Cowden's Disease with Pulmonary Hamartoma

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A case of Cowden's disease is reported. A 38-year-old man was admitted to our hospital because of an abnormal left lung shadow on a chest radiograph. There were no symptoms, although the patient had multiple papules on the nose and pharynx mucosa. There were a few fibromas on the axillas and the inguinal regions. The patient had thyroid goiters, gastrointestinal poliposis, and a pulmonary hamartoma. The latter has not been reported previously in Cowden's disease.

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Introduction

Cowden's disease was first described in 1963 by Lloyd and Dennis, who named the syndrome after their patient, Rachel Cowden (1). Cowden's disease has autosomal dominant inheritance and is characterized by multiple hamartomas of ectodermal, mesodermal, and endodermal origin. The most frequent findings are mucocutaneous lesions. This disease is important because of the association of malignancy, particularly of the thyroid and breast. The present case has a pulmonary hamartoma. Such a hamartoma has not been reported previously.

Case Report

A 38-year-old man was admitted to our hospital on September 25, 1987 because of an abnormal left lung shadow on chest X-ray. There were no symptoms. At the age of 23, the patient was found to have multiple gastric polyps. When he was 36, colon polyposis was discovered. His mother had a thymic cyst and gastric polyps.

On physical examination, numerous verrucous papules were found on the face, especially on the nose, and on the upper lip. A few verrucous lesions could be seen on both axillas, groins and on the shoulders. Polypoid lesions were found on the pharynx. A nodule, 1.0 cm in diameter, was palpable in each lobe of the thyroid gland. A pedunculated polyp with hemorrhage was found on the anal mucosa.

Laboratory results on admission were as follows:

- Hemoglobin, 10.2 g/dl; hematocrit, 32.8%; serum total protein, 6.20 g/dl; serum albumin, 3.50 g/dl; serum iron, 43 µg/dl; stool occult blood, guaiac test (+), orthotolidine test (-).
- T-cell subset proportions were altered, with 29.8% CD4+ cells and 27.7% CD8+ cells. The CD4/CD8 immunoregulatory ratio was 1.08.

A posteroanterior chest radiograph revealed no abnormal findings (Fig. 1A). The lateral view showed a tumor shadow, 1.5 cm in diameter, in the left lower lobe (Fig. 1B). Chest CT scan revealed a well-circumscribed solitary nodule with a small focus of calcification in the left S10 (Fig. 2). Thyroid CT scan revealed a low density nodule in each lobe.

By gastroduodenoscopy, innumerous polyps were identified throughout the esophagus, stomach (Fig. 3), and duodenal bulb. On colonoscopy, multiple sessile polyps (2 to 3 mm) were noted in the rectosigmoid area. By bronchofiberscopy, transbronchial biopsy was performed on the tumor in left lower lobe. After admission, the patient had melena from the anus polyp and polypectomy was thus performed.

Biopsy specimens of lesions in various locations showed: fibromas of the axilla and groin, inflammatory polyps of the stomach and colon, hamartoma of the lung (Fig. 4A), and a hamartomatous polyp of the anus (Fig. 4B).

Discussion

Cowden's disease is an uncommon autosomal dominant condition and is characterized by multiple hamartomas.
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Fig. 1. Chest radiographs. A) The postero-anterior view of a chest radiograph reveals no abnormal shadow. B) The lateral view of a chest radiograph reveals a tumor shadow in the left lower lobe.

Fig. 2. A chest CT scan reveals a solitary nodule with a small focus of calcification in the left S10.

Fig. 3. Endoscopic examination reveals innumerable polyps in the stomach.

and neoplasms of ectodermal, mesodermal, and endodermal origin. Since the original report in 1963 by Lloyd and Dennis (1), who named the syndrome after their patient, Rachel Cowden, about 100 reports of cases have been published in the English language literature (2, 3). In the Japanese language literature, 20 reports of cases have been published since the report in 1983 by Shono et al (4). In 1972, Weary et al (5) proposed the name multiple hamartoma syndrome to describe the presence of multiple hamartomatous anomalies of various organs.

Mucocutaneous lesions were observed in all cases. Starink et al (6) revealed that the most frequent cutaneous lesions were facial papules, which were present in 95% of the patients. They consisted of multiple, small, skin-colored, smooth and keratotic papules concentrated around the orifices. Acral keratoses that were most numerous on the dorsal aspects of the hands and feet were seen in 95%. Small round translucent palmoplantar keratoses were seen in 91%. Oral mucosal lesions consisting of small flat papules were seen in 86%.

The most frequently reported internal abnormality in the syndrome is thyroid gland abnormalities, which were seen in 67% (7). The most common abnormality of the thyroid gland is goiter and adenoma. Starink et al (6) found a high incidence of gastrointestinal polyps (about 60%). Most polyps were described as lipomatous,
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Fig. 4. A) Hamartoma of the lung composed of cartilage (HE stain, ×10). B) Hamartomatous polyp of the anus composed of dilatation of epithelium and plasma cell infiltration into the interstitium (HE stain, ×10).

Hamartomas, hamartomatous, or inflammatory. The most important association in this syndrome is carcinoma. Breast cancer occurs in 28% of female patients, carcinoma of the uterine cervix in 3%. Thyroid gland carcinoma occurs in 3% and colon carcinoma in 3% (7).

Abnormalities of the respiratory tract reported in this syndrome include laryngeal polyps in three patients (8–10), a cyst of the lung (7), possibly low-grade adenocarcinoma of the lung (11), coin lesions (possibly hamartomas) (10), and possibly arteriovenous malformation (7). To our best knowledge, this is the first report of an association between Cowden’s disease and pulmonary hamartoma, which was diagnosed histologically. Gabrail and Zara (12) proposed the name of pulmonary hamartoma syndrome to describe the association between pulmonary hamartoma and other benign tumors or congenital anomalies. They believe that pulmonary hamartoma syndrome and Cowden’s disease are separate, because none of their patients with pulmonary hamartoma had the characteristic skin manifestations of Cowden’s disease, and there has been no reported association between Cowden’s disease and pulmonary hamartoma. But their study was not large enough to draw a specific conclusion. The association between pulmonary hamartoma syndrome and Cowden’s disease is not clear. Cowden’s disease with pulmonary hamartoma is probably more common than previously thought.

In conclusion, larger studies will be necessary to more accurately define the syndrome. Patients with Cowden’s disease should be examined carefully for the possibility of associated malignant tumors.

References