Cowden’s syndrome impacting on oral health: considerations for the oral healthcare worker

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Abstract

Cowden’s syndrome is a rare autosomal dominant genodermatosis characterised by multiple hamartomas affecting all three germ layers coupled with an increased risk of developing cancer, most commonly of the breast, thyroid and endometrium. Here, we present a case of Cowden syndrome in an adult male where the chief complaint is the inability to maintain adequate oral health as a direct result of the oral manifestations of the condition. We also highlight the role of the oral healthcare worker in recognising and, when appropriate, referring such cases for specialist opinion and management.

Key words: Cowden syndrome, hamartoma

Introduction

Cowden syndrome (CS) is a rare autosomal dominant (AD) genodermatosis characterised by multiple hamartomas affecting all three germ layers, and an increased risk of cancer. Loss of expression of PTEN (protein tyrosine phosphatase with homology to tensin), a tumour suppressor gene localised to chromosome 10q23.3, is observed in 85% cases (Scheper et al., 2006).

Clinical features of CS include pathognomonic mucocutaneous lesions and a predisposition to malignancy, particularly of the breast, thyroid and endometrium. Oral, the most common presentation of CS is in the form of multiple fibro-epithelial polyps. Other manifestations include nodular gingival hyperplasia, a high-arched palate, fissuring and lobulation of the tongue and, rarely, oral squamous cell carcinoma (Scheper et al., 2006; Woo and Abdelsayed, 2008).

This case report discusses an adult male with Cowden syndrome in which the oral manifestations of the disease were the chief source of complaint and had resulted in a significant impact on the patient’s quality of life. It highlights the role of the general dental practitioner in recognising and, when appropriate, referring such cases for specialist opinion and management.

Case report

A 34-year-old single, Caucasian male with a confirmed diagnosis of Cowden’s syndrome based on PTEN gene mutation was referred to the Oral Medicine Department by the Clinical Genetics Department for a large polyp on the tongue and generalised gingival enlargement. On direct questioning, the patient reported that the tongue polyp had been present for just over a year and was not growing in size. His chief concern was constant bleeding from his gums and a subsequent inability to maintain adequate oral hygiene.

The medical history included CS. The patient had no history of malignancies, had no gastrointestinal symp-
toms and his annual thyroid function tests had consistently revealed no abnormalities. His family history was positive for CS in his mother. She, too, had no history of cancer. She had had multinodular goitre and had subsequently undergone a total thyroidectomy. She had been on annual breast and endometrial screening. The referral letter stated that the patient had been a “dental phobic”, but on further questioning it transpired that he had been registered with a general dental practitioner, but he had felt that he did not know enough about CS to appropriately manage the patient. The patient smoked 20 cigarettes a day, for the past 18 years. He did not drink alcohol.

Extraoral examination revealed slight macrocephaly (Figures 1). Multiple trichilemmomas pathognomonic of CS were present on the forehead and the digits (Figures 1 and 2). Intraoral examination revealed a 1x1cm irregular polyp on the right lateral aspect of the tongue, with a slight ‘moth-eaten’ appearance (Figures 3 and 4). The gingivae were grossly enlarged in all quadrants, with heavy plaque accumulation on the teeth (Figures 5-7). The dentition was irregular with a class II Div 2 incisor relationship (Figure 7). Additionally, a high-arched hard palate was observed (Figure 8).

Investigations revealed a normal full blood count and thyroid function tests. The most recent thyroid ultrasound had revealed several small hypoechoic nodules within the left lobe of the thyroid measuring up to 6mm, but the gland was not enlarged. A 10-minute salivary flow rate assay was carried and revealed a normal flow rate. Saliva was cultured for Candida spp. and showed a high level of 5,600 colony forming units per ml.

The initial management consisted of treating the candidal infection with a one-week course of 10mg amphotericin lozenges, to be taken four times a day. Adequate oral hygiene and smoking cessation advice were given. Arrangements were made to excise the polyp on the tongue. The patient was referred back to the general dental practitioner to arrange for oral hygiene therapy. He remains on annual review in the Clinical Genetics and Oral Medicine Departments.

Discussion

Cowden’s syndrome (previously termed ‘multiple hamartoma syndrome’) is a rare autosomal dominant disease characterised by multiple hamartomas arising in all three germ layers (ectoderm, mesoderm and endoderm) and a remarkably increased risk of cancer. Loss of expression of PTEN, a tumour suppressor gene, accompanies the condition in the majority of cases (Pilarski and Eng, 2004). More than 200 cases have been reported in the literature since it was first described by Lloyd and Dennis (Guilherme et al., 2006).

PTEN mutation is observed in a number of other syndromes apart from CS, thus the development of the term ‘PTEN Hamartoma Tumour Syndrome’ (PHTS), in order to encompass all such disorders. These include Lhermitte-Duclos Disease, Bannayan-Riley-Ruvalcaba syndrome and Proteus syndrome (Zbuk and Eng, 2007).

