

## Schimmelpenning syndrome (Epidermal Nevus Syndrome): A case report

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### ABSTRACT

Epidermal nevus syndrome (ENS) describes occurrence of a nevus sebaceous or an epidermal nevus with other developmental anomalies of eye, skeletal, central nervous, cardiovascular and urogenital systems. We report here a neonate with an extensive nevus sebaceous (NS), congenital giant melanocytic nevus (CGMN), multiple small and large melanocytic nevi, central nervous system and eye abnormalities, and seizures fitting into this rare neurocutaneous disorder and briefly review the literature and current concepts.

### CASE REPORT

A 2-day-old male baby born to a 30-year-old primigravida at full term by forceps delivery was referred by the pediatric department for dermatologic consultation for the multiple extensive skin lesions the neonate had since birth. There was no history of any drug intake except haematinics and calcium, or exposure to radiation to the mother during the pregnancy. She was not diabetic and was not on any other medication. The parents were non-consanguineous. There was no family history of similar lesions in both the parents. Cutaneous examination of the baby revealed a single, giant, soft, black plaque with increased hair covering his scalp, neck, back and part of the chest. The surface of the plaque was rugose at many places (Fig. 1). There were multiple, firm, 0.5 cm, dome shaped papules within the plaque. A single, 3.0cm, soft, compressible swelling which could be easily pushed into a button shaped hole

in the skin was present on the surface of this black plaque in the interscapular region. In addition there were numerous black, indurated, papules, nodules and plaques (1.0-8.0cm) scattered all over the limbs, abdomen, face and neck (Fig. 2).

A single, linear, band shaped, yellow plaque with velvety surface was present on the face and scalp extending from the lower lip in the midline to the left temporal and parietal region of the scalp, and the left auricle traversing the chin, the submental and the left mandibular regions (Fig. 3). The plaque was thrown into cerebriform folds over the scalp. A firm pedunculated skin colored 1.0cm nodule was present within the yellow plaque over temporal region.



**Fig. 1** Congenital-giant-melanocytic-nevus (bathing-trunk nevus) on the scalp, neck, trunk and arms with multiple smaller nevi.

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The left ear lobe was larger than the right. Giant hairy pigmented plaque and the yellow cerebri-form plaques were present concomitantly on the same areas over temporal and parietal regions of the scalp (Fig. 4). On the chin and submental area only the yellow plaque was present whereas on the trunk only the hairy plaque was present. His nails, palms, soles, oral cavity and genitalia were normal.



**Fig. 2** CGMN on the scalp, trunk and arms with multiple small and large nevi.



**Fig. 3** Linear yellow band shaped plaque of nevus sebaceous in the midline on the face.



**Fig. 4** Concomitant CGMN and NS on the scalp.

His cardiovascular, respiratory and skeletal system examinations were normal clinically. However, ophthalmic examination revealed multiple melanocytic patches on the inner aspects of eyelids and encroachment by the pigmented lesions over the cornea in both eyes. Limbal dermoid was found in the right eye (Fig. 2). Pupils were normal. Fundus examination revealed retinal pigment hypertrophy in both eyes, and choroid retinal atrophy in the right eye.

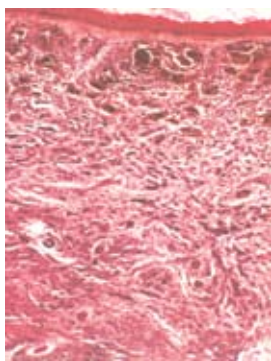
Clinical diagnoses of congenital-giant-melanocytic-nevus (CGMN) for the large dark lesion on the trunk, face, and scalp; multiple congenital melanocytic nevi (CMNs) for the numerous dark lesions on the trunk, face, and limbs; nevus sebaceous (NS) for the yellow cerebri-form linear plaque on the face and scalp and skin tag or accessory tragus for the pedunculated skin colored nodule within the NS on the temporal region were made.

Laboratory investigations revealed normal CBC and clinical chemistry. Serum calcium and phosphate levels were normal. The urinalysis, chest x-ray, x-ray examination of long bones and skull, ECG and echocardiography were normal. Ultrasonography of the abdomen and chest did not reveal any visceral abnormality.

