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CASE REPORT

# Incontinentia pigmenti associated to cleft palate. Case report and literature review

## *Incontinencia pigmentaria asociada a fisura palatina. Reporte de un caso y revisión de la literatura*

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**ABSTRACT**

Incontinentia pigmenti (IP2, Block-Sulzberger Syndrome) is a rare x-linked dominant genetic skin disease mainly affecting females. Its manifestations, among many others, consist of a series of skin, dental ocular and neurological disorders. **Patient and method:** 14 month old female patient. At birth vesicular lesions were observed in legs, underarms (armpits) and buttocks area. Upon breaking, the lesions developed into erythematosus and desquamative lesions. Other observed signs were vertex alopecia and cleft palate. **Results:** The clinical geneticist confirmed the presence of X-linked dominant syndrome, since the mother presented the same lesions at birth. The patient was referred to the maxillofacial service for cleft palate treatment. **Conclusions:** Skin alterations present at birth might precede others in the dental area, they thus warrant preparation for further prevention and treatment phases.

**RESUMEN**

La incontinencia pigmentaria (IP2, síndrome de Block-Sulzberger) es un raro caso de genodermatosis de herencia ligado a X dominante, afectando en su mayoría a mujeres. Consiste en una serie de manifestaciones de la piel, desórdenes dentarios, oculares, neurológicos y otros. **Paciente y métodos:** Paciente género femenino de 1 año 2 meses en el que al nacer se observan lesiones vesiculosas en extremidades inferiores, zona glútea y axilas que se rompen quedando lesiones eritematosas y descamativas. Destacaba además zona de alopecia en vertex y paladar fisurado. **Resultado:** Visto por genetista clínicamente se confirma el cuadro de herencia ligada a X dominante, ya que la madre presentó las mismas lesiones al nacimiento. Además es derivada al Servicio Maxilofacial para tratar su paladar fisurado. **Conclusiones:** Alteraciones cutáneas que se presenten al nacimiento pueden anteceder a otras en el área estomatológica, estando así preparados para etapas de prevención y tratamiento.

**Key words:** Incontinentia pigmenti, Bloch-Sulzberger syndrome, cleft palate.
**Palabras clave:** Incontinencia pigmentaria, síndrome de Bloch-Sulzberger, fisura palatina.

## INTRODUCTION

Incontinentia pigmenti (IP2) also called Bloch Sulzberger syndrome, is a rare genodermatosis described by Garrod and characterized by Bloch-Sulzberger, Siemens and Bardach during the 1920's.[1,2] It is a neuroectodermal disorder affecting skin, teeth eyes, as well as the nervous system.[1-3] It is an X dominant linked congenital abnormality (Xq28).[4] The patronymic IP2 described the histological characteristic of the melanin pigment incontinence of epidermis basal layer melanocytes and its consequent presence in the superficial dermis, which constitutes the final phase of this dermatosis.[1]

IP2 clinical manifestations are varied, even in members of the same family. Skin manifestations are generally the first to appear.[5,6] The most frequent manifestation is vertex alopecia, appearing in 38 to 50% of patients.[3,7] 7 to 40 % of patients present affected nails. These skin manifestations can change through the patients` life. Hyperpigmented lesions can even disappear.[8]

Skin abnormalities appear in four differentiated clinical stages.

The first stage appears at birth, and is characterized by vesicles, which adopt a linear pattern or in groups in limbs and face. After one month, they can

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disappear, appear anew, or be replaced by irregular papules and inflammatory lesions.

The second stage is characterized by hyperkeratotic lesions which generally appear when the patient is about one month old.

The third stage takes place generally when the patient is three to six months old, when grayish-brownish macules appear in the reticular pattern.

During the fourth or «burn out» phase pale, depigmented lesions appear and there is an observed absence of hair.[9]

Whenever present, eye manifestations (symptoms) are severe and generally associated with neurological damage. Thirty five porcent of patients will present ophthalmologic problems, the most common of which is strabismus.[10] Manifestations in central nervous system include among others, mental retardation, microcephaly, convulsive episodes (seizures) and cerebral (brain) atrophy.[3,7,11]

Second only to dermatological manifestations, dental manifestations are the most frequent; 90% of patients are afflicted by them.[12,13] These symptoms, persist during the life of the patient, while skin manifestations do not. Both dentitions are affected. Hypodontia is the most common manifestation, followed by conical and peg teeth and late eruption as well as other less frequent alterations such as impacted or fused teeth. There are reports of IP cases with figurative lip and palate as minor manifestations of the disease.[14,15] This study shows a patient with cleft palate (CP) associated to a dominant autosomal syndrome as is the case for IP2.

