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Case Report

Cowden syndrome: A case report

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ABSTRACT

Cowden syndrome or multiple hamartomas syndrome are other names for Cowden disease. It is a hereditary condition with autosomal dominant inheritance pattern, marked by the presence of hamartomas that are capable of affecting any organ and run the risk of developing into cancer. The main cause of Cowden syndrome is usually attributed to a PTEN (phosphatase and tensin homolog) mutation, a tumor suppressor gene that causes unchecked cell division, which gives rise to cancer and hamartomas. Bannayan-Riley-Ruvalcaba syndrome is another condition that shares characteristics with Cowden syndrome. Patients with this syndrome usually have macrocephaly and mucocutaneous lesions. The majority of Cowden syndrome patients eventually acquire cancerous tumors, usually in the breast, thyroid, or endometrium. Studies show that the prevalence is higher in women, and most of the cases documented in the literature involve people of Caucasian heritage. According to certain estimates, the prevalence of Cowden syndrome is roughly 1 in 2,000,000 individuals.

1. Introduction

Riley and associates first recognized a complex of symptoms in a group of patients from a single family in 1960, and they named this trait autosomal dominant. In 1963, Lloyd and Dennis went on to describe this condition.[1] They looked at Rachel Cowden, a 20-year-old patient with a number of abnormalities, such as scrotal tongue syndrome, thyroid adenomas, papillomatous papules, fibrocystic breast disease with malignant degeneration, changes in the central nervous system, and family members with a mild manifestation of the condition.[2]

2. Case Report

A 27-year-old woman who came to the Department of Oral Medicine and Radiology with a primary complaint of a forward-positioned upper jaw for the past three years. The patient reported experiencing bleeding from the gums and oral malodor. She is currently receiving homeopathic treatment for infertility and underwent nasal septum surgery eight years ago. On extraoral examination, there was no gross facial asymmetry, nor were there any abnormalities observed in the temporomandibular joint or in the salivary gland and lymph nodes. Intraoral examination indicated the presence of enlarged gingiva, restorations associated with tooth 14, and missing teeth 15, 25, 44, 46, 34, and 36. Additionally, there were pit and fissure caries noted in teeth 17, 24, and 26.

An incidental finding included multiple white papillomatous growths on the anterior gingiva, affecting both the attached gingiva and interdental papillaappearance.(Figures 1 and 2) Onpalpation, the lesion watender, soft to firm in consistency.

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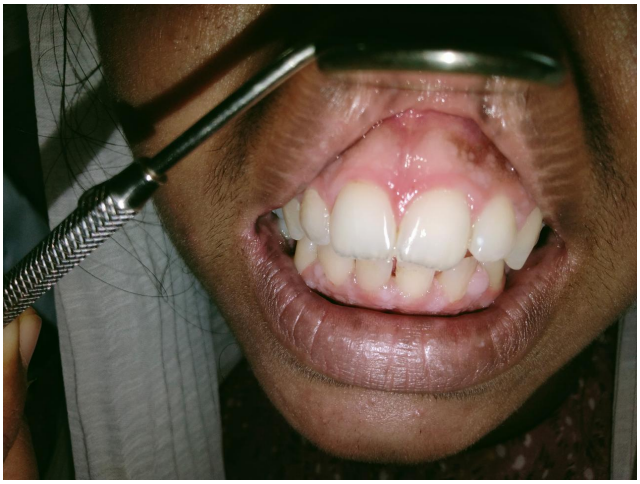

Figure 1: Shows multiple white papillomatous growth (papules) present on the anterior gingiva involving the attached gingiva and interdental papilla with respect to maxillary anterior region

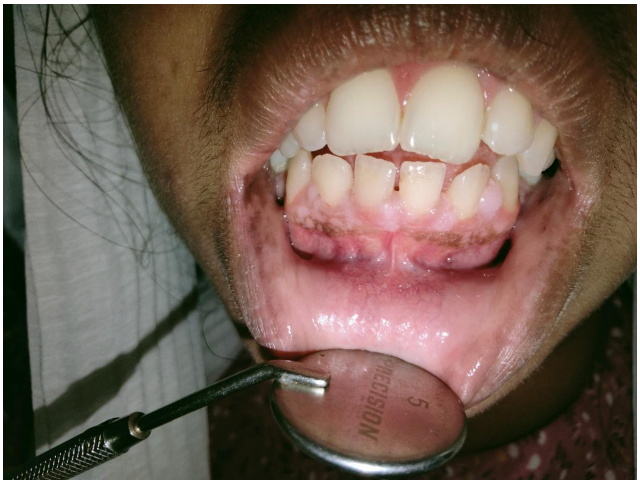

Figure 2: Shows multiple white papillomatous growth (papules) present on anterior gingiva involving attached gingiva and interdental papilla with respect to mandibular anterior region

The extraoral findings indicate the presence of multiple small skin colored papules on the flexor aspect of the hands and legs, referred to as Trichilemmoma. (Figure 3)

The patient was referred to a gastroenterologist for further evaluation.

