

原文題目(出處)：	Multiple Hamartoma syndrome with characteristic oral and cutaneous manifestations. Case Rep Dent 2013, Article ID 315109
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報告日期：	102/12/10

內文：

一、Abstract

1. To present a case of Cowden's syndrome and emphasize the importance of continued cancer surveillance in these patients.
2. A case of Cowden's syndrome of a 30-year-old female patient who came with a complaint of multiple growths in the oral cavity of a three-month duration.
3. Cowden's syndrome is associated with the development of several types of malignancies, especially breast carcinoma and thyroid carcinoma, which is why early recognition and regular and vigilant surveillance of individuals with the syndrome are important.

二、Background

1. Cowden's syndrome (CS), also termed as multiple hamartoma syndrome (MHS), was first described in 1940 by Salem and Steck.
2. It is a rare genodermatosis, of autosomal dominant inheritance and variable phenotype, principally characterized clinically by multiple hamartomas of ectodermic, mesodermic, or endodermic origin. It results most commonly from the mutation in the PTEN gene on the arm.
3. It is associated with an increased risk of malignancy, particularly cancers of the breast, thyroid, endometrium, and to a lesser extent, renal system. The rare occurrence of this disease and the synchronous association of various malignancies with this disease emphasize the importance of a thorough diagnostic work-up and management of the patients with Cowden's syndrome.

三、Case report

1. Age/sex: 30-year-old female
2. Chief complaint: Multiple growths in the oral cavity of three months duration.
3. Present illness: Initially, she had noticed only two growths in the right and left retrocomissural areas. Gradually they increased in number, involving the entire oral cavity. The lesions were not associated with any symptoms. Previously, she was prescribed corticosteroid ointment and multivitamins by a local doctor, but she found no relief.
4. Past history:
 - (1) A left breast abscess 12 years back which was drained.
 - (2) A growth in the left lower back region which was excised 10 years back.
 - (3) No medical records available for proper evidence
 - (4) Family history:(-)
5. General physical examination
 - (1) Vital signs: in the normal range
 - (2) Inferior palpebral conjunctiva: pallor

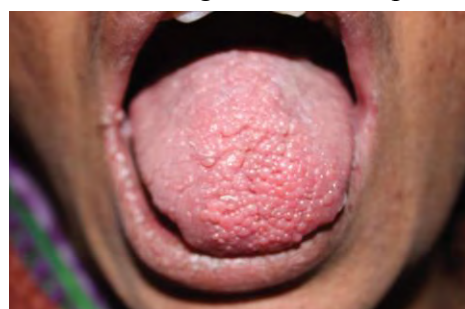
- (3) A scar was noticed over the lower back region on the left side
6. Extraoral examination:

- (1) Small multiple skin colored, flat topped papules over the skin of forehead and malar bones, measuring around 1 to 5mm in diameter → trichilemmomas.



7. Intraoral examination:

- (1) Multiple papillomatous papules involving all the mucosal surfaces.
 (2) Cobblestone appearance spherical coral pink in color
 (3) Size: 1 to 5 mm
 (4) Consistency: soft to firm
 (5) Tenderness: (-)
 (6) The lesions on the retrocomissural areas were larger in size and paler.



四、 Discussion of the diagnosis

1. A provisional diagnosis of Cowden syndrome was made on the basis of the presence of trichilemmomas and mucosal lesions. There were more than 6 cutaneous papules or trichilemmomas and oral papillomatosis → Criteria 1

Pathognomic criteria	Major criteria	Minor criteria
(i) facial trichilemmomas	(i) breast carcinoma	(i) thyroid lesions
(ii) acral keratosis	(ii) thyroid carcinoma	(ii) mental retardation
(iii) papillomatous papules	(iii) endometrial carcinoma	(iii) G I Hamartomas
(iv) mucosal lesions	(iv) macrocephaly	(iv) fibrocystic breast
	(v) Lhermitte-Duclos disease	(v) lipomas
		(vi) fibromas
		(vii) genitourinary tumors

Criteria 1 (Mucocutaneous lesions alone)	(i) 6+ facial papules with 3+ being trichilemmomas (ii) cutaneous facial papules and oral mucosal papillomatosis (iii) oral mucosal papillomatosis and acral keratosis (iv) 6+ palmar or plantar keratosis
Criteria 2	Two major criteria with one being Lheimitte-Duclos disease or macrocephaly
Criteria 3	One major and threeminor criteria
Criteria 4	Four minor criteria

2. Orthopantomogram: generalized alveolar crestal bone loss.
3. Laboratory investigations:
- (1) Hematological investigation: anemia
- (2) Biopsy specimen of papules from lower labial mucosa, buccal mucosa, and gingiva: hyperplastic stratified squamous epithelium with mild

inflammatory evidence in the connective tissue suggestive of nonspecific epithelial hyperplasia.

