Thyroid Disease Associated with Cowden Syndrome: A Meta-Analysis

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Abstract

Background: While Cowden Syndrome (CS) patients are known to harbor a propensity for thyroid disease, the exact incidence, pathology, and surgical management of thyroid disease in CS have yet to be fully delineated.

Methods: We perform a meta-analysis of the literature and present a representative case report.

Results: Review of published journal articles yielded 554 citations that fulfilled the inclusion criteria with 95 articles meeting the inclusion and exclusion criteria. A total of 181 cases were subsequently analyzed. Of the 181 patients, there were 99 females (54.7%), 77 males (42.5%), and no gender was reported in 5 cases (2.8%). The age at presentation ranged from 3 days to 78 years with mean and median ages of 38 years and 39 years, respectively. Ninety-six patients (96/181; 53.0%) were reported to have thyroid disease. Thyroid abnormalities were most commonly found on examination prior to diagnosis (37/96; 38.5%). Surgical management of thyroid disease was performed in 80.2% (77/96) of patients with thyroid disease with total thyroidectomy being the most common operation reported (23/77; 29.9%). Thyroid pathology reported with CS patients included goiter (39/96; 40.6%), adenoma (24/96; 25%), unknown/unspecified pathology (8/96; 8.3%), follicular carcinoma (7/96; 7.3%), thyroiditis (7/96; 7.3%), papillary carcinoma (6/96; 6.3%), cancer (unknown type) (3/96; 3.1%), medullary carcinoma (1/96; 1%), and hyperthyroidism (1/96; 1%).

Conclusions: CS is composed of a multitude of common findings. Given the high prevalence of thyroid disease and notable potential of malignancy, careful monitoring of thyroid disease in CS patients is imperative. CS patients most commonly present with goiter and require total thyroidectomy.

Introduction

Cowden Syndrome (CS) is an autosomal dominant syndrome that was first diagnosed in 1963 and was named after Rachel Cowden, the first affected individual. Common manifestations of CS include mucocutaneous lesions (such as trichilemmoma, acral keratoses, and verruroid or papillomatous papules), thyroid abnormalities (such as goiter, adenoma, and carcinoma), breast lesions (such as fibroadenoma, fibrocystic disease, and adenocarcinoma), macrocephaly, and genitourinary abnormalities (such as uterine leiomyoma) (2). The diagnostic criteria for this syndrome have also undergone several revisions with the most recent criteria outlined by Eng in 2000 (3). CS is caused by a mutation in the tumor suppressor PTEN gene (phosphatase and tensin homolog on chromosome 10). CS patients are known to be at significant risk for a multitude of medical conditions including breast cancer, gastrointestinal lesions, mucocutaneous lesions, and macrocephaly.

Materials and Methods

- Query of the United States National Library of Medicine PubMed database between 2001 and January 2010 was performed using the terms “cowden syndrome OR cowden’s syndrome OR cowden disease OR cowden’s disease.”
- Articles published during or after the year 2001 were included.
- Original articles, reviews, case reports, and case series were included.
- Articles were excluded if they were written in a language other than English, did not present cases of CS, or did not include patient information to qualify for a diagnosis of CS.

Results and Discussion

The most common thyroid pathologies reported in CS patients were goiter and adenoma. Seventeen patients (17/96, 17.7%) had thyroid carcinoma. In the report by Starink et al., it was noted that CS patients had a 68% rate of goiter/adenoma, 3% rate of hypothyroidism, 2% rate of hyperthyroidism, 2% rate of thyroglossal duct cyst, and a 3% rate of follicular adenocarcinoma (4). Salem and Steck noted a 59% incidence of goiter or adenoma in CS patients, a 6.5% incidence of thyroiditis, and a 6.5% incidence of thyroid carcinoma (5). Finally, Hansen et al. reported the incidence of thyroid carcinoma as 7% (6). Thus, the thyroid pathology findings in our analysis are similar to previous reports with the exception of thyroid carcinomas. In our review of 181 cases presented in the current literature, 53 patients had known thyroid abnormalities with 42.5% of all CS patients requiring surgical intervention for their thyroid disease. Our incidence of thyroid disease in this population is similar to previous reports of 50-70% (7).

Patient Details

A 33 year old female was referred from her primary care physician to our head and neck clinic for a left thyroid goiter. The patient was status post a right hemithyroidectomy at age 18 for a benign goiter. Fine needle aspiration of the left thyroid gland revealed follicular pathology. Past medical history revealed uterine leiomyoma, phyllodes tumor of the breast, and thyroid disease. On physical examination, the patient had numerous mucosal lesions with fibromas in the bilateral buccal mucosa regions and near the tonsillar regions. The patient had papillomatous/verruccous lesions over the entire dorsum of the tongue. The patient underwent thyroidectomy and excision of the buccal mucosal lesion. The pathology from this operation revealed a benign multinodular goiter of the left hemithyroid (Figure 1) and a fibroma of the buccal mucosa (Figure 2). Given the thyroid abnormalities, mucocutaneous lesions, history of breast and uterine lesions, and family history, the patient was referred to her primary physician for further evaluation/monitoring and genetic testing for CS.

Table 1. Thyroid Disease associated with Cowden Syndrome

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age at Presentation</th>
<th>Thyroid Disease</th>
<th>Surgical Management of Thyroid Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>3 days to 78 years</td>
<td>Goiter (40.6%)</td>
<td>Total Thyroidectomy (80.2%)</td>
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<tr>
<td></td>
<td></td>
<td>Adenoma (25%)</td>
<td>Hemithyroidectomy followed by</td>
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<td></td>
<td></td>
<td>Unspecified Pathology (8.3%)</td>
<td>Total Thyroidectomy (6.5%)</td>
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<tr>
<td></td>
<td></td>
<td>Follicular Carcinoma (7.3%)</td>
<td>Hemithyroidectomy (15.6%)</td>
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<tr>
<td></td>
<td></td>
<td>Thyroiditis (7.3%)</td>
<td>Unknown Operative Intervention (48.1%)</td>
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<td></td>
<td></td>
<td>Papillary Carcinoma (6.3%)</td>
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<td></td>
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<td>Cancer (Unknown Type) (3.1%)</td>
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<td></td>
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<td>Medullary Carcinoma (1%)</td>
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</table>

Conclusions

- Thyroid disease is a significant concern for patients with Cowden Syndrome.
- In our review of 181 cases presented in the current literature, 53% had thyroid disease with 42.5% of all CS patients requiring surgical intervention for their thyroid disease.
- Recognition of this syndrome is important given the high incidence of thyroid disease and associated morbidity and potential mortality.

References