3. Discussion

Cowden syndrome is typically caused by an inherited mutation in the PTEN tumor suppressor gene.This gene is essential for the synthesis of a protein that controls cell division.Similar mutations in the PTEN gene are also found in other conditions, such as Bannayan-Riley-Ruvalcaba syndrome and segmental overgrowth lipomatosis arteriovenous malformation epidermal nevus (SOLAMEN) syndrome.[3,4]

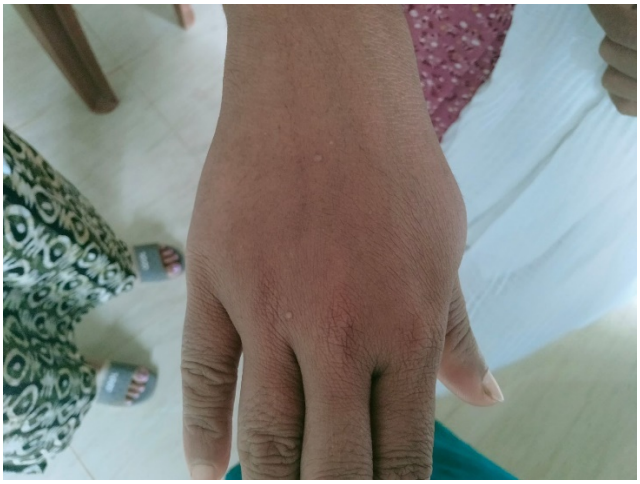

Figure 3: Shows presence of multiple small skin coloured papules on the flexor aspect of the hands - Trichilemmomma

A higher risk of cancer, especially thyroid and breast cancers, exists for people with Cowden syndrome. Non-medullary thyroid carcinoma is found in 3–10% of cases, whereas breast cancer is the most frequently associated malignancy, occurring in 25–50% of cases.[1]

The histopathological analysis of Cowden syndrome varies depending on the specific lesion being biopsied. Trichilemmomas, for instance, often exhibit pale glycogenated cells attached to the epidermis and linked to an associated hair follicle, with peripheral palisading observed.[5]

Intraorally the lesions present themselves as papillomatous or cobblestone patterns and generally are of the color of the surrounding mucosa. The tongue and the lips are most commonly involved in mucosal lesions, but any part of the mouth can be involved. (circumvallate papilla)Skin colored to yellow-brown, warty papules or nodules are a more specific finding in CS, representing sclerotic fibroma.Clinically, the syndrome is linked to gastrointestinal hamartomas, benign and malignant thyroid lesions, mucocutaneous lesions, developmental delays, breast cancer, and benign breast conditions like fibrocystic disease.[1]

Kay et al recommended that diffuse glycogenic acanthosis and colonic polyps be considered pathognomonic for Cowden Syndrome (CS).[6]

Despite its rarity, a high degree of clinical suspicion is necessary to diagnose this potentially cancerous condition. The diagnostic criteria established by the International cowden syndrome consortium are used for identifying CS.

To meet the criteria,

1. There must be at least three main characteristics, at least one of which must be gastrointestinal

hamartomas, Lhermitte-duclos disease, or macrocephaly.

2. Three minor criteria and two major criteria are satisfied.

Table 1: The international cowden syndrome consortium criteria [7]

	Major	Minor
1	Cancer of the breast.	Autism spectrum disorder
2	Endometrial cancer (epithelial)	Colon cancer
3	Thyroid cancer(follicular)	Esophageal glycogenic acanthosis (≥3)
4	Gastrointestinal hamartomas (including ganglioneuromas but excluding hyperplastic polyps :≥3)	Lipomas (≥3) Mental retardation (i.e, IQ ≤75)
5	Lhermitte-Duclos disease(adult)	Renal cell carcinoma
6	Macrocephaly (≥97 percentile :58 cam for females, 60cm for males)	Testicular Lipomatosis
7	Macular pigmentation of the glans penis	Thyroid cancer(papillary or follicular variant of papillary
8	Multiple mucocutaneous lesions(any of the following): 1. Multiple trichilemmommas (≥3, atleast one biopsy proven) 2. Acral keratoses (≥3 palmoplantar keratotic pits and/or acral hyperkeratotic papules) 3. Mucocutaneous neuromas (≥3) 4. Oral papillomas (particularly on tongue and gingiva), multiple(≥3) OR biopsy proven OR dermatologist diagnosed	1. Thyroid structural lesions (e.g adenoma, multinodular goiter) 2. Vascular anomalies (including multiple intracranial developmental venous anomalies)

Although the characteristics of cancers associated with Cowden syndrome/PHTS (PTEN Hamartoma Tumor Syndrome) have not yet been fully understood, it is common for them to involve the inactivation of the PTEN gene. [8]

Currently, there is no cure for Cowden syndrome due to its genetic nature.Nonetheless, genetic counseling may be helpful, especially if other family members are also susceptible to receiving a diagnosis. [1]

Regular and proactive screening is essential for the early detection and management of potential malignancies because of the increased likelihood of malignancies occurring in the breast, thyroid, and other organs linked to this syndrome. Regular self-examinations, surveillance, and yearly mammograms or magnetic resonance imaging (MRI) are advised for breast cancer, provided that there are risk factors or clinical suspicions. [1]

Patients with this syndrome are usually affected by either follicular or papillary thyroid cancers. [8]

Surgical intervention, anti-cancer medication therapy, and intravenous radioiodine therapy are among the treatments used. Depending on the lymph node involved and the degree of progression, surgical treatment options include adenomectomy, subtotal thyroidectomy, or total thyroidectomy.It has been demonstrated that systemic retinoid treatment can control the skin lesions linked to CS. Rapamycin therapy is presently being tested in clinical trials and has demonstrated encouraging results in terms of CS skin manifestation regression. [7]

Patients may live closer to normal life spans if cancers are detected early, and the prognosis is fair. [7]

4. Conclusion

The clinical symptoms of Cowden syndrome do not always align with genetic research findings. However, recent advancements in genetic testing highlight the need to diagnose this condition using both clinical assessments and genetic analyses. Collaborating with genetic experts is essential to ensure accurate diagnosis and appropriate monitoring for malignant tumors. [9]

5. Source of Funding

None.

6. Conflict of Interest

None.

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