Familial Non-Medullary Thyroid Cancer (FNMTC)

What is FNMTC?

Familial non-medullary thyroid cancer (FNMTC) refers to non-medullary thyroid cancer, most commonly papillary thyroid cancer, occurring in **two or more first-degree relatives** in the absence of a recognized hereditary cancer syndrome.

Referral to Hereditary Cancer Program

Referral may be considered when there is suspicion of a syndromic cause of non-medullary thyroid cancer. Examples include:

- **PTEN Hamartoma Tumor Syndrome** (Cowden syndrome): macrocephaly, mucocutaneous lesions, multiple hamartomas, breast cancer, endometrial cancer, renal cancer, or gastrointestinal polyps.
- **DICER1** syndrome: childhood-onset multinodular goitre, thyroid cancer at a young age, pleuropulmonary blastoma, cystic nephroma, ovarian Sertoli-Leydig cell tumour, or other DICER1-associated tumours.
- **Familial Adenomatous Polyposis** (FAP): colorectal polyposis, colorectal cancer, desmoid tumours, congenital hypertrophy of the retinal pigment epithelium (CHRPE), or cribriform-morular thyroid carcinoma.
- **Carney Complex**: spotty skin pigmentation, cardiac or cutaneous myxomas, endocrine overactivity, or multiple endocrine tumours.
- **Werner syndrome**: premature aging, bilateral cataracts, short stature, diabetes mellitus, premature atherosclerosis, or multiple malignancies.

Referrals are generally not indicated for isolated FNMTC alone, as genetic testing has a low diagnostic yield and the genetic basis remains unknown in most families. If genetic testing is being considered, an **affected family member should be tested first whenever possible**, as testing an unaffected relative is unlikely to be informative.

Screening and Management

Evidence supporting thyroid ultrasound screening in unaffected relatives remains limited, and there is no consensus recommendation for routine screening of all individuals from FNMTC families. For families with only two affected first-degree relatives, routine ultrasound screening is generally not recommended.

In families with three or more affected first-degree relatives, annual thyroid palpation and ultrasound screening may be considered on an individualized basis following discussion of the potential benefits, limitations, and risk of overdiagnosis. Any thyroid nodules identified should be managed according to standard thyroid nodule guidelines.

Key Points

- FNMTC is non-medullary thyroid cancer occurring in ≥2 first-degree relatives without a recognized hereditary syndrome.
- A hereditary predisposition is more likely when ≥3 first-degree relatives are affected.
- Genetic testing has a low diagnostic yield in isolated FNMTC.
- If genetic testing is pursued, an affected family member should be tested first.
- Referral to the Hereditary Cancer Program is generally reserved for individuals with features suggestive of a syndromic hereditary cancer condition.
- Routine thyroid ultrasound screening is not recommended for most families but may be considered when ≥3 first-degree relatives are affected.