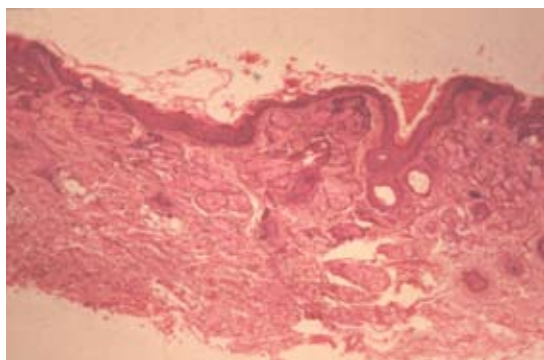
A CT scan of the brain showed a large non-enhancing CSF density cavity in the left temporal fossa and sylvian cistern. A fat density area was seen in the left CP angle in the cisternal region. Left fronto-temporo-parietal hypoplasia with agyria/pachygyria was noted in the left temporo-occipital region with associated lateral ventricular dilatation. Bone window demonstrated no bony erosion but showed pressure effect. Findings were suggestive of a large temporal arachnoid cyst with underlying temporal and fronto-parietal migration defect (agyria/pachygyria) and lipoma in the left

CP angle.

A skin biopsy from the CGMN on the trunk showed nests of nevus cells in the upper dermis. Spindle shaped melanocytes lying singly and in cords and melanophages were present in the deeper dermis (Fig. 5). Biopsy from the NS lesion on the temporal region showed acanthosis, papillomatosis and multiple mature sebaceous gland lobules in the upper dermis (Fig. 6). A biopsy from the site where both the CGMN and NS were present concomitantly showed features of nevus sebaceus in the upper dermis and nests of melanocytic nevus cells in the dermis in the same section (Fig. 7).

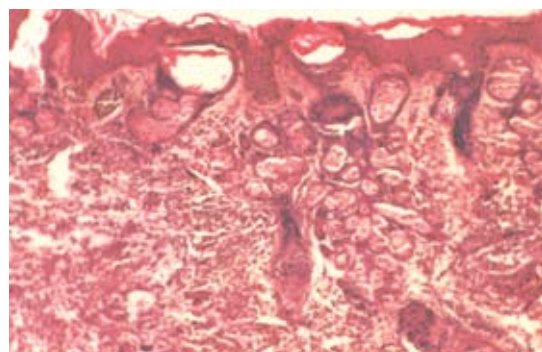


**Fig. 5** Biopsy from the CGMN showing nests and cords of nevus cells, and large spindle shaped melanophages through out the dermis. (H & E, x 10X)



**Fig. 6** Biopsy from the NS lesion on the temporal region showing acanthosis, papillomatosis, and multiple mature sebaceous gland lobules in the upper dermis. (H & E, x 4X)

A final diagnosis of Schimmelpenning syndrome (epidermal nevus syndrome - nevus sebaceous type) was made for this baby in view of the occurrence of multiple ocular and CNS anomalies



**Fig. 7** Biopsy from the concomitant CGMN and NS showing features of nevus sebaceus in the upper dermis and melanocytic nevus cells in the dermis in the same section. (H & E, x 20X)

in the presence of a NS, multiple CMN and a CGMN. The infant unfortunately died at home at the age of one-month following seizures, the nature of which could not be ascertained. There was no history of fever or symptoms suggestive of any infection or injury to the baby.

## DISCUSSION

ENS describes the association of sebaceous and/or verrucous naevi with other developmental defects, particularly of the central nervous system (CNS), eye and skeleton.<sup>1</sup> The first case of ENS reported by Schimmelpenning in 1957 had a NS on the head, ipsilateral colobomas of the upper eyelid, increased density of cranial bones, epileptic seizures and mental retardation.<sup>2</sup> Feuerstein and Mims in 1962 described two patients of 'nevus sebaceous with convulsions and mental retardation'.<sup>3</sup> The condition is known by several names such as Schimmelpenning syndrome, Feuerstein-Mims syndrome, Schimmelpenning-Feuerstein-Mims syndrome, ENS, Solomon syndrome, organoid nevus syndrome, linear naevus sebaceous syndrome (NSS), Jadassohn's nevus phacomatosis, Jadassohn's naevus sebaceous syndrome, Jadassohn-Schimmelpenning-Feuerstein-Mims syndrome.<sup>4</sup> Solomon et al had coined the term ENS.<sup>5</sup>

