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CASE REPORT

A 37-year-old female patient has had asymptomatic lesions in the oral cavity and on the lips since the age of 15. She had a history of thyroidectomy associated with the use of radioiodine for the treatment of follicular thyroid carcinoma, and follicular adenoma associated with Hashimoto's thyroiditis at age 23 years. Physical examination revealed normochromic, flat papules in the paranasal and perioral regions and on the lips, as well as hyperkeratotic papules on the dorsum of the hands (Figures 1 and 2). In the oral cavity, we noticed the presence of multiple, normochromic papules on the jugal mucosa, floor of the mouth and tongue (Figure 1). Biopsies of three lesions were performed: on the dorsum of the hand, compatible with benign acral keratosis; on the lip, forming a fibroepithelial polyp; and on the oral mucosa, with oral fibroma. High digestive endoscopy revealed duodenal hyperplastic polyps. Mammography was unchanged.

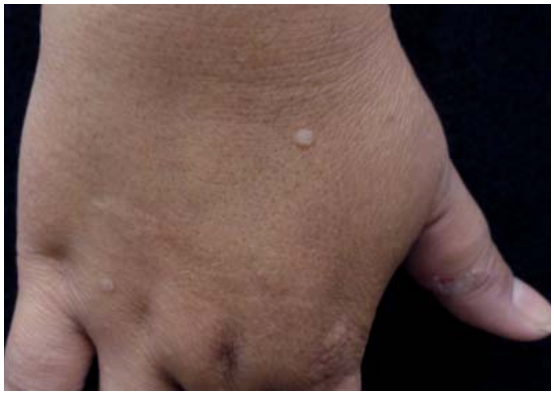

FIGURE 2: Normochromic keratotic papules on the dorsum of the right hand

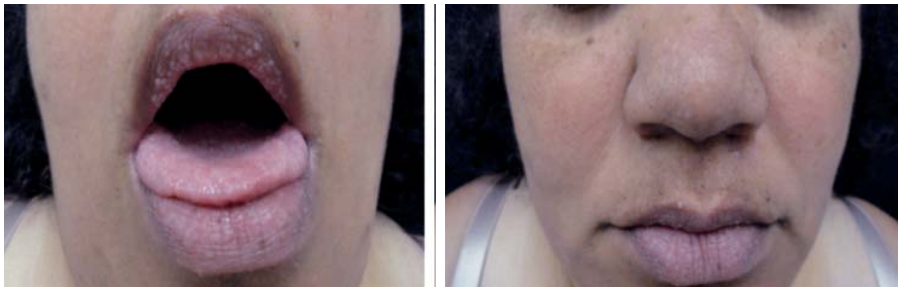

FIGURE 1: Hypochromic and normochromic papules in the perioral region, on the oral mucosa and on the lips

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DISCUSSION

Cowden's disease, also called Multiple Hamartomas Syndrome, was first described in 1963. It is an autosomal dominant syndrome with incomplete penetrance and variable expressivity. The disease has a prevalence of 1 per 200,000 inhabitants and is predominant in women.[1-6] Mutations of the PTEN tumor suppressor gene is present in 80% of cases. The classic dermatologic triad comprises multiple facial trichilemmomas, oral fibromas and benign acral keratoses benignas.[3,4] Changes become evident during the second and third decades of life.[2,7]

Included among the skin lesions presented by the patient and belonging to the syndrome are: flattened, normochromic, lichenoid papules with a central facial distribution; flattened, hyperkeratotic papules similar to flat warts on the dorsum of the hands; and polypoid and verrucous lesions in the oral mucosa.[2,3] Other associated mucocutaneous lesions include: lingua plicata with central fissure and hypertrophied lateral papillae, cobblestone oral mucosa, squamous and basal cell carcinoma, acanthosis nigricans, angiomas and lipomas.[1,4] Associations with Muir-Torre syndrome and melanoma have also been reported.[6,7]

The most commonly affected extracutaneous site is the thyroid. Neoplasia risk during life ranges from 3 to 10%.[6,7] Other affected sites are the breast, endometrium, gastrointestinal and genitourinary tracts, and central nervous system.[3,6]

Diagnosis is made by clinical criteria defined in 2000 in the International Cowden Consortion. However, some cases with atypical presentations do not meet all criteria (Chart 1).[5] The patient has four pathognomonic injuries: papillomas in the oral mucosa, oral mucosal lesions, benign acral keratoses, and facial trichilemmomas. One major criterion: confirmed thyroid neoplasia. One minor criterion: Hashimoto's thyroiditis.