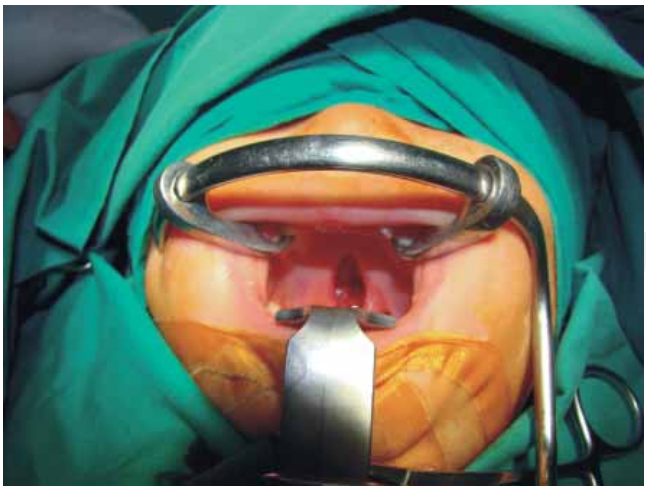

**Figure 1.** Preoperative image where cleft palate can be observed. Pin teeth can also be observed.

## CASE REPORT

14 month old female patient examined at the Hospital de Carabineros, Santiago, Chile, born from a 28 year old mother, delivered by caesarean section. At birth she weighed 3,163 grams, measured 49 cm and had a cranial perimeter of about 35 cm. At birth, vesicular lesions are observed in legs, buttocks area and armpits. Lesions break down upon cleansing (smearing) the skin, leaving erythematosus and scaly lesions. The condition was first diagnosed as bullous epidemiolisis. This diagnosis was later discarded. The patient also showed vertex alopecia and cleft palate *(Figures 1, 2 and 3).*

The patient was remitted to the ophthalmology department where a fundus oculi exam was performed.

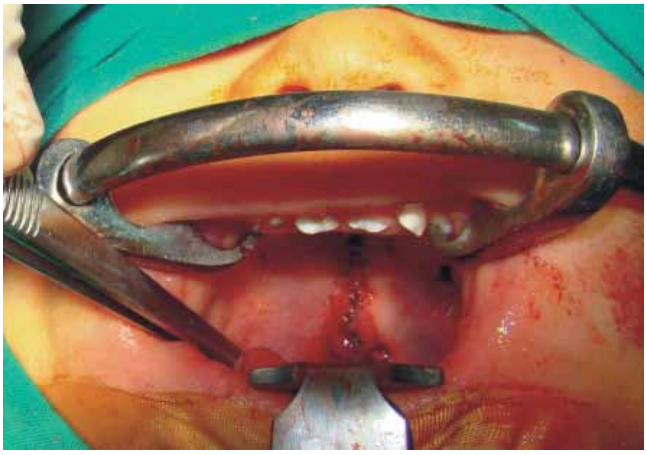

**Figure 2**. Postoperative image where the primary closing of the cleft palate can be observed.

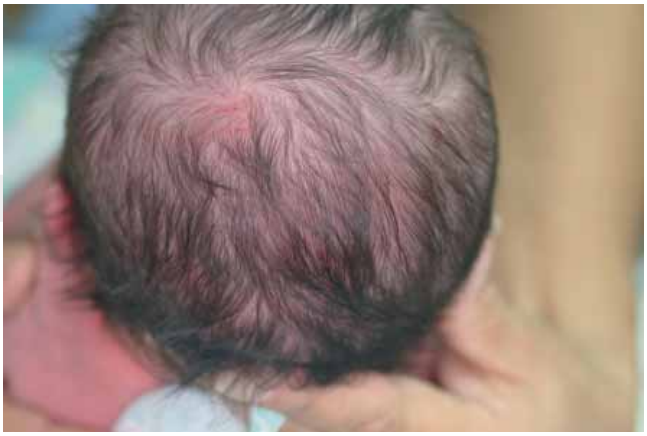

**Figure 3.** Image showing vertex alopecia, which is the most common clinical sign of incontinetia pigmenti.

Pigment epithelium was observed, with a generalized small amount of pigment; otherwise the rest was normal. The neurologist emitted an evaluation of normalcy. The dermatologist submitted diagnosis of pigment epithelium. A skin biopsy was performed. The sample was found to be well within normal histological boundaries, nevertheless it was deemed appropriate to take a new sample. The geneticist observed and confirmed a scheme of X linked dominant syndrome, since the mother presented the same lesions at birth. The patient was also remitted to the maxillofacial service due to her cleft palate. At ten months of age, the patient was operated for her cleft palate condition. The surgery functionally reconstituted the palatal velum (soft palate) muscular rings. The patient presented no postoperative complications.

