Oral manifestations of Cowden's disease. Presentation of a clinical case

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ABSTRACT

Cowden's disease, or multiple hamartoma syndrome, is an autosomal dominant genodermatosis, characterized by the presence of multiple cutaneous hamartomas, oral fibromas and benign acral keratosis. It affects multiple organs (breast, thyroids, stomach, colon), with the strong possibility of malignant neoplasia developing in these organs.

We present a case of this rare syndrome, highlighting the presentation of some clinical characteristics that, in suspected cases, can help to establish an early diagnosis of this disease, this being of great importance given the high frequency of tumors in people with this clinical picture.

Key words: *Cowden's disease, multiple hamartomas.*

RESUMEN

El Síndrome de Cowden o síndrome de hamartomas múltiples es una genodermatosis que se hereda de forma autosómica dominante, caracterizada por la presencia de múltiples hamartomas cutáneos, fibromas orales y queratosis acras benignas. Afecta a múltiples órganos (mama, tiroides, estómago o colon), pudiéndose presentar en estos órganos neoplasias malignas.

Presentamos un caso de este síndrome, por su rareza y por presentar unas características clínicas que se deben conocer para que a partir de un diagnóstico de sospecha podamos llegar a un diagnóstico precoz de esta enfermedad, hecho este de gran importancia pues son frecuentes los tumores en las personas que padecen este cuadro clínico.

Palabras clave: *Síndrome de Cowden, hamartomas múltiples.*

INTRODUCTION

Cowden's disease was described in 1963 by Lloyds and Dennis in a 20 year-old female with the surname Cowden, after whom this disease is named (1).

Cowden's disease is an extremely rare, autosomal dominant hereditary disease, characterized by the presence of mucocutaneous lesions, characteristically and diagnostically hamartomatous, with visceral involvement and with the formation of malignant neoplasia, primarily breast and thyroid, in adults.

To date, less than five hundred cases have been described in the literature worldwide. It affects females slightly more than males (6/4), and manifests in the second or third decade of life.

The etiology is unknown, although since 1993 it has been related with the presence of alterations in the PTEN gene (phosphatase and tensin homologue), on the long arm of chromosome 10 (10q23.31, 10q22.3) or MMAC1 (mutated in multiple advanced cancers), this normally acts as a tumor suppressor gene and on occasions is mutated in breast, prostate and brain tumors (2).

Clinically, it is recognized by the presence of typical mucocutaneous lesions, which appear in 80% of patients, being of greatest interest in the diagnosis of the so-called trichilemmomas or tricholemmomas (multiple lesions that correspond to benign tumors of hair follicles). These manifest as skin-coloured facial papules, similar to warts and which group together especially around the mouth, nose or outer ear (3,4).

Oral fibromas may also present as smooth whitish-pink papules on the mucosa of the oral cavity, when arranged in groups they give rise to a typical cobblestone image.

Less frequently, vitiligo, café au lait patches, melanosis or keratic papules may present in acral parts.

Another clinical sign is the presence of hamartomas or fibrocystic disease, typically with visceral, thyroid and breast involvement, and at any level of the female reproductive system, also gastrointestinal polyps and hamartomas of the central nervous system, hemangiomas, neuromas, and in some cases angioid streaks (5,7). Xerostomia and high-arched palate may present.

A high risk of malignancy in breast fibroadenomas exists in females, and in the thyroids in males, even at an early age. Carcinomas of the gastrointestinal tract may also appear.

The diagnosis of this disease is fundamentally clinical, with some diagnostic criteria having been established in 1983 (8) by the International Cowden Syndrome Consortium, which, following a revision in 2000, remains as shown in Table 1.

The early diagnosis of this disease is extremely important, since a diagnosis of Cowden's disease is always associated with a high risk of developing malignant tumors when appearing at a young age.

The differential diagnosis is made against tuberous sclerosis, some types of multiple endocrine neoplasia, Byars-Jurkiewicz syndrome, Gardner's syndrome, lipoid proteinosis, multifocal epithelial hyperplasia (oral lesions) and orofacial granulomatosis. Although the literature reports other possibilities for the differential diagnosis, above all cutaneous lesions, we believe that the overall picture discounts the majority of these diagnoses (9,10).

There is no curative treatment for this disease, although control of mucocutaneous lesions has been achieved with surgery, given that these do not respond to topical treatment. Facial trichilemmoma responds to laser treatment.

Table 1. Diagnostic Criteria for Cowden's Disease.
(The International Cowden Syndrome Consortium, 2000).

