



Case Report

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Gorlin-Goltz Syndrome: A Case Report

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Abstract

Nevoid basal cell carcinoma syndrome usually presents as an autosomal dominantly inherited syndrome with variable phenotypic expression. The aim of this study was to report a case of this syndrome based on clinical, radiographic, and histopathological findings. Male patient, 13-years-old, attended the Oral Diagnostic Clinic from State University of Paraíba, complaining of mandible swelling. On physical examination, left facial asymmetry was found, with mandible swelling and inflammatory submandibular lymphadenopathy. The patient also presented polydactyly. Panoramic radiography showed a multilocular well-defined mandibular radiolucency in anterior region. An incisional biopsy was performed, confirming the diagnosis of odontogenic keratocyst. Skull postero-anterior and thorax radiographic images were also performed, with no alterations. The patient was clinically diagnosed as having nevoid basal cell carcinoma syndrome with the presence of odontogenic keratocyst as a major criterion and the following minor criteria: Polydactyly, hypertelorism, Sprengel anomaly, deformed chest and prominent frontal bossing. The patient was referred to the physician for evaluation. Nevoid basal cell carcinoma syndrome has several distinct clinical characteristics and careful investigation is important, especially using imaging tests as complementary exams.

Keywords

Nevoid basal cell carcinoma syndrome, Gorlin syndrome, Odontogenic keratocyst

Introduction

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin-Goltz syndrome or Gorlin Syndrome, usually presents with dominant autosomal heritage, with variable phenotypic expression. It is usually caused by mutations in the *Patched Tumor Suppressor (PTCH1)* gene, located in chromosome 9q [1,2]. The mutation usually affects the germ cells resulting in vertical transmission but in as many as 40% of cases, the mutation affects somatic cells, and the syndrome occurs sporadically without other family members affected. NBCCS was described in 1960 by Gorlin and Goltz [3], who established the classic triad: Multiple nevoid basal cell carcinomas (NBCC), multiple odontogenic keratocyst [4,5] and bifid ribs [6,7].

The syndrome can be diagnosed only when the first signs and symptoms appear [8]. The presence of multiple odontogenic keratocysts in the jaws is very common [9], and may be the first and unique manifestation [10,11], being highly suggestive of the syndrome, even in the absence of other manifestations [12,13].

In addition, this syndrome is a condition that has a predisposition to cancer, being of fundamental importance to diagnose it as early as possible. Careful clinical examinations and imaging tests are of great value as a diagnostic aid [11].

The first health care professional to come into contact

with the patient may be the dental surgeon, due the presence of swelling on the face resulting from the keratocysts in the jaws [10,11]. So, this study aimed to report a case with unusual clinical manifestations in a young patient with NBCCS.

Case Presentation

A 13-years male patient attended the Oral Diagnostic Clinic from Campus VIII of the State University of Paraíba (UEPB), complaining of swelling in the mandible (Figure 1). The extra-oral physical examination found left facial asymmetry with localized mandible swelling on the left side and inflammatory submandibular lymphadenopathy. The patient also had polydactyly of the hands and feet (Figure 2). Sprengel anomaly was also found (Figure 3) and chest deformation. Basal cell carcinomas were not seen on the skin. The intraoral physical

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examination showed swelling in anterior region of the mandible, painless on palpation and with dental malposition (Figure 4). Panoramic radiography revealed a well-defined multilocular radiolucent lesion in anterior region of the mandible (Figure 5). An incisional biopsy confirmed the diagnosis of odontogenic keratocyst (Figure 6). Postero-anterior radiographies of the skull and the thorax were performed, and these did not show any notable changes such as calcification of falx cerebri and bifid ribs, or other bony anomalies typical of the syndrome. The patient was clinically diagnosed with NBCCS based on a keratocyst as a major criterion and the presence of five minor criteria: Sprengel anomaly (congenital scapular elevation), polydactyly, deformed chest, hypertelorism and prominent frontal bossing. The patient underwent surgical decompression and subsequent enucleation of the lesion and is being followed up by the Clinic team. The person responsible for the patient signed the Informed Consent Form when filling out the patient's medical record.

Discussion

NBCCS is a rare syndrome with large phenotypic heterogeneity which makes it difficult to diagnosis. More than 100 different clinical manifestations have been reported which in-



Figure 1: Facial asymmetry.



Figure 3: Sprengel anomaly (arrow).

