

Congenital tumors arising from nevus sebaceous in 2 neonates



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INTRODUCTION

Nevus sebaceous is a common congenital hamartoma of the follicular-sebaceous-apocrine unit. The lesions present at birth or during infancy as linear or elliptical, alopecic, yellowish-tan thin plaques, sometimes with a pebbly surface. The lesions often become thicker and more verrucous during puberty. Although the lesions are usually solitary, patients may rarely present with multiple lesions or extensive involvement. The majority of lesions occur in the head and neck region, with about 87% occurring on the face and scalp and 9% on the neck and trunk.^{1,2} Secondary neoplasms occur in about 10% of cases; most of which are benign and occur almost exclusively in adults.¹ The 2 most frequently associated tumors are syringocystadenoma papilliferum and trichoblastoma. Other relatively common secondary neoplasms include trichilemmoma, sebaceous adenoma, desmoplastic trichilemmoma, apocrine adenoma, and poroma.^{1,2} Different secondary tumors can arise concurrently. The incidence of basal cell carcinoma and other malignant neoplasms is considered relatively low, occurring in less than 1% of cases.¹⁻³ The risk of developing secondary tumors in childhood is extremely unusual, occurring in less than 2% of children with nevus sebaceous, and at birth is even rarer.⁴ We report 2 unrelated cases of congenital secondary tumors from nevus sebaceous, both with extensive cutaneous lesions, but without evidence of internal manifestations. We discuss the

clinical prognosis, genetic mutations, and potential systemic associations of extensive nevus sebaceous with secondary tumors.

CASE REPORTS

Patient 1 is a Chinese girl born at 36 weeks of gestation with an uneventful antenatal and perinatal course. At birth, there were extensive yellow-brown hairless plaques over the scalp, left cheek, chin, lip, trunk, and arms. Four exophytic tumors were seen arising from the scalp plaques, with the largest measuring 4.5 cm × 4 cm (Fig 1). In view of the extensive involvement, eye examination and cardiac echocardiogram were requested and showed normal results. Magnetic resonance imaging of the brain showed that the tumors arose from the scalp, with no intracranial extension and no structural brain abnormalities. Excisional biopsy of the scalp tumors showed the presence of both syringocystadenoma papilliferum and trichilemmoma arising from an underlying nevus sebaceous (Fig 2). Genetic studies of lesional skin for common mutations in the *RAS* genes were performed, with negative results. She underwent staged excision of the nevus sebaceous, and her growth and development are within normal limits at 3 years of age.

Patient 2 is a Cambodian girl who presented at 1 month of age with extensive skin-colored and hyperpigmented plaques on her scalp, forehead,

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Written informed consent was obtained from both patients' parents for publication of their clinical details and clinical photographs.

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Fig 1. **A**, Extensive nevus sebaceus involving the scalp, left cheek, chin, lip, trunk, and arms. **B**, Thick, verrucous yellowish nevus sebaceus plaques involving the lip and chin. **C**, Four exophytic red, fleshy tumors arising from the scalp nevus sebaceus.

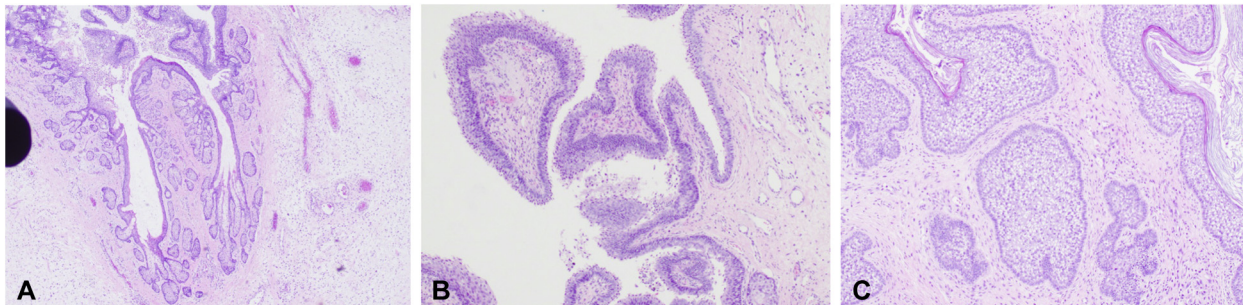


Fig 2. **A**, Scalp biopsy specimen showing acanthosis, papillomatosis, increased sebaceous glands, and ectopic apocrine glands, consistent with nevus sebaceus. This lesion transitions into a lesion of syringocystadenoma papilliferum superiorly. **B**, Scalp tumor showing multiple papillary structures lined by inner columnar and outer cuboidal cells, projecting into a cystically dilated invagination of the epidermis, with numerous plasma cells in the fibrovascular stroma of these papillary structures, consistent with syringocystadenoma papilliferum. **C**, Scalp tumor showing lobules extending from the epidermis into the dermis, composed of uniform small cells with round or oval vesicular nuclei, clear cytoplasm, and peripheral palisading, consistent with trichilemmoma. (**A-C**, Hematoxylin-eosin stain; original magnifications: **A**, $\times 40$; **B** and **C**, $\times 200$.)

temporal, preauricular, and perioral regions, ears, and lips. The lesions were present from birth. In addition, there were 2 reddish, lobulated, eroded tumors measuring 4 cm \times 3.5 cm \times 2 cm arising from the plaques over the parietal and occipital scalp that were also present from birth (Fig 3). The rest of her examination was normal. She underwent biopsy of the lip lesion and scalp tumor. Histologic examination of the lip lesion was consistent with nevus sebaceus, and histologic examination of the scalp tumor revealed a trichilemmoma (Fig 4). No further imaging was performed. At 2 years of age, she is healthy and developmentally appropriate.

