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Cowden's disease – its importance for otolaryngologists

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Abstract
Cowden's disease is a rare predominantly inherited disease, characterized by mucocutaneous lesions, gastrointestinal polyposis and benign or malignant thyroid and breast tumours. The report deals with a typical case of this disease with emphasis on its importance for otolaryngologists.

Key words: Cowden's disease; Head and neck neoplasms

Introduction

Cowden's disease (CD), known also as multiple hamartoma syndrome, is a rare predominantly inherited condition which is characterized by various ecto-, meso- and endodermal benign and malignant tumours that may affect the skin, oropharyngeal, laryngeal and gastrointestinal mucosa, thyroid and breast, as well as several other organs.

The first case of CD was described by Lloyd and Dennis (1963). They suggested that a specific group of symptoms was representative enough to form a new clinical entity, which they named by the family name of the first patient having this disease. Weary *et al.* (1972) reported five additional cases and proposed the name 'multiple harmartoma syndrome' as their patients presented with hamartomas of all three germ layers. Gorlin *et al.* (1976) listed it as 'multiple hamartoma and neoplasia syndrome'. Until now, a total of 106 cases of CD have been reported in the literature. As the most obvious signs of the disease are associated with mucocutaneous lesions, it is not surprising that most of the recorded cases appear in dermatological literature.

The aim of this report is to present an additional case of CD as well as to familiarize otorhinolaryngologists with signs and symptoms of this syndrome which have not yet been described in our literature.

Case report

B.M., a 46-year-old woman had noted numerous papulous lesions on her face and neck since childhood. At the age of 14, she underwent partial thyroidectomy for benign adenomatous changes in the gland. A year later she had radical mastectomy for intraductal breast carcinoma. In 1966, at the age of 19, she was for the first time admitted to the University Department of Otorhinolaryngology and Cervicofacial Surgery in Ljubljana because of speech- and swallowing-related problems. On physical examination, multiple 1–2 mm diameter flesh-coloured papules and papillomas were seen on her face and neck (Figure 1). Numerous papules and papillomas were present also on the buccal mucosa, gingivae and mobile tongue which had a cobblestone appearance. Similar, though much more pronounced, changes were found at indirect laryngoscopy on the anterior oropharyngeal wall including valleculae (Figure 2), epiglottis, posterior parts of aryepiglottic and ventricular folds, as well as in both pyriform sinuses. Most of pharyngeal and laryngeal masses were removed by direct laryngoscopy. Histopathological exam-

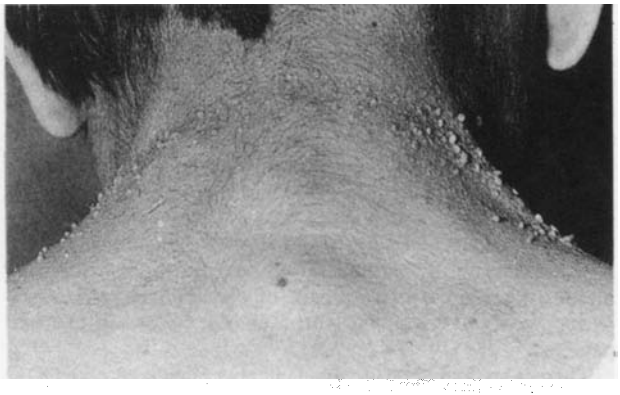

FIG. 1
Cutaneous lesions involving the posterior neck region.

