Birt-Hogg-Dubé syndrome: identifying patients at risk of renal cell carcinoma, pulmonary cysts and pneumothoraces

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DESCRIPTION

A 42-year-old woman attended the dermatology outpatient department (OPD), with a 2–3 year history of multiple firm flesh-coloured papules localised to her cheeks, periauricular and auricular area (figures 1 and 2). These lesions developed when the patient was in her late 30s. They were asymptomatic. She also had multiple fibroepithelial polyps (skin tags). She had a family history of similar skin lesions (2 sisters and her father). Her medical history was significant for mild hidradenitis suppurativa. A punch biopsy of lesional skin was performed—histology showed focal increase in perivascular dermal connective tissue, in keeping with an angiofibroma (figures 3 and 4). Genetic testing confirmed a heterozygous variant in the folliculin (FLCN) gene, consistent with a diagnosis of Birt-Hogg-Dubé syndrome.

Birt-Hogg-Dubé syndrome is an autosomal-dominant condition. It has characteristic cutaneous findings, including fibrofolliculomas, angiofibromas, fibroepithelial polyps and trichodiscomas.

Figure 1 Multiple firm flesh-coloured papules—right post-auricular area.

Figure 2 Multiple similar lesions affecting nasal bridge and ala.

Figure 3 H&E stain—angiofibroma, left earlobe.

Figure 4 Masson’s trichrome—highlighting fibrosis in an angiofibroma, left earlobe.
Extra cutaneous findings include pulmonary cysts, spontaneous pneumothorax and renal cancer. Management is focused on early diagnosis and treatment of renal cancer. The FLCN gene, located on the short arm of chromosome 17 (17p11.2), is responsible for this syndrome. It codes for the protein folliculin, thought to be an oncogene suppressor protein. It has also been linked to the mammalian target of rapamycin signalling pathway, a serine/threonine protein kinase that regulates cell growth, proliferation and survival.

Following diagnosis of Birt-Hogg-Dubé syndrome, our patient had a renal ultrasound and thorax/abdomen CT to assess for pulmonary or renal disease. These revealed a benign renal cyst with no evidence of pulmonary cysts. She will require long-term follow-up and screening for renal carcinoma.

Learning points

- Multiple angiofibromata are associated with several genetic conditions including tuberous sclerosis, multiple endocrine neoplasia type 1 (MEN1) and Birt-Hogg-Dubé syndrome.
- Skin examination can help detect patients who may be at risk of certain malignancies and who may therefore benefit from regular cancer screening.
- Diagnosing a genetic condition has implications for both the patient and all family members.

REFERENCES