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

Cowden Syndrome

Cowden syndrome (CS) is part of the *PTEN* hamartoma tumour syndrome, which also includes Bannayan-Riley-Ruvalcaba syndrome (BRRS), *PTEN*-related Proteus syndrome (PS), and Proteus-like syndrome. This syndrome is associated with germline *PTEN* gene mutations that are inherited in an autosomal dominant manner.

CS is a multi-system condition characterized by hamartomatous overgrowth of tissues. It is associated with a high risk for benign and malignant tumors of the thyroid, breast, and endometrium. Affected individuals usually have macrocephaly as well as specific skin findings (trichilemmomas and papillomatous papules) identified by their late 20s.

Referral Criteria

- family member with a confirmed *PTEN* gene mutation – refer for carrier testing
- consider referral for *PTEN* assessment if personal and/or family history includes the following:
    - breast cancer, epithelial thyroid (follicular or other non-medullary) cancer, endometrial carcinoma AND
        - skin findings: trichilemmomas, papillomatous papules (oral, facial), acral keratosis, palmoplantar keratosis
        - macrocephaly (occipital frontal circumference ≥ 97th percentile)
    - Lhermitte-Duclos disease (cerebellar dysplastic gangliocytoma)
- other features that have been associated with Cowden syndrome include: thyroid lesions (e.g., adenoma, multinodular goiter), intellectual disability, hamartomatous intestinal polyps, fibrocystic disease of the breast, lipomas, fibromas, renal cell carcinoma, other genitourinary tumors, genitourinary malformation, uterine fibroids.

Estimated Lifetime Cancer Risks for *PTEN* mutation carriers

breast cancer	85%
thyroid cancer (usually follicular)	35%
endometrial cancer:	28%
renal cancer	34%
colon cancer	9%
melanoma	6%

Cancer Risk Management Recommendations for adult *PTEN* 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.

Risk management for *PTEN* mutation carriers includes an annual physical exam and consideration of the following cancer screening and potential risk-reducing options.

Breast cancer:

- women should be breast aware
- annual breast MRI from age 30-65
- annual mammograms beginning at age 30 (continue as long as clinically indicated)
- clinical examination of the breast and regional nodes by an experienced healthcare professional every 12 months, in conjunction with appropriate breast imaging
- consider risk-reducing bilateral mastectomy, which reduces breast cancer risk by over 90%. The decision to have this surgery is complex and requires discussion regarding benefits and risks in the context of a woman's general health, life expectancy and personal health
- risk-reducing medications (e.g. tamoxifen, raloxifene, anastrozole, exemestane) can almost halve the risk of developing hormone receptor positive breast cancer. The decision to use such medication requires discussion about the relative benefits and the risks of side effects

Endometrial cancer:

- prompt investigation of any unusual bleeding between menstrual periods or after menopause
- there is no evidence to support the effectiveness of endometrial cancer screening. Some women with Cowden syndrome may consider annual endometrial biopsy with transvaginal ultrasound, starting at age 30-35
- risk-reducing hysterectomy may also be considered

Colon cancer:

- colonoscopy every 5 years beginning at age 35 or 5-10 years younger than the earliest colon cancer diagnosis in the family

Thyroid cancer:

- annual thyroid ultrasound

Other:

- consider renal ultrasound starting at age 40, then every 1-2 years
- regular dermatological evaluation may be indicated for some patients
- education regarding general signs and symptoms of cancer

Additional Information

A comprehensive review of this syndrome is available at Gene Reviews
https://www.ncbi.nlm.nih.gov/books/NBK1488/

References available on request.
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