五、Treatment and management

1. Surgical excision of the lesions present on the right and left retrocommissural areas, the lower labial lesions
2. Gingivectomy with surgical contouring of the lower anterior gingiva was performed for esthetic reasons.
3. Thyroid ultrasonography and thyroid function tests and endoscopy for gastric polyps →no abnormality
4. Rule out malignancies of the endometrium and breast→ referred to a gynaecologist for appropriate screening.
5. Mammography → no evidence of malignancy was found
6. Follow up to monitor the lesions as well as to perform continued cancer surveillance.

六、Discussion

1. Cowden's syndrome is a rare multiple hamartoma disorder. This syndrome is one of a group of heterogeneous disorders known collectively as the *PTEN* hamartoma tumor syndrome (PHTS).
2. Cowden's syndrome is clinically characterised by multiple mucocutaneous hamartomatous lesions and neoplasias of the breast, thyroid gland, and gastrointestinal tract.
 - (1) Mucocutaneous lesions include flesh-colored flat-topped cutaneous facial papules ranging from 1 to 5mm in diameter, most of which are trichilemmomas.
 - (2) Multiple oral papules are present on gingival, labial, and palatal surfaces of oral cavity. They measure around 1 to 3 mm, and they coalesce to give a cobblestone appearance to the mucosae.
 - (3) Palmoplantar keratosis is another type of mucocutaneous lesions observed in Cowden's syndrome .
 - (4) Because the development of associated malignancy may take several years, these mucocutaneous lesions may serve as important clinical markers in identifying patients at high risk of malignancy of the breast and thyroid.
3. Women with Cowden's syndrome have a 30% to 50% risk for breast cancer. Therefore, women should carry out monthly self-examinations, and professional physical examinations should be performed once every three months. Mammography is suggested to be performed twice a year. Some authors have recommended prophylactic bilateral mastectomy, particularly in women with an extensive fibrocystic breast disease or breast carcinoma. Thyroid should be examined for any abnormalities. Thyroid function tests and ultrasonography of the gland should be performed as baseline diagnostic examinations. Fine needle aspiration or surgical biopsies are indicated if any lesion is identified. In addition, complete blood cell count, liver and renal function tests can be performed at the baseline .
4. Other investigations which could be carried out are gastrointestinal endoscopy, endometrial examination, radionuclide scans to detect any malignancies, molecular genetic analysis for phosphatase and tensin homolog (*PTEN*), and immunohistochemical staining for PTEN.
5. Treatment for Cowden's syndrome is only cosmetic.

- (1) The facial papules can be treated physically by CO₂-laser ablation, surgical removal, or chemically removed by topical 5-fluorouracil.
- (2) Systemic therapy with acitretin 0.75mg/kg/day has been reported to give good cosmetic results for all mucocutaneous lesions . Surgical management of the mucocutaneous lesions includes cryosurgery, electrosurgery, dermabrasion, and laser abrasion.

七、Conclusion

Perhaps, the oral lesions could be the only sign of this disease. Hence, the identification of these lesions will help in early recognition of Cowden's syndrome which may in turn facilitate the early diagnosis of cancer. Hence, frequent follow-ups and continued cancer surveillance is vital for long term survival of these patients.

題號	題目
1	下列關於 Cowden's syndrome 的敘述何者為非? (A) 屬於一種 autosomal dominant disease (B) 常見到 facial trichilemmomas 此種症狀 (C) 和 PTEN 此基因有關 (D) 無法做為 cutaneous marker of breast cancer
答案 (D)	出處：Shafter's textbook of Oral Pathology(6 th edition)
題號	題目
2	(A) (B) (C) (D)
答案 ()	出處：