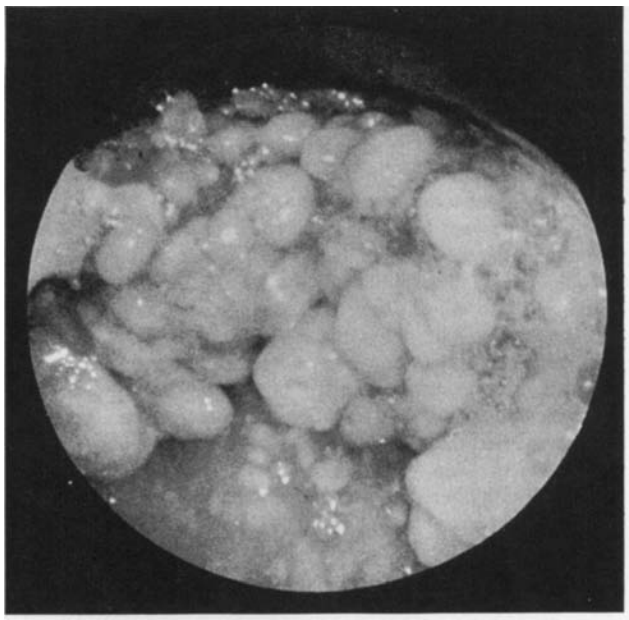

FIG. 2
Extensive confluent papillomatous lesions on the anterior pharyngeal wall.

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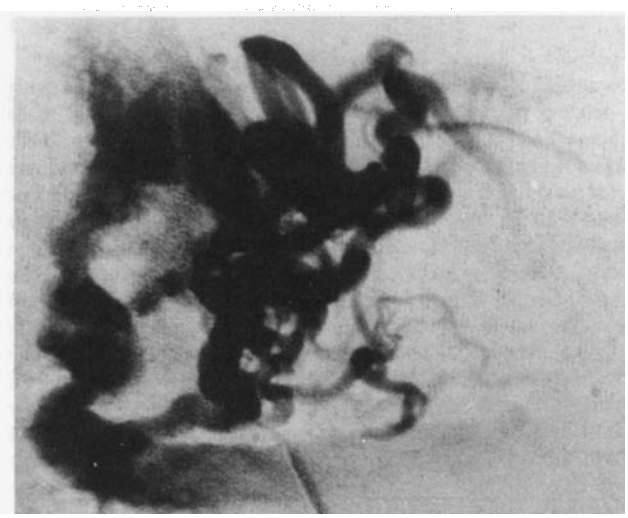

FIG. 3
Arterio–venous malformation in the right retroarticular region.

ination of the laryngeal lesions revealed a fibrovascular core covered with hyperplastic parakeratotic squamous epithelium.

In the following years, laryngeal and pharyngeal papillomas had been directoscopically removed six times already, the last such procedure being performed in 1981 when endoscopic examination revealed also polyposis of the oesophagus, stomach and intestine.

A cavernous haemangioma, 3 × 2 cm in size was excised from her right neck region in 1982, and a 2 × 2 cm lipoma from the opposite side of the neck two years later.

In 1990 she started to complain of tinnitus in her left ear. On examination, a soft pulsating tumour was palpated behind the left ear. An arterio–venous malformation 3 cm in diameter, which was fed by the left occipital artery and drained into the internal jugular vein through the sigmoid sinus, was confirmed on angiography (Figure 3). The patient refused surgery, and throughout the following two years her condition remained practically unchanged.

In 1991, the patient had rheumatoid arthritis of the small joints of the hands and feet diagnosed.

A regular follow-up examination in 1992 revealed a 3 × 4 cm large, hard, painless and poorly mobile swelling in the right submandibular region. The aspiration biopsy findings were suspicious for carcinoma. On directoscopy, numerous papillomas on the root of the tongue, and single papillomas in the larynx and hypopharynx were found. However, there was no evidence of changes for the suspicion of malignancy. Surgery included extirpation of the submandibular salivary gland and right-sided functional dissection of the neck. Histology confirmed an undifferentiated carcinoma of the right submandibular salivary gland with metastases in two cervical lymph nodes. The patient received post-operative irradiation. There were no signs of recurrence found on the last follow-up examination 10 months after completed therapy.

The patient's son, who was born when she was 23 years old, presented with mucocutaneous lesions and an extensive gastrointestinal polyposis characteristic of CD.

Discussion

CD, the pathogenesis of which remains unknown, is characterized by mucocutaneous lesions, gastrointestinal polyposis, thyroid gland tumours and benign or malignant breast tumours.

