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**Author:**

[Resende, Cristina](#), Hospital de Braga  
[Araujo, Catarina](#), Hospital de Braga  
[Vieira, Ana Paula](#), Hospital de Braga  
[Ventura, Filipa](#), Hospital de Braga  
[Brito, Celeste](#), Hospital de Braga

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**Abstract:**

Schimmelpenning syndrome (SS) includes an organoid nevus that follows the lines of Blaschko and defects of brain, eyes, bones, or other systems.

We report a case of a 3-month old female infant, who presented with several thin plaques, with irregular borders, yellowish color, which had a verrucous appearance, following the lines of Blaschko, mainly occupying the left side of posterior trunk, the left face, the right side of the anterior trunk, and the right upper limb. These plaques had been present since birth. In addition, she had a flat salmon to yellow nevus on the left parietal and temporal region of the scalp, with a bald patch. She was diagnosed after birth with an interauricular communication.

The skin biopsy from the lesion of the right arm revealed an epidermal nevus that occupied the epidermis completely. Routine and other complementary laboratory blood tests, including



platelet count, [thyroid function](#) tests, 25-hydroxy-vitamin D, parathyroid hormone, and plasma and urinary levels of calcium and phosphorus were negative. Cerebral magnetic resonance and renal ultrasound were normal. The diagnosis of SS was established.

She is being followed in the clinics of Dermatology, Cardiology, Pediatrics, and Pediatric Neurology. We report this case to point out the importance of investigating patients with epidermal nevus to identify associated conditions

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## Case Presentation

### Schimmelpenning syndrome

**Cristina Resende, Catarina Araújo, Ana Paula Vieira, Filipa Ventura, Celeste Brito**

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**Department of Dermatology and Venereology, Hospital de Braga, Portugal**

### Correspondence:

Dr. Cristina Resende  
Serviço de Dermatologia e Venereologia  
Hospital de Braga  
Sete Fontes – São Victor  
4710-243 Braga  
E-mail: cristinapresente@gmail.com

## Abstract

Schimmelpenning syndrome (SS) includes an organoid nevus that follows the lines of Blaschko and defects of brain, eyes, bones, or other systems.

We report a case of a 3-month old female infant, who presented with several thin plaques, with irregular borders, yellowish color, which had a verrucous appearance, following the lines of Blaschko, mainly occupying the left side of posterior trunk, the left face, the right side of the anterior trunk, and the right upper limb. These plaques had been present since birth. In addition, she had a flat salmon to yellow nevus on the left parietal and temporal region of the scalp, with a bald patch. She was diagnosed after birth with an interauricular communication.

The skin biopsy from the lesion of the right arm revealed an epidermal nevus that occupied the epidermis completely. Routine and other complementary laboratory blood tests, including platelet count, thyroid function tests, 25-hydroxy-vitamin D, parathyroid hormone, and plasma and urinary levels of calcium and phosphorus were negative. Cerebral magnetic resonance and renal ultrasound were normal. The diagnosis of SS was established.

She is being followed in the clinics of Dermatology, Cardiology, Pediatrics, and Pediatric Neurology. We report this case to point out the importance of investigating patients with epidermal nevus to identify associated conditions

**Keywords: Schimmelpenning syndrome, epidermal nevus syndrome, genomic mosaicism**

## Introduction

The epidermal nevus syndromes (ENSs) represent a group of distinct disorders that can be distinguished by the type of associated epidermal nevus (EN) and by the criterion of the presence or absence of heritability [1,2].

There are well defined epidermal nevus syndromes characterized by organoid nevi or by keratinocytic nevi [2]. Organoid nevi are epithelial nevi showing hyperplasia or structural changes of sebaceous glands [1,2]. The epidermal nevus syndromes characterized by keratinocytic nevi are defined by the presence of nonorganoid EN, showing differentiation exclusively to keratinocytes [1].

The use of the term organoid nevus syndrome when referring to a specific nosologic entity is misleading, because organoid nevus syndrome includes Schimmelpenning syndrome, Phacomatosis pigmentokeratotica, Nevus comedonicus syndrome, Angora hair nevus syndrome, and Becker nevus syndrome [1,2]. The term keratinocytic nevus syndrome includes Proteus syndrome, type 2 segmental Cowden disease, Fibroblast growth receptor 3 epidermal nevus syndrome, and Congenital hemidysplasia with ichthyosiform nevus and limb defects (CHILD) syndrome and should not also be used to design a specific disease[1,2].

Table 1 summarizes the most relevant features of well defined ENS [1,2].