Chart 1: Diagnostic criteria for Cowden´s syndrome

PATHOGNOMONIC CRITERIA	MAJOR CRITERIA	MINOR CRITERIA
	Breast neoplasia	Other lesions of the thyroid
	Thyroid neoplasia	Mental retardation
Facial trichilemmomas	Macrocephaly	Hamartomatous intestinal polyps
	Lhermitte-Duclos disease	Fibrocystic disease of the breast
Acral keratoses	Endometrial carcinoma	Lipomas
		Fibromas
		Tumors of the genitourinary tract
Papillomatous lesions		
Oral mucosal lesions		

Operational diagnosis if:

- One pathognomonic lesion, if there are: 6 or more facial papules, and 3 or more of them are trichilemmomas; or facial papules and papillomatosis in the oral mucosa; or papullomatosis of the oral mucosal and acral keratoses; or 6 or more palmoplantar keratoses
- Two major criteria, and one of them must necessarily be macrocephaly or Lhermitte-Duclos disease
- One major criterion and 3 minor criteria
- Four minor criteria

If there is one family member with confirmed diagnosis of Cowden´s syndrome, the diagnosis is made if:

- Presence of 1 pathognomonic criterion
- Any major criterion with or without minor criteria
- Two minor criteria

In the differential diagnosis, the following conditions shoud be excluded: Darier's disease, tuberous sclerosis, neurofibromatosis, juvenile polyposis syndrome, congenital pachyonychia, mucocutaneous hyalinosis, generalized hair follicle hamartoma, inverted follicular keratosis and other diseases associated with keratotic papules.[2]

Treatment consists of periodic dermatological examination of skin lesions, although the risk of malignancy is small. If the patient wishes so, excision of suspicious or aesthetically disfiguring lesions is performed.[6] Clinical and gynecological follow-up is necessary and should include exams that allow early detection of malignant neoplasms, such as mammography, endometrial biopsy, thyroid ultrasound and digestive endoscopy.[5,6] ❑

Abstract: The authors describe a case of Cowden´s syndrome in a female patient with classic cutaneous lesions, plus papillomatous lesions in the gastrointestinal tract and a previous history of thyroid carcinoma. Mucocutaneous lesions occur in 90% of Cowden's syndrome cases and are characterized by facial trichilemmomas, oral mucosal papillomas and benign acral keratoses. Sites of extracutaneous involvement include: the thyroid, gastrointestinal tract, breast and endometrial tissue. There is risk of malignancies in these organs and they need to be monitored with imaging tests. The early diagnosis of the syndrome by a dermatologist through mucocutaneous lesions enables the investigation and diagnosis of extracutaneous involvement.
Keywords: Hamartoma; Papilloma; Multiple Hamartoma Syndrome

REFERENCES

1. Farooq A, Walker LJ, Bowling J, Audisio RA. Cowden syndrome. Cancer Treat Rev. 2010;36:577-83.
2. Vettorato G, Souza PRM, Bozko MP, Lamb FM. Cowden's Disease or Mutiple Hamartoma Syndrome. An Bras Dermatol. 2003;78:209-13.
3. van der Velden JJ, Vreeburg M, Smeets EE, Schrander-Stumpel CT, van Steensel MA. Skin abnormalities in individuals with macrocephaly: Cowden disease from a dermatologist's point of view. Int J Dermatol. 2008;47:45-8.
4. Larumbe A, Iglesias ME, Illarramendi JJ, Córdoba A, Gállego M. Acral Keratoses and Inverted Follicular Keratosis Presenting as Cowden Disease. Actas Dermosifiliogr. 2007;98:425-9.
5. Ha JW. Autossomal Dominant Inherited Cowden's Disease in a Family. Clin Endosc. 2013;46:85-90.
6. Hammami S, Berriche O, Ali HB, Hellara O, Ansar F, Mahjoub S. Managing the risk of cancer in Cowden syndrome: a case report J Med Case Rep. 2012;6:225.
7. Jornayvaz FR, Philippe J. Mucocutaneous papillomatous papules in Cowden's syndrome. Concise report. Clin Exp Dermatol. 2008;33:151-3.

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