DISCUSSION

Nevus sebaceus is a fairly common, benign hamartoma occurring in about 0.3% of neonates. In rare cases where involvement is extensive, multi-systemic associations may occur, with various anomalies of the cardiac, ocular, skeletal, and central nervous systems, known as Schimmelpenning syndrome.^{5,6} Patients with central nervous system involvement may have major neurologic abnormalities, including cerebral deformities, cognitive impairment, and seizures, which may not be apparent in early life. These patients should be reviewed for growth and developmental assessments. Increased risks have been reported for

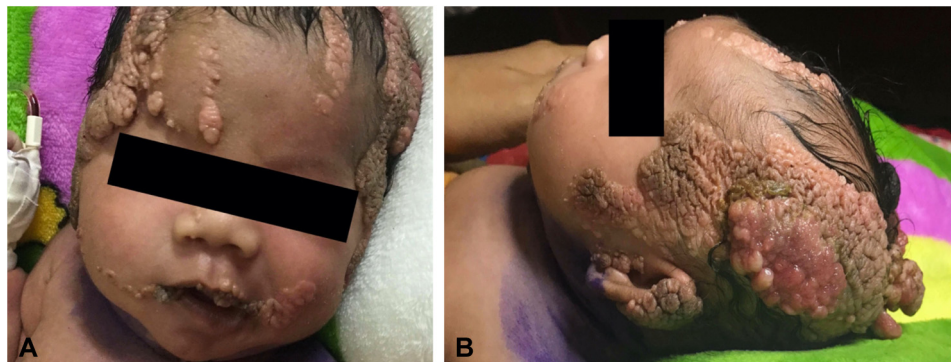


Fig 3. **A**, Extensive thick verrucous plaques over the scalp and face. **B**, Two reddish, lobulated, ulcerated tumors arising from the plaques over the parietal and occipital scalp.

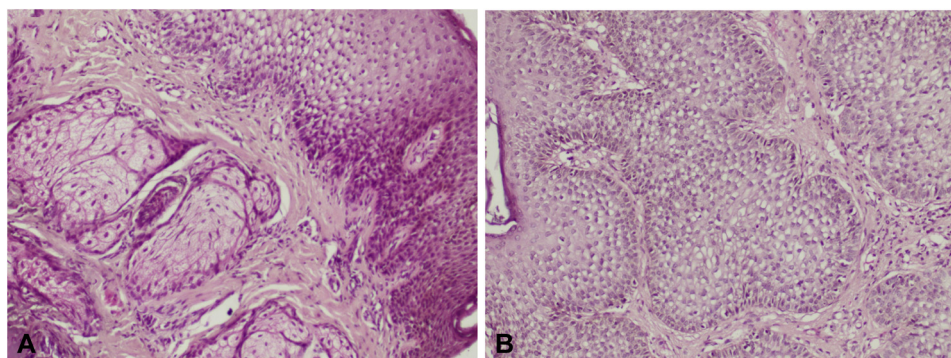


Fig 4. **A**, Lip lesion showing epidermal papillomatosis and acanthosis, increased number of enlarged sebaceous glands and ectopic apocrine glands, consistent with nevus sebaceous. **B**, Scalp tumor showing lobules extending from the epidermis into the dermis composed of uniform small cells with round or oval vesicular nuclei, clear cytoplasm, and peripheral palisading, consistent with trichilemmoma. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A** and **B**, $\times 200$.)

cerebral neoplasms, such as astrocytomas, optic gliomas, and cerebral hamartomas.⁷

At birth, sebaceous nevi often appear raised, with irregular surfaces. However, waning of maternal hormones leading to reduction in the size of the sebaceous glands often results in flattening of the lesion during infancy. At puberty, the lesions become more verrucous and hyperpigmented due to epidermal hyperplasia and sebaceous gland maturation. Nevus sebaceous is now considered a mosaic “RASopathy.”⁸ Recently, postzygotic mosaic mutations in *HRAS*, *KRAS*, and *NRAS* have been identified in lesions of nevus sebaceous.^{9,10} Common mutations include the c.37G>C:p.(Gly13Arg) variant in *HRAS* and the c.35G>A:p.(Gly12Asp) variant in *KRAS*. These mutations result in hyperactivation of the mitogen-activated protein kinase and phosphatidylinositol 3-kinase-AKT pathways in mutated cells. Mosaicism occurring earlier in embryogenesis has been shown to lead to more

severe and extensive phenotypes. This is shown in our cases, with patient 1 exhibiting more extensive disease than patient 2, likely because the mutation occurred earlier in embryogenesis in patient 1. We suggest that the negative results in *RAS* gene mutations in patient 1 are due to mosaicism or that such extensive lesions may have different mutations from commonly known genetic mutations.

Secondary neoplasms occur in about 10% of nevus sebaceous cases and are far more common in adolescence and adulthood.¹ Nevus sebaceous cells have pluripotent potential and can differentiate into follicular, sebaceous, apocrine, and eccrine cells and rarely even into muscle lineages. Secondary tumors occur because of increased cellular proliferation, caused by the same mutations that result in the activation of the mitogen-activated protein kinase and phosphatidylinositol 3-kinase-AKT pathways. The simultaneous occurrence of multiple tumors in nevus sebaceous has been well reported. They are

much more common in adulthood. Our 2 cases illustrate the rare occurrence of congenital secondary tumors from nevus sebaceous, both with extensive cutaneous lesions, but without evidence of internal manifestations.

Treatment options for nevus sebaceous include reassurance and education about the condition and its potential complications, regular clinical monitoring, or surgery in cases with widespread involvement or those with secondary tumors. For more extensive lesions, surgery may improve the cosmetic and psychosocial outcome; however, the optimal timing for surgery is still unknown.

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Conflicts of interest

None disclosed.

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