Basal Cell Nevus Syndrome: A Brief Guide and Memory Aid

Early diagnosis of this rare disorder will ensure proper management and initiation of prevention strategies.

By David A. Barzilai, MD, PhD and Robert Brodell, MD

Basal cell nevus syndrome (BCNS) is a rare autosomal dominant condition characterized by tumors, most notably basal cell carcinoma (BCC), and a wide variety of developmental abnormalities, with an estimated one case per 57,000-164,000 population. Mutations in the PTCH (patched) gene chromosome arm 9q is thought to be responsible. BCNS has 97 percent penetrance and variable expressivity; one third of cases are attributed to new mutations.

Although BCCs are nearly ubiquitous with this syndrome, sun exposure accelerates development.

Signs and Symptoms

BCNS remains a clinical diagnosis, based on recognition of associated developmental abnormalities affecting the skeletal system, the genitourinary system, central nervous system (CNS) and skin. The most characteristic of these include palmoplantar pits (defects in the stratum corneum), jaw cysts (diagnosed radiographically), and multiple BCC. Present in 50 percent of patients, palmoplantar pits are most specific for BCNS. These can be enhanced by soaking the hands in warm water for 10 minutes.

The first diagnostic clue is often multiple BCC arising in large numbers in a young patient. These lesions may occur as early as two years of age but generally start between puberty and 35 years of age often occurring in crops. They number from a few to over a thousand and may develop pigmentation with ulcerations as they mature. Jaw odontogenic keratocysts are another common presenting sign in 65-75 percent of affected patients. These cysts may be associated with pain, malocclusion, or swelling. Table 1 outlines major and minor criterion developed by Kimonis et al to facilitate diagnosis. Routine laboratory testing is not indicated. Skull radiographs help identify calcification of the falx cerebri and tentorium cerebelli and lytic bone lesions. A general skeletal XR survey may identify bifid, hypoplastic, fused or other rib defects, malformations at the occipitovertebral junction, or vertebral fusion. Panoramic radiography may reveal odontogenic keratocysts. MRI is indicated when medulloblastoma is suspected in young BCNS patients, and pelvic ultrasonography (US) may be performed at puberty as a baseline with follow-up US should symptoms present to suggest ovarian fibromas. Table 2 is a memory aid for some of the more common associated signs. Molecular testing is available to confirm the diagnosis when necessary.

Differential Diagnosis

Other conditions associated with multiple BCC include Rombo syndrome (atrophoderma vermiculatum of the face, multiple milia, telangiectases, acral erythema, and multiple BCCs) and Bazex-Dupre-Christol syndrome (follicular atrophoderma, congenital hypotrichosis and multiple BCCs). Arsenic ingestion and xeroderma pigmentosa have also been associated with multiple BCC. These conditions can be distinguished from BCNS by the absence of associated developmental defects listed in Table 1.

Treatment and Management

Larger BCC’s in BCNS may be excised.

Table 1. Diagnostic Criteria

2 major criteria OR 1 major and 2 minor criteria

Major Criteria
1. >2 BCCs or 1 BCC in patients younger 20
2. Histologically proven odontogenic keratocysts of the jaw
3. >2 palmar or plantar pits
4. Bilamellar calcification of the falx cerebri
5. Fused, bifid, or markedly splayed ribs
6. One or more first-degree relatives with NBCCS.

Minor Criteria:
1. Macrocephaly
2. Congenital malformations (e.g., cleft palate or lip, frontal bossing, coarse facies, and moderate or severe hypertelorism)
3. Skeletal abnormalities (e.g., Sprengel deformity, marked pectus deformity, marked syndactyly of the digits)
4. Radiologic abnormalities (e.g., vertebral anomalies, bridging of the sella turcica, modeling defects of the hands and feet, or flame-shaped lucencies of the hands and the feet)
5. Medulloblastoma or ovarian fibroma.
To avoid scarring, lesions with typical clinical features and limited thickness may be treated without biopsy utilizing cryotherapy, topical 5-fluorouracil cream 5% and imiquimod cream 5%.1–4 Other options include Mohs microscopic surgery, CO2 laser, electrodesiccation and curettage (ED&C), and photodynamic therapy. Radiation therapy is not recommended since this has been associated with increased numbers of BCCs in BCNS. Genetic counseling is advised.

Preventive measures include sun avoidance and aggressive use of broad spectrum sunscreens. Clinical surveillance at least every three months with full body skin examinations will promote early diagnosis and treatment, which is critical since smaller lesions are more responsive to non-surgical modalities, and BCCs occasionally metastasize. Follow-up should also include neurologic examination every six months.2 Ovarian and cardiac tumors may also develop and require excision. Medulloblastomas may require surgery, radiation, and chemotherapy.