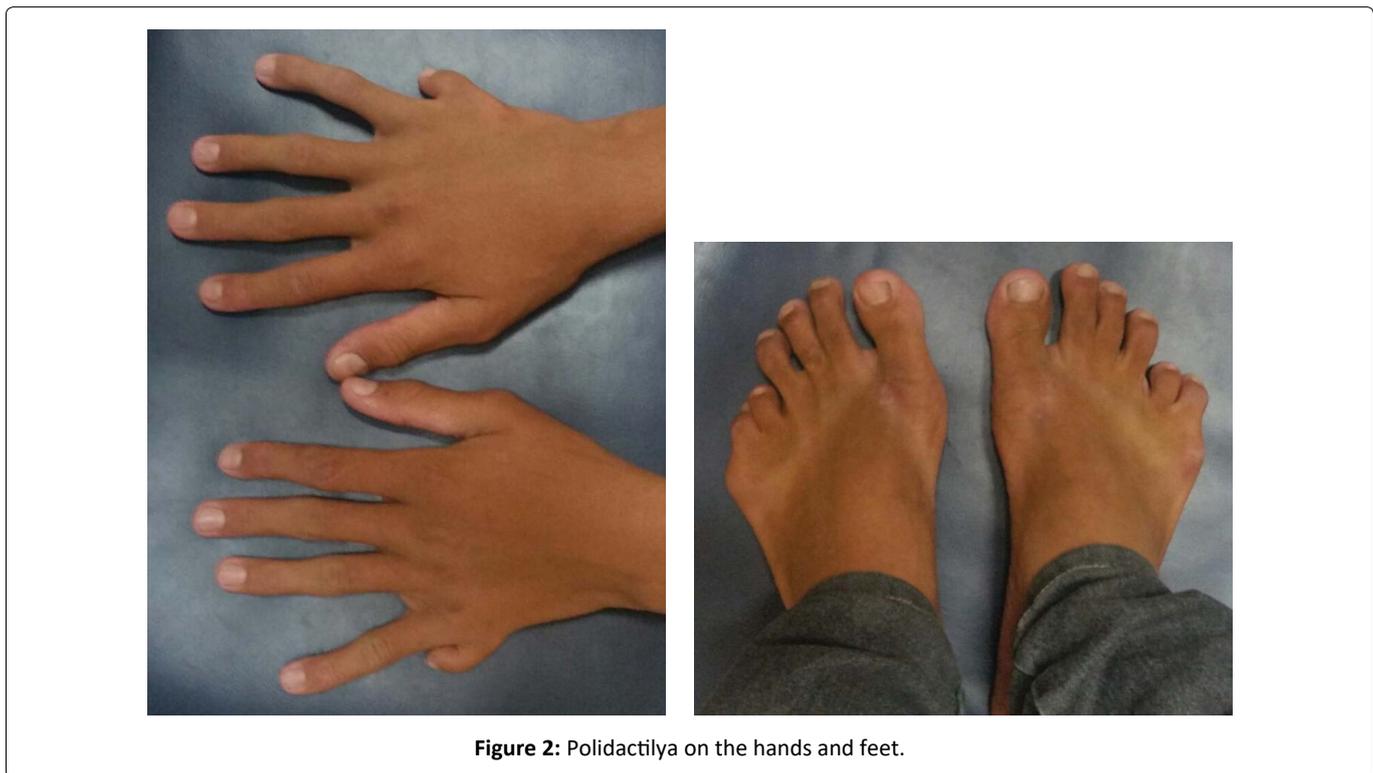


Figure 2: Polydactyly on the hands and feet.

clude skeletal, craniofacial, neurological, oropharyngeal, dermal, sexual, ophthalmic, and cardiac abnormalities [14-16].

The diagnosis is clinical and based on specific characteristics, requiring the presence of two major criteria (odontogenic keratocyst, nevoid basal cell carcinoma, palmoplantar pits), or a major criterion with two minor [1,17], or a major criterion associated with a minor one. Minor criteria include macrocephaly, congenital malformations, ocular and skeletal abnormalities, radiographic changes, among others. The syndrome should also be considered if there is a major criterion and a molecular confirmation. Gene mutation analysis confirms the diagnosis [18]. Although the patient in the present case had only one large odontogenic keratocyst in mandible (major criterion), he had other minor criteria such as Sprengel anomaly (congenital elevation of the scapula with rotation toward the spine with scoliosis), polydactyly in the hands and feet, prominent frontal bossing, hypertelorism and chest deformity (Pectus Excavatum).