Some authors include only those cases as ENS where the cutaneous component consists of a sebaceous nevus, verrucous epidermal nevus, syringocystadenoma papilliferum or nevus comedonicus.<sup>1</sup> However, Happle<sup>4</sup> describes nine well defined types of ENS that include conditions such as Schimmelpenning's syndrome, phacomatosis pigmentokeratolica (NS with papular nevus spilus), nevus comedonicus syndrome (with ipsilateral cataract), angora hair nevus (EN with overlying angora hair), Becker's nevus syndrome (Becker's nevus with ipsilateral breast hypoplasia), Proteus syndrome, type 2 segmental Cowden's disease, FGFR3 ENS, and CHILD syndrome in which an EN is present among constellation of signs and symptoms. Schimmelpenning syndrome is the best known ENS and many authors consider it as 'the classical ENS'. NS is the hallmark of this syndrome.<sup>4</sup> Virtually, all the cases of Schimmelpenning syndrome are sporadic and by definition exhibit mosaicism.<sup>4</sup> The etiology of nevus sebaceous syndrome is presumed to be due to alterations of ectodermal and mesodermal blastoderm in early embryogenesis.<sup>6</sup> It is postulated that the mutation is an autosomal gene that is lethal unless rescued by mosaic state.<sup>7</sup>

Additional cutaneous abnormalities seen in some patients include infantile haemangiomas, naevi flammei, hypochromic naevi, café au lait macules, congenital melanocytic naevi, Spitz naevi, follicular hyperkeratosis and dermatomegaly.<sup>1</sup>

Significant developmental anomalies occur in approximately 1.7% of all neonates, however the incidence is more (10%) in children with EN.<sup>8</sup> The risk correlates poorly with the number and extent of skin lesions. Skeletal deformities reported in the ENS include kyphosis, scoliosis, cystic and lytic changes, hypertrophy and atrophy, short

limbs and syndactyly.<sup>5,9</sup>

A wide variety of neurological abnormalities have been identified in about 50% of patients with ENS.<sup>10,11</sup> Neurological abnormalities are much more frequent in patients who have sebaceous naevi on the head and neck.<sup>1, 11</sup> Seizures, especially infantile spasms, occur in some 50% of patients, many of whom have underlying structural abnormalities of the CNS. Mental retardation also occurs in about 50% of cases. Spastic hemiparesis affects about 20% of patients. Conductive and sensorineural deafness and cranial nerve palsies have also occurred in patients of ENS.<sup>1</sup>

The commonest structural CNS abnormalities reported in ENS are ipsilateral gyral malformations, and complete or partial hemimegalencephaly.<sup>12-16</sup> Vascular malformations, hemiatrophy, posterior fossa abnormalities, lateral ventricle enlargement, porencephaly, agenesis of the corpus callosum, hamartoma, and intracranial or intraspinal lipomas have been reported.<sup>1</sup> Our patient had a large temporal arachnoid cyst with underlying temporal and fronto-parietal migration defect (agyria/pachygyria) and a lipoma in the left CP angle.

Some 35-70% of patients have ocular abnormalities,<sup>1</sup> the commonest of which is involvement of the eyelid or conjunctiva by the epidermal naevus as seen in our patient too. These can sometimes cause trichiasis or interference with lid closure. Other ocular problems have included colobomas of the eyelid, iris and retina, retinal dysplasia, conjunctival lipodermoids and choristomas.<sup>17,18</sup> Cortical blindness, microphthalmia, macrophthalmia, anophthalmia, corneal opacities and cataracts have also been reported.<sup>1</sup>

Many other non-cutaneous abnormalities have now been reported in association with epidermal naevi, including a variety of cardiac and genito-

urinary abnormalities. In addition to these structural and anatomical malformations, biochemical abnormalities resulting in rickets have rarely been reported in patients of ENS/NSS.<sup>19-21</sup> Debulking the epidermal naevi has led to biochemical improvement as well as correction of rickets suggesting that these epidermal naevi, or the associated intraosseous angiomatous tumours, secrete a substance that induces renal phosphate loss. However there have been instances where no biochemical improvement has been observed despite the surgery.<sup>21</sup>

Benign as well as malignant transformation may occur in these patients' epidermal naevi. The incidence does not differ from when such naevi occur without associated abnormalities.<sup>1</sup> However a high incidence of systemic malignancies have arisen in patients with epidermal naevi, often at a very early age, a fact that still needs investigations and an explanation.<sup>22</sup>