1/ Criterios patognomónicos	Son todas las lesiones mucocutáneas de cualquier tipo. (triquilemomas faciales, queratosis, lesiones papilomatosas y mucosas).
2/ Criterios mayores	Carcinoma de mama, carcinoma de tiroides, macrocefalia, hamartomas múltiples en cerebelo o enfermedad de l´Hermitte Duclos, y carcinoma endometrial.
3/ Criterios menores	Otras enfermedades tiroideas, retraso mental, hamartomas y tumores gastrointestinales, enfermedad fibroquística mamaria, lipomas, fibromas, y malformaciones o tumores genitourinarios.
Para el diagnóstico se requieren una de las cuatro posibilidades siguientes:	A.- Presencia exclusiva de lesiones mucocutáneas aisladas: 6 pápulas de las cuales tres correspondan a triquilemomas, o queratosis acral o un mínimo de seis lesiones de queratosis palmo-plantar.
	B.- Presencia de dos criterios mayores, uno de los cuales debe ser obligatoriamente macrocefalia o enfermedad de l´Hermitte Duclos.
	C.- Presencia de 1 criterio mayor y tres menores.
	D.- Presencia de cuatro criterios menores .

CLINICAL CASE

A 56-year-old female attended our clinic for the extraction of a radicular remnant. During the clinical examination, multiple papular lesions were discovered on the gingiva, which tended to group together resulting in a cobblestone effect (Fig 1). The lower labial mucosa had a corrugated arrangement (Fig 2), and numerous papules appeared on the tongue creating a moriform appearance (Fig 3). A polypoid lesion on the jugal mucosa was removed at the same time as the biopsy of the gingiva was taken, the result of which was an inflammatory hyperplasia, the lesion of the jugal mucosa resulted to be a fibroepithelial polyp.

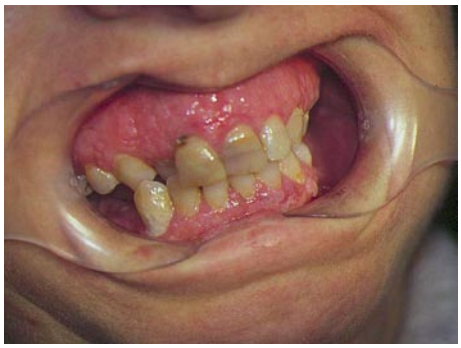

Fig. 1. Numerous papules on the gingiva giving rise to a cobblestone appearance.

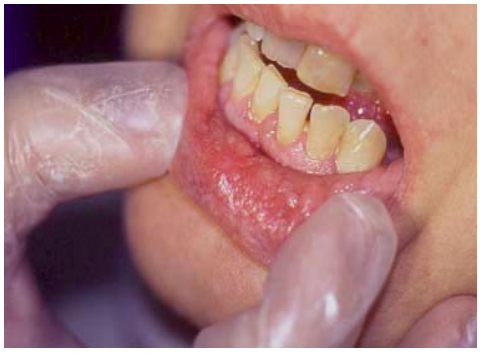

Fig. 2. Corrugated appearance of the labial mucosa.

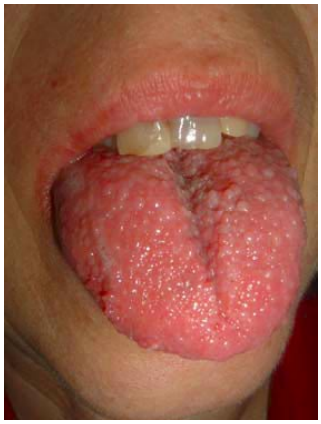

Fig. 3. Moriform appearance of the tongue due to the enormous amount of papules.

In the anamnesis, the patient referred to having been operated on for goiter on two occasions, and also for bilateral mammary cysts. The patient suffered from a gastric ulcer, esophagitis and polyps in the colon. Cutaneous lesions on the arms and soles of the feet had previously been extirpated on various occasions.

Given such an elaborate pathology, the full clinical history was requested from the hospital and summarized. The patient had previously undergone extirpation of thyroid colloid nodules, and on two occasions had been operated on for fibrocystic disease of the breast, she presented a gastric ulcer, and on various occasions, gastric and colonic polyps had been extirpated via endoscopy.

The lesions removed from the arm were Ackerman reactive inflammatory hyperplasias and those on the sole of the feet verruca plantaris.

Given these findings a diagnosis of oral involvement of Cowden's syndrome was made.

DISCUSSION

A rare case of this disease is presented, possessing the diagnostic criteria of the International Cowden Syndrome Consortium, as represented by four minor criteria (Appendix D).

This disease is slightly more predominant in females (6/4), with a predilection for Caucasians, clinical characteristics presented in our patient.

It is notable in this case that, in spite of being previous labeled as having Cowden's disease, at no point was an examination of the oral cavity or a biopsy of the lesions carried out. Perhaps because the malignancy of lesions of the oral mucosa is not described, or because the lesions are asymptomatic that the patient had not previously consulted a dentist.

Although this is usually a genetically determined disease, in this case no other member of the family is affected. However, the fact that this may be a spontaneous mutation cannot be discounted, as occurs in sporadic cases of breast, prostate or brain cancer (11).

Mutations of the PTEN suppressor gene have been noted in 80% of patients with Cowden's disease, with more than 80 different mutations being described (12, 13).

We agree with Mignoma (14) in that the dentist should be familiar with the clinical picture of this disease since its early diagnosis is extremely important, due to the high probability of cancer, fundamentally breast and thyroid, occurring in these patients, found to be as much as one third of cases by some authors (15).

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