Cowden syndrome (CS) is a genetic disorder characterized by multiple benign tissue growths (i.e., hamartomas) and an increased risk of developing specific cancers, such as breast, thyroid, kidney, endometrial, or colorectal cancer (Genetics Home Reference, 2012). This genetic syndrome was named after a person diagnosed with the disorder (Lloyd & Dennis, 1963). CS is part of a larger syndrome called PTEN hamartomatous syndrome, which also includes Bannayan-Riley-Ruvalcaba syndrome, PTEN-related Proteus syndrome, and Proteus-like syndrome (Eng, 2014).

Basic Genetics

Cowden syndrome is transmitted from parent to child through an autosomal dominant pattern of inheritance. An autosome is a chromosome that does not convey gender, therefore an autosome is any chromosome other than the sex chromosomes X and Y. Genetic disorders that are transmitted on autosomal chromosomes occur in males and females. Dominant means the genetic condition may occur (i.e., be expressed) when only one copy of the genetic mutation is present. CS is most frequently caused by a mutation in the PTEN gene (Genetics Home Reference, 2012). A healthy PTEN gene suppresses tumors from forming. A mutation in the PTEN gene leads to uncontrolled cell growth, formation of hamartomas, and can potentially lead to the development of certain cancers. Hamartomas are an overgrowth of normal appearing and functioning mature cells that resemble, but are not, true tumors (MedlinePlus, 2014). CS is also caused by mutations in the KLLN, SDHB, or SDHD gene, but they are less common than PTEN (Genetics Home Reference, 2012).

Diagnosis

Penetrance refers to the proportion of individuals with a genetic mutation that actually develop the clinical manifestations of the genetic disorder in the presence of a genetic mutation (Genetics Home Reference, 2014). The expected penetrance of the PTEN gene is 90% by late in the second decade of life and 99% in the third decade of life with skin manifestations as the most common finding (Eng, 2014).

The diagnosis of CS can be made via genetic testing or by assessment of clinical findings. Genetic testing may include full sequencing or multiplex ligation-dependent probe amplification of a single gene or a panel of genes. Full sequencing of a gene involves examining one base pair at a time, much like the spell-checking function on a word-processing computer program. Multiplex ligation-dependent probe amplification helps to identify deletions and duplications of genetic information that full sequencing cannot recognize (Stuppia, Antonucci, Palka, & Gatta, 2012). Panels of genetic tests allow for the full sequencing and multiplex ligation-dependent probe amplification of multiple genes related to a more global genetic problem such as a family history of breast, thyroid, kidney, endometrial, or colorectal cancer. To confirm the clinical diagnosis of CS, a panel test that includes the PTEN gene and closely matches the cancers seen in a family would be ordered.

Cowden syndrome is associated with numerous clinical findings that can be isolated findings. However, many of these findings can also be associated with other syndromes. Some clinical findings were previously felt to be pathognomonic (i.e., distinctively characteristic) for CS, but a systematic analysis of diagnostic criteria by Pilarski et al. (2013) did not provide evidence for any pathognomonic clinical features of CS. Major and minor diagnostic criteria have been established to help the healthcare provider sort through physical findings and make a clinical diagnosis of CS. See Figure 1 for a listing of these criteria. The major and minor criteria from Figure 1 are used, as described in Figure 2, to make a clinical diagnosis.

Physical assessment is a quick, easy, noninvasive, and inexpensive method to screen for CS. Macrocephaly is one of the major criteria of CS (Mester, Tirot, Rybicki, Frazier, & Eng, 2011). The occipital-frontal circumference, or head circumference, is measured in centimeters just above the ears and around the largest portion of the head. Macrocephaly is identified when the head circumference is at or above the 97th percentile for the gender and height of an adult (Bushby, Cole, Matthew, & Goodship, 1992). Common skin findings in CS include trichilemmomas (i.e., small, skin-colored papules on the face, ears, and neck) (DermNet NZ, 2013), plantar keratotic pits (i.e., indentations that are best seen after soaking the hands and feet in warm water), and acral hyperkeratotic papules (i.e., thickened, callous-like tissue). Oral findings often include papillomas (i.e., hamartomas) of the gingiva and the buccal mucosa, giving it a cobblestone appearance.