. He has been kept under regular follow-up of dermatologist.

CONCLUSION

Whenever a clinician detects a congenital nevus in a patient, a thorough clinical examination and relevant investigations should be done keeping in mind the organ systems involved with different types of nevi. Proper counseling should be done to the parents regarding the condition, its associations, progress, and future morbidities. Regular follow-up with concerned specialties needs to be stressed.

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