A fusiform nodule on the flank

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Case report

An otherwise healthy 61-year-old female presented with a skin tumor on the left flank, which had been present since her early adulthood. The tumor gradually enlarged during the first 2–3 years and then stabilized in size. There were no symptoms from the tumor. On examination, a red to violaceous, shiny, polypoid, fusiform nodule with firm consistency, measuring approximately 3.0 cm × 2.0 cm, was noted on her left flank (Figure 1). There were also many skin tumors on her face and scalp, most of which were dome-shaped, smooth surfaced, violaceous, firm nodules measuring several millimeters in diameter. These tumors were 1-cm dermal nodules that caused pain; others were rounded, skin-colored, firm papules with a size of approximately 5 mm in diameter around her nose. An excisional biopsy specimen was obtained from the tumor at the flank.

Histopathologic examination revealed a tumor occupying the reticular dermis, which was composed of aggregations of neoplastic cells arranged in a jigsaw puzzle pattern. The aggregations consisted of neoplastic cells with two different appearances: (1) peripheral cells aligned in a palisade with small, dark staining columnar nuclei surrounded by a scant cytoplasm, and (2) cells with nuclei that were larger and paler, and that had a more abundant pale cytoplasm. Each aggregation was surrounded by a rim of homogenous eosinophilic basement membrane-like material. Globules of the same material were also present within the aggregations themselves (Figure 2).

The patient then underwent several sessions of surgical removal for other tumors on the face and scalp, and pathology exams showed cylindroma, spiradenoma, trichoepithelioma, or combinations of them (Figure 3A: cylindroma + trichoepithelioma; Figure 3B: cylindroma + spiradenoma). She reported that two of her younger brothers and sisters also had similar skin tumors, but they were not as numerous as hers.

Figure 1  A fusiform nodule on the patient’s left flank.

Figure 2  Peripheral columnar cells and central cells with abundant cytoplasms (H&E, 400×).

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**Diagnosis**

Cylindroma and Brooke-Spiegler syndrome.

**Discussion**

Cylindroma is a common benign adnexal tumor, which is most often seen on the head, neck and scalp. It usually presents as a dome-shaped, shiny nodule. Scalp lesions may grow to a large size and coalescence of numerous lesions is known as a “turban tumor.” Development on the trunk or polypoid appearance is exceptional. There is a marked female preponderance of cylindroma (up to 9:1). Familial cases have been described and are typically associated with multiple tumors. Multiple cylindromas may be associated with trichoepitheliomas and spiradenomas, a constellation known as Brooke-Spiegler syndrome, which is inherited in an autosomal dominant fashion. Patients with this syndrome occasionally develop multiple basal cell adenomas, milia, organoid nevi, and basal cell carcinoma. There is a high penetrance in affected families, but the individual clinical manifestation is highly variable.

Brooke-Spiegler syndrome is caused by germline mutations in a single gene, called CYLD, located on chromosome 16q12–q13. Most of the mutations, which are mainly located at the C-terminal half of the CYLD coding sequence, lead to the formation of truncated proteins. The function of CYLD is not fully understood. It belongs to a family of ubiquitin-specific proteases, and interacts with NEMO, the regulatory subunit of the inhibitor κB kinase complex, tumor necrosis factor receptor-associated factors (TRAFs), and TRAF-interacting proteins; it negatively regulates the nuclear factor κB signal transduction pathway. Inhibition of CYLD enhances activation of the nuclear factor κB and leads to increased resistance to apoptosis and advanced carcinogenesis.

Mutation screening of the CYLD gene should be considered for patients with multiple cylindromas and/or trichoepitheliomas, as well as for their relatives. Early identification of Brooke-Spiegler syndrome may improve therapeutic management to avoid complications such as disfigurement and malignant transformation.

Treatment modalities of these tumors reported in the literature are mainly ablative, including surgical removal, cryotherapy, electrodessication, topical trichloroacetic acid application, and CO₂ and Er:YAG laser. It has been reported that the effect of CYLD mutation can be reversed by application of salicylates or prostaglandin A. This finding may provide directions for future novel therapy for this syndrome.

**References**