Among the major criteria, the presence of multiple keratocysts (affecting 74% [1] to 90% [16] of the patients) and calcification of falx cerebri is also quite prevalent [7,9,11,16,19],

in addition to palmoplantar pits [17]. The patient in the present case presented with one large keratocyst in the mandible with a multilocular pattern. Keratocysts in syndromic patients can present, on average, five per patient, in addition to a higher recurrence rate after enucleation compared to non-syndromic patients. Because of this, it is recommended follow-up for a long period (annually for five years and biannually, for the entire life of the patient) [7,11,20]. Khaliq, et al. [11] when evaluating seven syndromic patients, found that all had multiple keratocysts as the first manifestation of the syndrome, most of which were located in the mandible (77%), in an unilocular pattern (71%), associated with teeth (88%). As treatment, the patient of the present case initially received a conservative approach (cystic decompression), due to the large extent of the lesion, followed by enucleation, the most common treatment for keratocysts [21].

However, despite being prevalent major criterion, the patient of this case did not present palmoplantar pits, but he was alerted to their appearance and the possibility of malign-



Figure 4: Intraoral exam with tooth malposition.

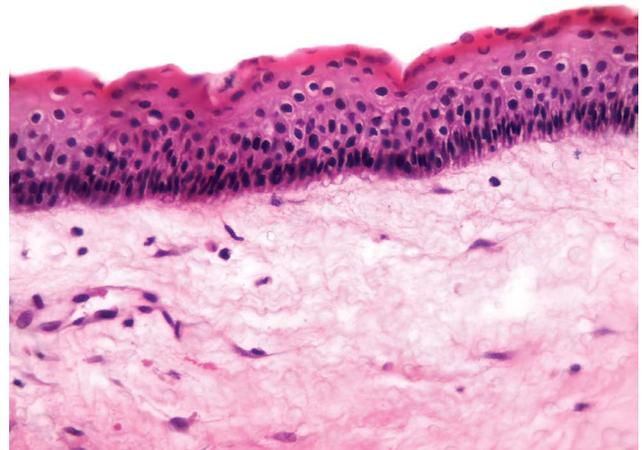


Figure 6: Parakeratinized epithelium, with a corrugated surface, basal layer with columnar and hyperchromatic cells, in palisade and with a discrete inverted nuclear polarity (400x).



Figure 5: Large radiolucent multilocular area in the anterior region of mandible, dislocating teeth.

nant transformation into nevoid carcinomas [1]. In addition, he was referred to the dermatologist for evaluation. Often the basal cell carcinomas of the skin in these patients are the most challenging to manage and produce the most morbidity. The Posterior-Anterior (PA) radiography of the patient's skull did not demonstrate calcification of falx cerebri, although this is the most frequent radiographic alteration found in syndromic patients [2,15]. All syndromic patients evaluated by Santos, et al. [16] and by Khaliq, et al. [11] presented calcification of falx cerebri.

Among the most prevalent minor criteria of the syndrome are the presence of skeletal anomalies, especially in the ribs [13,17]. However, the evaluation of chest radiography did not show any noticeable changes in the ribs of the patient.

Because NBCCS is a hereditary condition, genetic counseling is mandatory in order that family members, especially children, can be genetically tested or followed. For this, radiographic exams, which have a low cost, must be used [14]. As the syndrome is of autosomal dominant inheritance, offspring have 50% risk of being affected [1,14,22]. However, some syndromic patients can present a new spontaneous mutation [23,24], with no history of an affected family member [15]. In the present case, it was not possible to assess the rest of the patient's family.

As the treatment is multidisciplinary, the early referral of the patient to other professionals is essential for the diagnosis of other changes and possible interventions. The patient must be followed up by different specialists, especially dermatologists, due to his high predisposition to basal cell carcinomas and neoplasms [25]. Carcinomas associated with the syndrome are diagnosed often in young patients (mean 25-years-old), in unexposed areas of the body [1,7].

However, due the relative rarity and phenotypic variability, this syndrome is usually diagnosed late [26]. Our 13-year-old patient had earlier indications of the syndrome, such as polydactyly, Sprengel anomaly, prominent frontal bossing and hypertelorism, but it was only due to the swelling in the face that the family sought the health professional and the final diagnosis of NBCCS was confirmed.

This case presents an alert to dentists that, the NBCCS should at least be considered in any patient with a biopsy proven odontogenic keratocyst, and the patient should be examined for other features of the syndrome as well as family history of jaw cysts. If other major or minor criteria are present, referral to other specialists would be in order to document as soon as possible other features of the syndrome that could lead to a more definitive diagnosis.

Final Considerations

NBCCS presents well-defined clinical criteria for its diagnosis and the performance of molecular tests is indicated only in a few particular cases, due to its high cost. A helpful complementary diagnostic tool of great importance is the imaging tests that are relatively inexpensive but are critical to discover the keratocyst.

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