NS has tendency to develop tumors mostly benign, later on in life.<sup>1</sup> The lifetime risk of malignant transformation is probably less than 5%. Most of the reports indicate a low risk of malignancy in NS and hence do not recommend prophylactic surgical excision however it can be recommended for cosmetic reasons. Sebaceous naevi occur in about 0.3% of all neonates.<sup>1</sup> ENS/SNS occur in 1 in 10000 live births.<sup>1</sup> CMN are considered to be present in 1-2% of new borns.<sup>23</sup> Giant type of CMN is rare.<sup>24</sup> The exact incidence is difficult to ascertain but Castilla *et al*<sup>25</sup> described one CMN >10 cm per 20445 subjects in a study of 500,000 infants in South America. Co-occurrence of ENS with CGMN as seen in this child is an extremely rare event.<sup>26</sup>

Demerdjieva Z *et al*<sup>27</sup> recently described occurrence of circumscribed lesions of aplasia cutis

within the sebaceous nevus on the scalp, a phenomenon named as didymosis aplasticosebacea. Lam J *et al*<sup>28</sup> reported a patient having sebaceous nevus syndrome, CNS malformations, aplasia cutis congenita, limbal dermoid, and pigmented nevus (giant congenital melanocytic nevus) with neurocutaneous melanosis, a distinct syndromic entity and gave it the acronym SCALP syndrome. The term didymosis aplasticosebacea was coined by Happle and Koneg.<sup>29</sup> They described it as an example of twin spot phenomenon.<sup>29</sup> The lesions of ACC and NS tend to be directly adjacent or in close proximity. Twin spotting has been defined as a phenomenon in which a heterozygous cell can give rise to different homozygous daughter cells.<sup>29</sup> Our patient also had a combination of NS, CGMN, CNS and eye abnormalities but did not have any aplasia cutis emphasizing that constellation of organs or systems involved may vary and be very broad in the spectrum of ENS.

CMNs have been divided into three size ranges; small (<1.5 cm), large (1.5 - 20.0 cm) and giant lesions (> 20 cm).<sup>24</sup> The latter rare type is also known as garment or bathing-trunk naevus because of its distribution.<sup>24</sup> With time, the surface may become rugose or warty and nodules can develop within a large CMN. The hairy component is present in 95% of lesions. There may also be a large number of smaller congenital naevi as seen in our patient. Associated abnormalities such as meningeal involvement, spina bifida or meningocoele when the CGMN is present over the vertebral column, or club - foot and hypertrophy or atrophy of the deeper structures of a limb have been reported. Other hamartomas, such as vascular naevi, lipomas or von Recklinghausen's disease, may be found in patients with extensive congenital pigmented naevi.<sup>24</sup> The risk for developing malignant trans-

formation is highest among the large/giant CMNs; the lifetime risk being 4-5%.<sup>30</sup> The lesion is cosmetically and psychologically very disturbing and distressing to the parents. It also presents a great challenge to manage. Several approaches such as surgical excision, curettage, dermabrasion, and laser ablation have been tried for reduction of pigment and risk of malignant transformation, however the results have been variable, generally poor and difficult to assess.<sup>31-33</sup> Spontaneous improvement has been reported rarely.<sup>24</sup>

The management of NSS requires a team work with care being provided by dermatologist, pediatrician, neurologist, ophthalmologist, radiologist, orthopedics, psychologist and cosmetic or general surgeon. A regular follow up is mandatory for patients with NSS as symptoms related to different organ systems may appear at different times. All children with extensive ENS should at least undergo the non-invasive investigations such as a thorough ophthalmologic examination, CT scan of the head, ultrasonogram of abdomen, and serum calcium and phosphate level estimation. If a large or giant CMN is present over the scalp or back in the midline, MRI to rule out structural CNS abnormality is a fair approach.<sup>24</sup> Prophylactic surgical removal of CGMN is recommended if practical and feasible as soon as possible as malignant transformation commonly occurs before puberty in such lesions compared to smaller CMNs. Follow up of such patients is mandatory as they have increased risk of CNS melanoma, symptomatic neurocutaneous melanosis, neurodevelopmental delay and seizures.<sup>28</sup>

Our patient had the unusual combination of a NS, CGMN, CNS and ocular anomalies. Interestingly the NS and CGMN were present concomitantly over a same location as well as present in different

areas of the body. The contiguous areas showed features of both the nevi in the same biopsy. Unfortunately the child died following seizures and an autopsy was not conducted to rule out any other organ involvement.

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