Case Series

Nonmedullary thyroid carcinoma in kindreds: A case series and review of familial papillary thyroid carcinoma

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ABSTRACT

Papillary thyroid carcinoma (PTC) is the most common thyroid cancer, comprising approximately 85% of cases. Familial PTC (FPTC) accounts for 5–10% of papillary thyroid carcinoma (PTC) cases and often presents more aggressively with higher rates of lymph node metastasis, distant spread, and recurrence. In this report, a 53-year-old man was diagnosed with a Hurthle cell predominant nodule with a focus on papillary carcinoma following a routine checkup and family history revealing three first-degree relatives with PTC. He underwent a total thyroidectomy which was managed with thyroxine and regular follow-up. His 46-year-old wife, in a consanguineous marriage, also opted for evaluation due to the family history. Ultrasound and fine-needle aspiration cytology revealed multifocal papillary carcinoma, leading to total thyroidectomy and similar management with thyroxine. The report highlights the clinical significance of recognizing FPTC in families with multiple affected members, stressing that early intervention can minimize the need for extensive surgery, including lymph node dissection and radioactive iodine therapy. By identifying FPTC early, clinicians can improve outcomes, reduce recurrence rates, and tailor treatment to avoid more invasive procedures, emphasizing the need for proactive management in familial thyroid cancer cases.

Key words: Early diagnosis and treatment, Familial papillary thyroid carcinoma, Screening

Papillary thyroid carcinoma (PTC) is the most common thyroid cancer accounting for about 85% of the cases [1]. Etiological factors include radiation exposure, benign thyroid diseases, and familial syndromes, [2]. Although most of the PTCs are sporadic (around 90%), familial causes constitute about 5–10% of the cases [2]. Familial cancers tend to be more aggressive compared to sporadic cases in terms of lymph node spread, distant metastases, and recurrence rates. Identifying familial PTC is challenging given the low incidence. When two or more first-degree relatives (like parents, siblings, or children) are diagnosed with the disease without a history of familial syndromes or risk factors that are frequently linked to non-medullary thyroid cancer (NMTC), the condition is identified as familial PTC (FPTC), the most common type of familial NMTC (FNMTC) [3,4]. Although the familial variant of the disease (FNMTC) is still a less well-characterized clinical entity, it has become more common than previously documented due to the rising occurrence of papillary thyroid cancer (PTC) around the world in recent years [5].

We report a family (married couple and their family members) diagnosed with papillary carcinoma thyroid and present a literature review of FNMTC, highlighting the clinical significance of recognizing FPTC in families that improves outcomes and overall quality of life.

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Case 1

A 53-year-old gentleman presented with incidental thyroid nodules during a routine health checkup. His medical history was otherwise not significant. He reported that three other family members (first-degree relatives) had been diagnosed with papillary carcinoma of the thyroid. His mother, grandmother, and maternal aunt were diagnosed with papillary thyroid carcinoma during their 40s–50s. Clinical examination was unremarkable.

On investigating further, a neck ultrasound showed a 1.4 × 1 cm thyroid imaging, reporting, and data system V nodule in the right lobe of the thyroid. Fine-needle aspiration cytology (FNAC) of the nodule was atypia of undetermined significance - Bethesda III. Considering the strong family history, the patient was given treatment options. He opted for a total thyroidectomy and underwent the same. The final histopathology report (HPR)

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revealed that the right thyroid lobe showed an exophytic nodule of size 1.51 × 1 × 1 cm with features of hurthle cell predominant nodule. A 1 × 1 mm focus of papillary carcinoma was also seen in the right lobe. The case was discussed in a multidisciplinary board meeting and planned for follow-up. He was started on thyroxine and was kept under observation.

Case 2

Considering the above findings, his wife, married by consanguinity, a 46-year-old lady, wanted to evaluate herself, and a neck ultrasound was done which showed a 6 × 6 mm nodule in the left lobe of the thyroid. Clinical examination was unremarkable. FNAC of the nodule was Bethesda III. She was planned to be kept under follow-up, however, due to a strong family history, the patient wanted surgery and underwent a total thyroidectomy. The final HPR showed multifocal papillary carcinoma thyroid- 3 focus with the largest focus 6 × 6 mm. The case was discussed in a multidisciplinary board meeting and planned for follow-up. She was started on thyroxine and was kept under observation.

Both patients were followed up with neck ultrasounds at 3 and 6 months, which demonstrated normal findings.

DISCUSSION

The first reported familial thyroid cancer was in 1955, reported by Robinson and Orr when monozygotic twins underwent total thyroidectomy in Kansas City [6]. FPTC is better described when three or more family members have papillary carcinoma thyroid rather than two members only because the chance of it being sporadic is higher when only two members are diagnosed [7]. It may also be associated with benign thyroid diseases, such as long-standing multinodular goiter, thyroiditis, and adenomatous nodules. There is no proper consensus on the number of family members affected to call it FPTC [8]. In a study by Charkes *et al*., the sporadic case incidence rate was 62–69% if only two individuals were affected compared to 6% when three or more individuals were affected [4]. In our case series, our patient had more than three family members diagnosed with papillary carcinoma thyroid confirming the FPTC.

The pathogenesis and genetic background of FPTCs are poorly understood. Based on the available literature, it is likely to be polygenic and autosomal dominant with incomplete penetrance. There is ongoing research on susceptibility genes linked to FPTCs [9,10]. FPTCs tend to be more aggressive compared to their sporadic counterparts. It has higher rates of multifocality, bilaterality, extrathyroidal invasion, distant metastasis, lymph node metastasis, recurrence, larger tumor size, and more malignant lymph nodes involved [11]. These factors often result in more aggressive treatment approaches, negatively impacting patient outcomes and quality of life. A study by Zhang *et al*. reports a retrospective analysis of 117 families with a history of FPTC, where they noted increased recurrence rates and aggressive disease features, such as lymph node involvement. This study also emphasizes the benefits of early detection through screening in improving outcomes [12]. In our cases, we mitigated these risks by diagnosing and managing the disease at an early stage, allowing for less invasive treatment and improved prognosis.

Although FPTC is a rare disease, all PTC patients should be asked about family history because most of the time FPTC goes undiagnosed. There is around a 3–6% chance that relatives have a history of PTC. These patients and their relatives need aggressive follow-up and screening. American Thyroid Association 2015 guidelines did not recommend neck ultrasound for screening [13,14]. However, given the rising incidence of FPTCs, families with three or more affected relatives should be offered screening. In our case, the couples have two daughters aged 16 and 18, and planned for proactive screening from 36 years of age. This comprehensive approach highlights the necessity of recognizing genetic patterns in thyroid cancer and advocating for heightened awareness and monitoring in at-risk families.

This case report signifies the importance of identifying FPTCs and with early diagnosis and treatment, the extent of the surgery and treatment as a whole can be minimized. In our cases, lymph node dissections and radioactive iodine therapy were avoided because the case was detected at very early stages emphasizing the importance of screening and early treatment of the same.

CONCLUSION

FPTCs though rare are a prevailing yet undiagnosed condition. Considering the aggressive nature of the disease compared to its sporadic counterpart needs a high index of suspicion and a thorough family history should be elicited. Based on the data that is now available, it is recommended that ultrasonography neck screening be done annually, beginning at age 10 years earlier than the youngest afflicted family member, and only in families with three or more affected members. Furthermore, a more aggressive care decision should be made with a lower threshold for the diagnosed instances in those families.

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