Multiple Endocrine Neoplasia Type 2 (MEN2)

MEN2 is an autosomal dominant condition caused by germline mutations in the RET gene. About 20-25% of medullary thyroid cancers (MTC) are associated with MEN2. MTC is more often bilateral and/or multifocal with MEN2 compared to sporadic MTC.

There are 2 clinical subtypes of MEN2 with implications for management:

MEN2A: MTC, pheochromocytoma, parathyroid adenoma/hyperplasia. Familial MTC is a subtype of MEN2A.

MEN2B: early onset aggressive MTC, marfanoid habitus, medullated corneal nerve fibers, ganglioneuromas of the lips/tongue or GI tract, pheochromocytoma

MEN1 is a separate syndrome that is associated with tumours of the parathyroid, pituitary and/or gastro-entero-pancreatic tract.

Referral Criteria

Note: close relatives include children, brothers, sisters, parents, aunts, uncles, grandchildren & grandparents on the same side of the family. History of cancer in cousins and more distant relatives from the same side of the family may also be relevant.

- family member with a confirmed RET gene mutation – refer for carrier testing
- person with medullary thyroid cancer (MTC) diagnosed at any age
- person with pheochromocytoma AND hyperparathyroidism
- person with MTC and features of MEN2B
- person with pheochromocytoma OR hyperparathyroidism, AND a close relative with MTC, pheochromocytoma OR hyperparathyroidism
- a person with features described above and family history of related tumours
- family history of close relatives with features described above

Referral of children is appropriate for this syndrome because it may inform their medical management.

Lifetime Cancer Risks for RET mutation carriers

Lifetime MTC risk is close to 100%. Several groups have proposed risk stratification based on the mutation locations within the RET gene, which appear to be associated with age of onset and aggressiveness. MTC risk with any RET mutation is significantly higher than in the general population.

Pheochromocytoma risk is 30-50% and may also vary by mutation location.

The risk of parathyroid disease is 20-30% (except for MEN2B).
Cancer Risk Management Recommendations for RET mutation carriers

Note: The recommendations provided below are general in nature. Individualized recommendations based on personal and/or family medical histories may be provided through Hereditary Cancer Program assessment and/or by other specialists involved in a person’s current care.

Medullary thyroid cancer

- thyroidectomy is recommended in childhood (timing may be directed by location of RET mutation), followed by annual serum calcitonin monitoring
- prior to surgery: annual serum calcitonin levels and neck ultrasound beginning at age 3 (or at age 6 months for highest risk mutations)

Pheochromocytoma

- annual medical review, blood pressure and biochemical screening (24-hour urinary catecholamines and fractionated metanephrines) beginning at age 8 or age 20, depending on mutation
- abdominal MRI and/or CT if pheochromocytoma is suspected clinically and/or if plasma or urinary catecholamine values are increased

Parathyroid (MEN2A only)

- annual serum calcium (total and ionized) and fasting parathyroid hormone levels, beginning at age 8 or age 20, depending on mutation

Additional information

The following websites offer support and information which may be helpful to people living with MEN2:

- AMEND: www.amend.org.uk
- American MEN Support: http://amensupport.org/
- Thyroid Cancer Canada: https://www.thyroidcancercanada.org/

References available on request.

Reviewed October 2017, Revised April 2021