## DISCUSSION

Incontinentia pigmenti is considered a ectodermal and mesodermal mixed poly-dysplasia. It affects females at a 37:1 rate, and is more common in Caucasians. In Carney´s review of 653 cases, 593 were female and 16 male (3). There are at least 900 cases described in literature but prevalence of IP2 is unknown.[7,9]

Carney, in his 1979 publication, found that 79.8% of patients presented alterations in hair, eyes, teeth and central nervous system as well as other abnormal structures. *Table I* shows criteria proposed for IP2 diagnosis.

IP2 presents distinctive abnormalities in teeth, which must be taken into account once the teeth start to erupt. Hypodontia, delay in eruption pattern and conical crowns might be found in these cases. These changes are similar to those observed in hypohidrotic ectodermal dysplasia. Some authors suggest there is a relationship between IP2[6] and the aforementioned dysplasia. Therefore, the clinical operator must be aware, with the help of regular monitoring, including proper oral examination, of the possible onset of any abnormality which might compromise the patient s oral health.

The results of Carney[3] study showed that 1.1% (5 cases) presented cleft lip or palate abnormalities which could include arched palate, palate and lip cleft, palate hypoplasia and partial lip cleft.

In 1976, Brett[15] published a case which included cleft lip and palate. The patient experienced difficulties when feeding and was intubated for a few weeks. Samman reported in 1959 an IP2 case with partial cleft lip and palate among other skin and dental alterations as well as hemiplegia.[16] Yell contributed with a

**Table I.** Diagnostic criteria for incontinentia pigmenti (IP)*.

| • No incidencia of IP in at least 1 first-degree female relative | • Evidence of IP in at least 1 first-degree female relative |
|---|---|
| **Major criteria** | |
| Typical neonatal rash<br>Erythema, vesicles, eosinophilia<br>Typical hyperpigmentation<br>Mainly on trunk<br>Following blaschko lines<br>Fading in adolescence<br>Linear, atrophic, hairless lesions | Suggestive history or evidence of typical rash<br>Skin manifestation of IP<br>Hyperpigmentation<br>Scarring<br>Hairless streaks<br>Alopecia at vertex<br>Anormalous dentition<br>Wooly hair<br>Retinal disease<br>Multiple miscarriages of male fetuses |
| **Minor criteria (supportive evidence)** | |
| Dental involvement<br>Alopecia<br>Wooly hair, abnormal nails | |
| At least 1 major criterion is necessary to make a firm diagnosis of sporadic IP. Minor criteria, if present, will support the diagnosis; because of their high incidence, complete absence should induce a degree of uncertainty | The diagnosis of IP is likely in a first-degree female relative of an affected female patient if any of the mentioned minor criteria are present, alone or in combination |

*According to Landy and Donnai.[5]

rare case of bilateral cleft lip and palate.[17] In a report of 40 IP2 cases it was found that two sisters and their mother suffered isolated cleft palate.[18]

All this comes to show that cleft palate cases are difficult to find in scientific literature.

According to Jones & al statistics, of a total 574 patients, the percentage of syndrome-associated clefts was 13.8% of lip and palate clefts. Of a total 328 patients 41.8% presented isolated cleft palate. Of a total 46 patients, 78.3% showed velopharyngeal insufficiency. It was then considered a syndrome due to the fact that the examined infant associated to the cleft two or more major malformations or three or more minor malformations unexplained through family history. This supports the theory, as well as is the case in our paper, that syndromes are more frequently associated to isolated cleft palate (CP).[19]

Our patient presented typical IP2 skin characteristics distinctively found in stage 1. There were also observable signs in hair and ophtalmological alterations. The mother`s clinical history was of the essence to later arrive to a confirmed diagnosed hypothesis upon consultation with the geneticist. When the infant was ten months old, she underwent cleft surgery. This protracted timing was a result of respiratory conditions which precluded the observation of optimal timing for palate surgery according to our cleft palate surgical protocol.

The velum (soft palate) reconstructive surgery was performed without incidents. Good quality muscular tissue was encountered to achieve reconstruction of muscular rings. The patient recovered total functionality of velopharyngeal sphincter. We therefore can suggest that treatment of this manifestation of the condition can be carried out without special considerations when programming surgery.

Even though IP2 is considered a rare condition it must be taken into account when examining oral and dental anomaly cases in infants presenting other major manifestations associated to the dental scheme. In these cases, the role of the dentist is all important. The dentist must be aware of any clinical or radiographic finding of the condition to be able to differentiate it from other forms of ectodermal dysplasia. The dentist must as well be aware of the fact that, alterations present at birth can precede other alterations in the stomatological area, thus enabling him to be prepared to perform treatment and prevention stages of these alterations.

Some authors support the idea that IP2 is randomly related to CLP cases,[18] we arrive at the question of whether there really is an analogy between the syndrome and CP condition.

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