**Table 1.** The diagnostic hints of well-defined epidermal nevus syndromes

Schimmelpenning syndrome	Linear or systematized nevus sebaceous and epidermal nevus, with variation often depending upon anatomic site (head and neck versus trunk, respectively). It could include cerebral, ocular and skeletal defects.
Phacomatosis pigmentokeratotic	Coexistence of nevus sebaceous and papular nevus spilus
Nevus comedonicus syndrome	Nevus comedonicus with ipsilateral ocular, skeletal, or neurologic defects
Angora hair nevus syndrome	A linear epidermal nevus with long soft white hair
Becker nevus syndrome	Becker nevus and breast hypoplasia
Proteus syndrome	Nonepidermolytic keratinocytic nevus of a soft, flat type and cerebriform connective tissue nevi of palms or soles; asymmetric macrodactyly
Type 2 segmental Cowden disease	Linear Cowden nevus ( nonepidermolytic keratinocytic nevus of a soft and rather thick, papillomatous type). PTEN germline mutation
Fibroblast growth receptor 3 epidermal nevus syndrome	Nonepidermolytic keratinocytic nevus of a soft type and mosaic FGFR3 mutation R248C
CHILD syndrome	Congenital hemidysplasia with ichthyosiform nevus and limb defects. Lateralized, inflammatory skin lesions NSDHL mutations

Schimmelpenning syndrome is a well-characterized entity within the group of organoid nevus syndromes. Its dermatological hallmark is a linear or systematized organoid nevus, which follows the lines of Blaschko with strict midline separation [3, 4, 5]. Nevus sebaceous is usually present at birth and shows a salmon to yellow color [3,6]. It is often located in skin regions in which the sebaceous glands are more abundant: scalp, forehead, and ocular and palpebral regions [3,6]. There is a lack of hair in the area of the nevus and the hair in surrounding zones shows a colorless appearance [3,7]. The lesion is typically relatively flat during the initial stages of infancy, but at puberty often thickens, assuming a verrucous nature because of the androgen-dependence of sebaceous glands [3,4,7]. The clinical and histopathological features of nevus sebaceous change with age: in infancy and childhood (before puberty) the nevus is relatively flat, owing to the quiescence of sebaceous glands. However, papillomatous epithelial hyperplasia with hypoplastic sebaceous glands and hair follicles are observed. At puberty ( under hormonal influence), nevus sebaceous often becomes hyperkeratotic and hyperplastic sebaceous and apocrine glands are seen by microscopic examination. Benign and malignant neoplastic changes characterize a third stage in a minority of cases [3,7].

We report the case of a child with an EN that followed the lines of Blaschko. She had an interauricular communication, diagnosed after birth, apparently without any other ectable extra-cutaneous lesions.

## Case report

A 3-month-old female infant, the first child to non-consanguineous parents, was delivered at 40-week gestation by spontaneous vaginal delivery following an uneventful pregnancy and delivery. Her birth weight, length, and head circumference were in the 25th-percentile.

She was referred to the Department of Pediatric Dermatology with a history of a verrucous nevus of the face, neck, and trunk, present since birth.

She was diagnosed after birth with a congenital cardiac malformation (interauricular communication), a moderate left-to-right shunt, an increased pulmonary blood flow, and diastolic overload of the right ventricle. She had normal psychomotor development for age. Her family history was not contributory. She was not taking any medication.

