Acta Scientific Otolaryngology

Volume 3 Issue 4 April 2021

Case Report

A Rare Case of Cowden Syndrome Presenting as Multinodular Goitre

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Received: March 15, 2021

Published: : March 24, 2021

Abstract

Screening for cancer associated with syndromes is a very common practice nowadays. Nodular Thyroid disease is very uncommon in childhood and adolescence when their family is having history of nodular thyroid disease which has been diagnosed with benign or malignant disease.

Keywords: Cowden Syndrome; Thyroid Disease; Cancer; PTEN Gene

Introduction

Cowden syndrome is one such condition. Cowden syndrome is an autosomal dominant condition with variable expression associated with mutation in PTEN gene on arm 10q [8]. It causes hamartomatous [2,3] neoplasm of any organ cases. In this syndrome, the phenotypic presentation of a patient and their relatives must be observed carefully. By 20 years of age, skin lesions are seen in all cases, by 40 years of age, one of the malignancy is seen. Skin lesions (90 - 100%), multinodular thyroid (66 - 75%) with prevalence of 1 in 200,000 (US Study). Review of English literature shows only 300 reported Cowden syndrome. Patients with germ-line mutation associated with this syndrome are at increased risk of developing a varied range of tumours over their lifetime.as a result, appropriate counselling and follow-up are necessary [1].

Case Report

An 18 years old thin built macrocephalic female patient presented with 10 x 5 x 4 cm in size thyroid swelling for 2 years which was gradually increasing in size with firm consistency over the right thyroid lobe. Multiple papular lesion (1 - 3 mm) seen on upper and middle-third of face. Multiple papules giving cobblestone appearance on gingiva, corrugated appearance on lips and moniform appearance on tongue. Similar findings were seen on her younger sister. Based on clinical profile, CBC, urine analysis, thyroid profile, USG neck, FNAC neck swelling, USG whole abdomen, breast and skin lesion biopsy were advised for investigation.

Image 1: Patient with multinodular goiter.

Image 2: Facial lesion showing trichilemmoma.

Image 3: Mucosal lesions, moniform appearance of tongue.

Image 4: Mucosal lesions on tongue.

Image 5: Corrugated appearance on lips, pappilomatosis.

Results

CBC, urine analysis and thyroid profile were not significant. USG neck findings and FNAC suggested multinodular goitre. Skin biopsy showed benign trichilemmomas [10].

Image 6: Skin lesion biopsy.

Skin lesion biopsy showing following findings [11]:

1. Compact hyperkeratosis with focal parakeratosis.
2. A focal proliferation of eosinophilic epithelium emanating from the under surface of the epidermis.

3. Uniform basaloid cells with oval nuclei and abundant pale cytoplasm.
4. Attempts at cornification.
5. Palisading of peripheral cells.
6. Telangiectasia at the base of the lesion.

Image 7: Multiple fibroadenomas with cystic swellings breast in USG.

USG findings are:

- Right breast- ill-defined hypoechoic areas noted.
- Left breast- round to oval approximately 21 x 10 mm homogenous lesions noted at 12 o' clock position.
- Round to oval homogenous lesions 12.9 x 9.6 mm noted at 2 o' clock position.
- Round heterogenous lesion with calcific foci within of approx. 11 mm x 8.9 mm size at 9 o' clock position.
- Impression- b/l multiple fibroadenoma.
- USG whole abdomen showed mild septate uterus.
- Right hemithyroidectomy was done and specimen sent for histopathological examination with following findings [5,6].

HPE

Gross: Right hemithyroidectomy specimen measuring 7.5 cm x 5.5 cm x 3 cm. Outer surface capsule intact. Cut surface has variable areas of colloid filled hemorrhagic nodules.

Microscopic section studied from right lobe shows fibrocartilaginous capsule surrounding numerous follicles of varying shape and size lined by flat to cuboidal follicular cells and filled with thick and thin colloid. The interfollicular areas show foci of haemmorrhage with few haemosiderin laden macrophages diagnosed as multinodular goitre.

Image 8: Right hemithyroidectomy specimen.

Based on history, clinical examination, HPE and biopsy skin, Cowden syndrome with multiple cutaneous papillomatosis, oral fibromas, multinodular goiter and fibrocystic disease of breast was diagnosed.

