BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority
Hereditary Cancer Program

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

RET testing for an eligible **affected index** case can be ordered by an endocrinologist or oncologist using the appropriate Cancer Genetics Lab requisition.

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.
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