The Cowden Syndrome: A Case Report

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Abstract We report on a 42-year-old woman who presented a mild mental retardation, a dolichocephaly, multiple papules scattered throughout the body, two scars cervicotomy with a stage II heterogeneous goiter with a discrete hypothyroidism. The Cowden syndrome has been suspected by the dermatologist. Histopathological examination of the thyroid nodule was in favor of a micro-invasive carcinoma. The mammography showed multiple breast nodules, ACR2 class with a malignant histology. The esophagogastroduodenoscopy showed small gastric and duodenal polyps pinhead and the nasofibroscopy revealed nasopharyngeal polyps with decreased mobility of the vocal cords. The genetic study could not be performed. It seems essential to insist that the dermatologist must suspect the Cowden syndrome in all patients with mucocutaneous lesions. Weakened by her divorce, unsightly look, the heavy monitoring and the vital risk require psychological support as there is currently no specific treatment.

Keywords Cowden syndrome; Thyroid carcinoma; Breast cancer; Gastrointestinal polyps

1 Introduction
The Cowden syndrome (CS) is a rare disease but under diagnosed, it’s an autosomal dominant disorder (Kumar et al., 2016). Patients have multiple trichilemmomas, oral papillomatosis, cutaneous keratosis, goiters, gastrointestinal polyps, and breast cancers. The possibility of malignant transformation for thyroid and breast is great (Molvi et al., 2015).

2 Case report
A 42-year-old woman, non-consanguineous parents, divorced without children, with a family history of goiter in the maternal grandmother consulted in our department. There were no similar cases or family neoplasia. Our patient had papules lesions at age 16 and one year later she developed a left nodular goiter which motivating consultation in general surgery where a left thyroidectomy was performed with a benign histology. Then, the patient was lost sight of for 10 years. At age 27, she had a recurrence of goiter, and a subtotal thyroidectomy was performed with a benign histology. Then, a Levothyroxine therapy was prescribed for two years. But, the patient stopped the treatment and any follow-up on its own initiative. At age 37, worried by the large spread of papules mainly on the face but not by the second recurrent of goiter, she consulted a dermatologist who suspected a Cowden syndrome. Thereafter, she was referred to our department. The physical examination revealed a mild mental retardation, a dolichocephaly, multiple papules scattered throughout the body (Figure 1), two scars cervicotomy with a stage II heterogeneous goiter (presence of a 2 cm hard but not adherent nodule without lymphadenopathy or compression) with a discrete hypothyroidism (TSH=8.2 μIU/ml). The Thyroid ultrasonography showed multiple echogenic and hyperechoic nodules formations of 20 mm on the left. The cytology of the left nodule was in favor of a hyperplasia and important hemorrhage. The mammography revealed multiple breast nodules, ACR2 class. The esophagogastroduodenoscopy showed small gastric and duodenal polyps pinhead and the nasofibroscopy revealed nasopharyngeal polyps with decreased mobility of the vocal cords. The genetic study could not be performed. We addressed the patient after substitution in Levothyroxine to the surgery to perform a subtotal thyroidectomy after euthyroidism. Due to the importance of adhesions, surgeons have been able to practice only a left lobo-isthmetomy. Histopathological examination revealed a micro-invasive carcinoma. Three months later, she underwent a subtotal thyroidectomy at the ENT department. A few months
later, the patient underwent removal of the breast with a malignant histology followed by chemotherapy and radiotherapy.

Figure 1 Mucocutaneous lesions

3 Discussion

The Cowden syndrome is an autosomal dominant disease predisposing to cancers with a variable penetrance, associated with a mutation in a tumor suppressor gene (PTEN at locus 10q23.2) or KILLIN or phosphatidylinositol 4,5-bisphosphate-3 kinase catalytic subunit alpha (PIK3CA) or AKT1 genes (Bennett et al., 2010; Orloff et al., 2013).

The most common manifestations, and which are described in our patient, are the mucocutaneous lesions in 99-100% of patients (Eng, 2000), the gastrointestinal visualisable polyps in 85%, the dolichocephaly in 80%, the thyroid gland affections in 67% (Capitan Canadas et al., 2006) and the breast diseases in 50-76% (Lee et al., 1997; Masmoudi et al., 2011; Capitan Canadas et al., 2006). But, some authors reported cases of CS with Lhermitte-Duclos disease (a dysplastic cerebellar gangliocytoma which is a rare tumor of the cerebellum) preventing as ataxia (Arun et al., 2015), intestinal ganglioneuromatosis (Vinisky et al., 2013), esophageal polyposis (Norimura et al., 2013), rare association of polydactyly (Molvi, 2015), and malignant peripheral nerve sheath tumor (Taylor et al., 2015).

Furthermore, diagnostic criteria have been established first by Salem and Steck (Guimaraes et al., 2002). Then the recommendations of the International Cowden Consortium revised the classification (familiar forms of CS) by adding endometrial and renal cell carcinoma (Eng, 2000). In the case of our patient, the mucocutaneous lesions, the dolichocephaly, the thyroid carcinoma, the nasopharyngal and the gastric and the duodenal polyps, and the breast cancer were in favor of the diagnosis of Cowden syndrome.

In our case, the delayed diagnosis has earned four thyroid surgeries with serious psychological and medical repercussions that could have been avoided by a prophylactic total thyroidectomy. Our patient had gastrointestinal polyps that need monitoring to detect degeneration without forgetting a gynecological and urinary screening and a dermatological examination.

Otherwise, the family investigation is not always easy, and a careful examination and especially a genetic counseling are required. Weakened by her divorce, unsightly look, the heavy monitoring and the vital risk require psychological support as there is currently no specific treatment. The gene therapy is a promising research.
It seems essential to insist that the dermatologist must suspect the CS in all patients with mucocutaneous lesions.

4 Conclusion
Although the Cowden syndrome is a rare disease, serious consequences involve the vigilance of the endocrinologist who must be alarmed by the concurrent of a goiter or a thyroid cancer with specific skin lesions confirmed by a dermatological examination.

Author’s contributions
By signing this letter each of us acknowledges that she or he participated sufficiently in the work to take public responsibility for it.

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