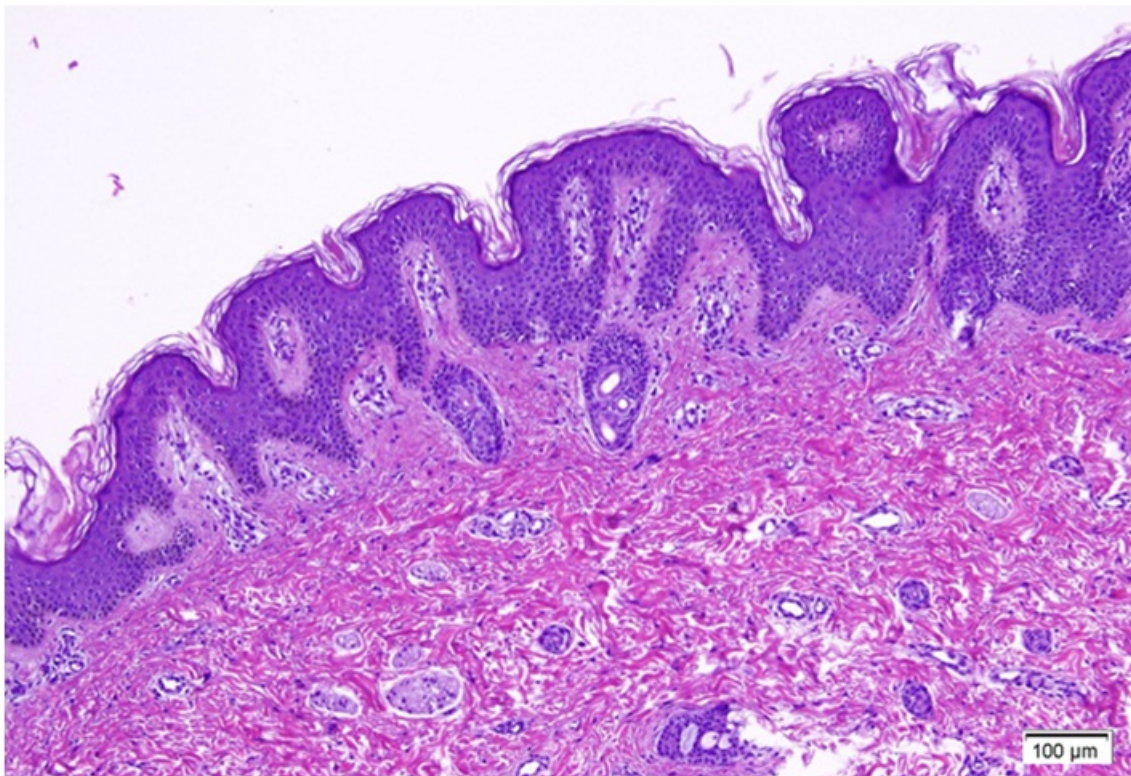






On cutaneous examination, there were several thin verrucous plaques with irregular borders and yellowish color following the lines of Blaschko, which mainly occupied the left side of the posterior trunk, the left face, the right side of anterior trunk, and the right upper limb (Figures 1, 2 and 3). In addition, she had a flat salmon to yellow nevus, 8 cm in diameter, on the left parietal and temporal region of the scalp. There was lack of hair in the area of the nevus (Figure 4). The remainder of the physical examination was normal, except for the presence of a systolic outflow murmur in cardiac auscultation.

Routine and other complementary laboratory blood tests, including platelet count, thyroid function tests, 25-hydroxy-vitamin D, parathyroid hormone, plasma and urinary levels of calcium and phosphorus were negative or within the normal range.



A skin biopsy from the lesion of the right arm revealed an epidermal nevus, which occupied the epidermis completely (Figure5). The infant was further evaluated to exclude central nervous system and renal structural abnormalities. Cerebral magnetic resonance and renal ultrasound were normal.

The parents were referred for a genetic counseling consultation. The risk of recurrence in future generations is somewhat increased, but still rather low (< 1%). It is not possible to make a prenatal diagnosis for future pregnancies.

# Discussion

We report a patient with an organoid nevus that follows the lines of Blaschko. This non-random cutaneous pattern probably arises from a postzygotic mutation occurring during embryogenesis [4,8,9]. According to this theory, SS is likely caused by an autosomal lethal mutation that survives by genetic mosaicism [4,8]. The mutated cells, which are presumably incompatible with intrauterine life persist only in close proximity to normal cells [9]. An individual with a mosaic state could not transmit the mutation to offspring because if transmitted, the zygote would die in utero [4]. Mosaicism was thought to arise either from a postzygotic mutation or from a half-chromatid mutation occurring before fertilization in one or two gametes forming the zygote [7,10]. To explain the rare exceptions from the rule of nonheritability, the concept of paradominant inheritance has been proposed by Happle [4,7]. Happle theory could explain the segmental pattern of SS with the mosaic distribution of lesions along the lines of Blaschko, the sporadic occurrence, and the discordance between monozygotic twins, but awaits molecular confirmation [8].

Schimmelpenning syndrome could be coupled with many extracutaneous features, mainly involving the brain, eye, and skeletal systems [2]. The most common neurologic abnormalities are seizures, mental retardation, and cognitive development delay. Cerebral magnetic resonance is the preferred structural imaging technique to delineate the central nervous system structural abnormalities [3,11]. The most frequent ophthalmologic abnormalities in SS include strabismus, lipodermoids, and colobomas; as a consequence, the loss of vision of the involved eye may occur [3]. Vascular malformations are found in 12.6 to 33% of patients with SS [8]. Skeletal abnormalities exist in 50% of patients with SS [3]. Intraoral lesions also may be found, including linear squamous cell papilloma of the mucosa, fibromatous enlargement of the tongue, and benign fibrous histiocytic lesions of the mandible [8,12,13]. In SS genitourinary abnormalities are also described in 10% of cases, namely: hydronephrosis, double collecting system, horseshoe kidney, cystic kidney, hypospadias, cryptorchidism, testicular and paratesticular tumors, nephroblastomatosis, ureteropelvic junction obstruction, and vitamin-D resistant rickets [1,3]. It is described in the literature that 12% of patients with SS have different types of cardiac malformations [3].

Our patient has a nevus sebaceous on the left face and on the left parietal and temporal region of the scalp. She also has an epidermal nevus on the right side of anterior trunk and on the right upper limb. We have only done a biopsy of the nevus of the right arm, which revealed an epidermal nevus. We have not done a biopsy of the scalp because the sebaceous glands tend to be underdeveloped before puberty. In light of this, we think that is preferable to delay the scalp biopsy until puberty.

Our patient had an interauricular communication since birth, apparently without any other detectable extra-cutaneous lesions. The management of patients with SS needs to be individualized and a multidisciplinary approach is mandatory for optimal management, with possible collaboration of several specialties such as dermatologists, pediatricians, pediatric neurologists, dermatopathologists, plastic surgeons, geneticists. Occasionally others, such as pediatric endocrinologists, cardiologists, nephrologists and orthopedists are required [2,3].

In the past, the malignant potential of an organoid nevus has been overestimated [1]. There is no need to remove the organoid nevus prophylactically for cancer prophylaxis; their surgical removal may be considered mainly for psychosocial and cosmetic reasons [1]. The patient and/or family should be reassured that in SS the risk of recurrence is somewhat increased but still rather low [1,10].

The prognosis of SS depends on the presence and the severity of associated internal defects [10].

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