Among these various anomalies, mucocutaneous lesions are the most characteristic and consistent sign of the disease. Cutaneous changes, which are usually distributed over the face and neck, consist of many 2–5 mm papular or papillomatous lesions. Similar changes often occur also on the dorsal surfaces of the hands. Microscopically, some cutaneous lesions show acanthotic areas of follicular origin with foci of sebaceous glands in their centres, whereas others exhibit markedly irregular acanthotic epidermis with hyperkeratosis (Gorlin *et al.*, 1976). Similar, mucous lesions are regularly present in CD. Numerous small papules can be found particularly on the gingivae, buccal area and palate, where papillomatous and verrucoid lesions are generally seen on the mobile tongue, and oropharynx. As in our patient, these papillomas microscopically do not differ from solitary lesions in otherwise healthy patients. Our case seems particularly interesting because of the extensive pharyngeal and laryngeal involvement, since there are only few such cases associated with CD reported in the literature (Weary *et al.*, 1972). As changes in these sites cannot be detected without the help of indirect or direct laryngoscopy, a majority of reports on dermatological and gastroenterological mucocutaneous lesions are confined to the description of the oral cavity, and accordingly, the real incidence of CD involvement in the appointed sites remains unknown.

Gastrointestinal polyposis can affect entire digestive tract or only parts. Polyps, which can range from one millimeter to several centimeters in diameter, are most often encountered in the colon and rarely in the small bowel, stomach and oesophagus. They are present in about 75 per cent of these patients. Their pathology varies and is not specific for this disease. It does not appear that there is any association between polyps in CD and gastrointestinal cancer (Carlson *et al.*, 1984; Snover, 1987).

Goitre, adenomas and carcinoma of the thyroid gland occur in up to two thirds of patients with CD (Salem and Steck 1983; Chen *et al.*, 1987). It has also been found that fibrocystic disease of the breast is encountered in more than two-thirds of female patients with CD, whereas in about a half of these patients mammary carcinoma may occur (Civatte *et al.*, 1978; Brownstein *et al.*, 1979). Frequently, the disease is accompanied by lipomas and various types of haemangiomas, as was also the case in our patient.

Other anomalies occasionally accompanying CD are manifold and variable: mental retardation, uterine hypoplasia, miscarriage, pectus excavatum, pathological fractures, parotid harmartoma, meningioma of the external ear canal, and others (Weary *et al.*, 1972; Gentry *et al.*, 1974; Nuss *et al.*, 1978; Rosenberg-Gertzman *et al.*, 1980; Ortonne *et al.*, 1980; Leiber and Olbrich, 1981; Brenner and Hutterer, 1982; Taylor *et al.*, 1989). Because of their rarity, it seems that they represent only accidental findings in these patients.

As presented, the clinical picture and the course of disease in our patient has all the characteristics of CD; there were four leading symptoms (mucocutaneous lesions, gastrointestinal polyposis, tumours of the thyroid gland and breast) as well as the second most frequent sign of the disease (lipomas and haemangiomas) present. Also both carcinomas, which in our patient appeared within the span of 31 years, comply with the picture of this syndrome. Although carcinoma of the submandibular salivary gland in CD patients has not been reported in the literature so far, apart from the thyroid and breast there have been many other malignant tumour sites reported: bladder (Hauser *et al.*, 1980), kidney (Taylor *et al.*, 1989), colon (Burnett *et al.*, 1975), ovary and uterus (Carlson *et al.*, 1984), acute myelogenous leukaemia (Ruschak *et al.*, 1981), malignant melanoma (Siegel, 1975). Therefore, a thorough clinical examination was recommended to rule out the presence of concomitant malignancy (Swart *et al.*, 1985) along with a careful follow-up of these patients.

There is no doubt that the actual number of patients with CD is much higher than suggested by rare reports from the literature. Due to the lack of awareness of this entity, many cases of CD remain unexplained and misinterpreted for various other diagnoses. It is difficult to understand that despite many symptoms evident in the head and neck region (affected skin, lesions in the mouth, pharynx and larynx, tumours of the thyroid, haemangio-

mas and lipomas on the neck), CD has received negligible attention from otorhinolaryngologists so far. Nevertheless, their better knowledge of this condition will result in a higher rate of correct diagnoses, which is also of utmost importance in early detection of more severe sequelae of this disease, i.e. malignant growth that may develop during its course.

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