Clinical features of CS include pathognomonic mucocutaneous lesions (trichilemmomas) and a predisposition to malignancy, particularly adenocarcinoma of the breast (25-50%), thyroid cancer (3-10%), endometrial cancer, and renal cell carcinoma (Lachlan et al., 2007). Other features include thyroid abnormalities, fibrocystic breast lesions, gastrointestinal lesions, macrocephaly, and genito-urinary abnormalities (Scheper et al., 2006). It is worth noting that cancer risk has only been clearly demonstrated in Cowden’s syndrome of all the PHTS disorders (Zbuk and Eng, 2007).

Orally, the most common presentation of CS is in the form of multiple fibro-epithelial polyps. Other oral features include nodular gingival hyperplasia, a high-arched palate, fissuring and lobulation of the tongue and, rarely, oral squamous cell carcinoma (Chaudhry et al., 2000). Xerostomia can also accompany the condition (Woo and Abdelsayed, 2008). The difficulty in maintaining adequate oral hygiene as a direct cause of the manifestations of the disease can lead to a vicious cycle of periodontal disease and rampant dental caries, as well as a significant impact on the quality of life.

CS can present in a variety of forms and in many instances not all the ‘classic’ signs of the disease are present, particularly when it is difficult to establish a positive family history, or when PTEN gene mutation is absent. As such, we suggest following the recent International Cowden Consortium operational criteria for the diagnosis of Cowden Syndrome in 2007 (Lachlan et al., 2007 – Table 1).

The diagnosis of CS is usually made on the presence of pathognomonic criteria alone if there are six or more facial papules (three of which must be trichilemmoma), or in the presence of orofacial papillomatosis, or the identification of 6 or more palmoplantar keratosis lesions (Lachlan et al., 2007). Diagnosis can also be made based on different combinations of minor and major criteria. We direct the reader to the National Comprehensive Cancer Network (NCCN) website for further details, which can be accessed at www.nccn.org

The prognosis of CS is guarded due to the high risk of cancer. The NCCN has published the following guidelines to help with the long-term management of CS:

- Annual physical examination
- Annual breast examination from age 25
- Annual mammography from age 30 and regular self-examination
- Thyroid baseline exam with ultrasound, starting at 18 years and annually thereafter
- FBC, CXR, urinanalysis and FNA’s for suspicious lesions
GI exam based on symptoms
Annual endometrial screening and blind biopsies starting at 35 (Lachlan et al., 2007).

Management of CS by the oral healthcare worker can be divided into three areas:
1. Treating individual oral lesions when necessary. Surgery, chemotherapy and radiotherapy and laser ablation have all been cited as suitable options for mucocutaneous lesions (e.g. fibro-epithelial polyps).
2. Aggressive oral hygiene advice and regular dental attendance. This is imperative to avoid a vicious cycle precipitated by the manifestations of the disease that can hinder oral hygiene regimes.
3. Vigilant monitoring for malignancies that may arise in the orofacial region.

Hence, the management of CS not only entails a multidisciplinary approach that can involve the clinical geneticist, oncologist, general surgeon and other medical specialties but it also presents as an area for oral healthcare workers from different backgrounds to cooperate for the best interest of the patient, be it the general dental practitioner, dental hygienist or whether it is specialists from oral medicine or special care dentistry. In our case, the importance of clear communication and appropriate referrals between all different specialties is also an obvious and important take-home message for the oral healthcare worker involved in the management of these rare, yet challenging, cases.

Figure 1
Extraoral view showing slight macrocephaly

Figure 2
Individual trichilemmoma on the middle finger

Figure 3
Extraoral photograph of the dorsum of the tongue showing large polyp on the right border

Figure 4
Higher quality photograph demonstrating the ‘moth-eaten’ appearance of the polyp

Figure 5
Gross hypertrophy of the anterior gingivae

Figure 6
Left lateral view showing gingival hypertrophy
References


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Pathognomonic criteria

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<th>Mucocutaneous lesions:</th>
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<tr>
<td>- Trichilemmomas</td>
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<tr>
<td>(facial)</td>
</tr>
<tr>
<td>- Acral keratoses</td>
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<tr>
<td>- Papillomatous lesions</td>
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<td>- Mucosal lesions</td>
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<tr>
<td>Lhermitte-Duclos disease (cerebellar dysplastic gangliocytoma)</td>
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Major criteria

| - Breast cancer  |
| - Thyroid cancer  |
| - Macrocephaly  |
| - Endometrial carcinoma  |

Minor criteria

| - Other thyroid lesions (e.g. goitre)  |
| - Mental retardation (I.Q. < 75)  |
| - Hamartomatous intestinal polyps  |
| - Fibrocystic disease of breast  |
| - Lipomas  |
| - Fibromas  |
| - Genito-urinary tumours  |