Discussion

Cowden syndrome is an autosomal dominant condition with variable expression associated with mutation in PTEN gene on arm 10q [8]. It causes hamartomatous neoplasm of any organ [2,3]. By 20 years of age, skin lesions are seen in all cases, By 40 years of age, one of the malignancy is seen. Skin lesions (90 - 100%), multinodular thyroid (66 - 75%) with prevalence of 1 in 200,000 (US Study). Review of English literature shows only 300 reported Cowden syndrome cases internationally till date.

Affected tissues are those having higher rate of proliferation, such as [7]:

- Epidermis - Trichilemmoma
- Oral and gastrointestinal mucosa -Papillomatosis
- Thyroid - Carcinoma
- Uterus - Fibroids
- Breast – Fibroadenoma.

An operational diagnosis of Cowden syndrome is made if an individual meets any one of the following [9]:

1) Pathognomonic mucocutaneous lesions combined with one of:
   a. ≥ 6 facial papules, of which 3 or more must be trichilemmomas.
   b. Cutaneous facial papules and oral mucosa papillomatosis.
   c. Oral mucosal papillomatosis and acral keratosis.
   d. ≥ 6 palmoplantar keratosis.
2) ≥ 2 major criteria.
3) 1 major and ≥ 3 minor criteria.
4) ≥ 4 minor criteria.

International Cowden syndrome consortium (ICSC) criteria

Pathognomonic criteria	Major criteria	Minor criteria
Adult Lhermitte-Duclos disease	Breast cancer	Other thyroid lesions (adenoma multinodular goitre)
Mucocutaneous lesions:	Epithelial thyroid cancer (non-medullary), especially follicular thyroid cancer	Intellectual disability (iq <75)
Trichilemmomas	Macrocephaly (> 97th percentile)	Hamartomatous intestinal polyps
Acral keratoses	Endometrial carcinoma	Fibrocystic disease of the breast
Papillomatous lesions		Lipomas
Mucosal lesions		Fibromas
		Genito-urinary malformation
		Uterine fibroids

Table

Conclusion

Management includes:

- Cowden syndrome is a very rare disease and only a handful of cases are reported from India.
- Although skin manifestations are present, systemic examination is more important to rule out internal malignancy.
- Genetic counselling and regular follow up is necessary to prevent transmission and early detection of any neoplasm.
- Counseling of patients regarding increased risk of malignancy, esp. Thyroid cancer and breast cancer in females.
- Instruct the patient for early signs of most common cancers for which they are at risk.
- Sirolimus(mtor) inhibitor show promising results in treatment of disease.

Bibliography

1. Lee EJ., *et al*. "Multiorgan involvements of Cowden disease in a 50-year-old woman: a case report and literature overview". *Journal of the Korean Society of Radiology* 69 (2013): 251-255.
2. Neumann S. "Cowden syndrome with an ovarian tumor (multiple hamartoma syndrome) (in German)". *Chirurg* 62 (19911): 629-630.
3. Smpokou P., *et al*. "PTEN hamartoma tumour syndrome: early tumour development in children". *Archives of Disease in Childhood* 100 (2015): 34-37.
4. Tan MH., *et al*. "Lifetime cancer risks in individuals with germline PTEN mutations". *Clinical Cancer Research* 18 (2012): 400-407.
5. Milas M., *et al*. "Should patients with Cowden syndrome undergo prophylactic thyroidectomy?" *Surgery* 152 (2012): 1201-1210.
6. Francis GL., *et al*. "Management guidelines for children with thyroid nodules and differentiated thyroid cancer". *Thyroid* 25 (2015): 716-759.
7. Hobert JA and Eng C. "PTEN hamartoma tumor syndrome: an overview". *Genetics in Medicine* 11 (2009): 687-694.
8. Nelen MR., *et al*. "Localization of the gene for Cowden disease to chromosome 10q22-23". *Nature Genetics* 13 (1996): 114-116.
9. Eng C. "Will the real Cowden syndrome please stand up: revised diagnostic criteria". *Journal of Medical Genetics* 37 (2000): 828-830.
10. Alimonti A., *et al*. "Subtle variations in Pten dose determine cancer susceptibility". *Nature Genetics* 42 (2010): 454-458.

11. McBride KL., *et al*. "Confirmation study of PTEN mutations among individuals with autism or developmental delays/mental retardation and macrocephaly". *Autism Research* 3 (2010): 137-141.