Successful treatment of multifocal intracerebral and spinal hemangiomas with propranolol

To the Editor: Multifocal infantile hemangioma (MIHs) is defined by the presence of at least 5 cutaneous infantile hemangiomas (IHs). Extracutaneous involvement may occur, with an estimated mortality rate of 5%. Central nervous system (CNS) disease is exceptional.

A full-term male newborn was hospitalized with 50 small superficial and deep subcutaneous IHs, without heart failure or hepatomegaly (Fig 1). At day 2 of age, ultrasound imaging showed a focal liver IH measuring 14 mm with arteriovenous shunting, a testicular IH, and multiple hyperechogenic lesions visualized by transfontanellar imaging. Cerebral and spinal magnetic resonance imaging (MRI) confirmed the presence of MIH in the brain and in 3 spinal locations, with multiple gadolinium enhancements seen on T1-weighted images, sometimes surrounded by slight edema (Fig 2, A). No other visceral IHs were detected. Thyroid function and echocardiography were normal.

Treatment with propranolol 1 mg/kg daily was started on day 8 of life. Heart rate, blood pressure, blood glucose level, and electrocardiogram results were normal before and after initiating propranolol therapy. The dose was increased to 3 mg/kg daily by day 18. There were no adverse effects and he was discharged home on day 23.

At day 29, clinical regression of subcutaneous lesions was observed and the liver lesion had decreased by a few millimeters on ultrasound imaging. At day 45, MRI showed a decrease in number and size of the CNS IHs. At day 60, all subcutaneous IHs had disappeared. At day 100, the liver and testicular IHs were undetectable. At day 180, edema and contrast enhancement of the brain and spinal cord lesions were no longer visible on T1-weighted MR images (Fig 2, B). The child’s growth and psychomotor development were normal. One year after starting treatment, only a few superficial cutaneous IHs remained and the MRI findings were unchanged. It was planned to continue propranolol 3 mg/kg daily until 18 months of age and then progressively reduce the dose, with repeat imaging studies to monitor for rebound IH growth.

CNS disease in MIH is exceptional. Two cases with extensive CNS involvement treated with systemic corticosteroids had neurologic sequelae and side effects. Three cases of cerebellar IH are reported;

Fig 1. Multifocal infantile hemangioma: numerous superficial reddish and subcutaneous blue hemangiomas at birth.

Fig 2. Magnetic resonance imaging of central nervous system infantile hemangiomas (IHs) before (A) and after (B) initiation of propranolol treatment. A, One spinal and numerous intracerebral IHs with multiple gadolinium enhancements are seen on T1-weighted images (red arrows), some with surrounding edema (red circle). B, Edema and contrast enhancement are no longer visible on T1-weighted images at 6 months.

2 were treated with surgical excision. Recently, an isolated cerebellar IH associated with MIH was treated effectively with propranolol. Our case of MIH with multiple cerebral and spinal lesions was also successfully treated with propranolol, with rapid improvement by day 45 and disappearance of lesions on neuroimaging at 6 months.

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Syringocystadenoma papilliferum developing over hyperkeratosis of the nipple in a pregnant woman

To the Editor: Syringocystadenoma papilliferum (SCAP) is usually a solitary lesion that most commonly occurs on the scalp. Rarely, lesions have been described on the breast. It usually presents at birth or develops in childhood as a warty crusted papule. Although there is increasing evidence for apocrine histogenesis, eccrine origin could also be a possibility as well as derivation from pluripotent cells. In approximately one third of cases, it is associated with organoid nevus; it has also been described in association with nevus comedonicus. Here we report, to the best of our knowledge, the first case of SCAP developing over hyperkeratosis of the nipple.

A 27-year-old woman in her thirty-fifth week of first pregnancy presented with a 5-week history of enlarging asymptomatic skin lesion on the nipple of her right breast (Fig 1, A). She had had an asymptomatic verrucous hyperpigmented plaque diffusely involving the right nipple for 5 years that was diagnosed as hyperkeratosis of the nipple (HNA) based on biopsy findings of hyperkeratosis, keratotic plugging, acanthosis, papillomatosis, and a sparse perivascular lymphocytic infiltrate (Fig 1, B). The HNA was stable until a new 0.5-cm skin-colored papule developed over the HNA starting in her thirtieth week of gestation. The patient was otherwise healthy. Shave excision of the newly developed lesion revealed papillary foci in continuity with the surface squamous epithelium. These papilla had a bilayered epithelium of inner columnar cells showing decapitation secretion and outer flattened cells as well as a fibrovascular core containing abundant plasma cells (Fig 1, C and D). These findings were consistent with SCAP.

First described in 1923, HNA is a benign condition of unknown origin. It is usually bilateral, affecting young adult women and occurring as a hyperpigmented verrucous lesions on the nipple (17%), areola (25%), or both (58%). Although HNA shares clinical and histopathologic features of epidermal nevus, it is usually acquired after puberty and is not associated with systemic disease. In 1938, Lévy-Franckel classified HNA into 3 types. Type 1 is an extension of epidermal nevus. Type 2 is usually associated with several other dermatoses including ichthyosis, Darier disease, or lymphoma. Type 3 is the isolated nevoid variant. Hormonal factors may contribute to its etiopathogenesis in that lesions appear or worsen in pregnancy or with hormonal therapy.

There are yet no reports of an association of HNA with SCAP or other tumors. The fact that HNA shows features of an epidermal nevus and may theoretically be an extension of epidermal nevus makes the development of different neoplasms, including SCAP, within it possible, similar to what has been reported with nevus sebaceous and nevus comedonicus. The basic defect producing the hamartomatous process in epidermal nevi that may result in immature cells capable of differentiating into follicular and glandular cells and tumors could also be playing a role in SCAP development over HNA. This is especially true given that a recent study demonstrated that SCAP could itself be a hamartomatous tumor arising from pluripotent cells.

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