ANSWER TO PHOTO QUIZ (PAGE 198)

ASYMPTOMATIC FACIAL PAPULES AS A MARKER OF GENETIC SYNDROME

DIAGNOSIS

Fibrofolliculomas. Birt-Hogg-Dubé syndrome (BHD).

Birt-Hogg-Dubé (BHD) is a rare autosomal dominant disorder caused by a germline mutation of the FLCN gene characterised by the presence of benign hair follicle tumours, kidney tumours, pulmonary cysts and recurrent spontaneous pneumothoraces. This syndrome has a great variability in clinical features and patients can present with any combination of manifestations.

The most common systemic finding in BHD is lung cysts, with a 50-fold increased risk of spontaneous pneumothorax. Pneumothoraces in these patients have a high rate of recurrence and pleurodesis is recommended after the first episode.[1,2]

Patients with BHD are at increased risk of developing bilateral, multifocal, renal cell cancers which are the most dangerous complication of this disease. Multifocal and bilateral tumours are seen frequently but most of them tend to be indolent.

Cutaneous findings are common, and sometimes may be the first manifestation of the disease as in the present case. Histology of these lesions most often reveals fibrofolliculomas, but trichodiscomas, perifollicular fibromas, and angiofibromas have also been reported.[3]

There are clinical criteria for the diagnosis of this syndrome. Major criteria are the presence of at least five individual fibrofolliculomas and/or trichodiscomas lesions appearing in adulthood with at least one histologically confirmed and/or presence of a pathogenic PLCN germline mutation. Minor criteria are multiple lung cysts located basally with no other apparent cause (with or without pneumothorax); renal cancer that is either early onset (age < 50 years), multifocal or bilateral or mixed chromophobic/oncocytic histology; or a first-degree relative with BHD syndrome.

To rule out pulmonary or renal manifestations, a baseline chest X-ray or CT scan and abdominal ultrasound must be performed. Currently there are no published guidelines for renal cancer or pulmonary cyst screening in asymptomatic BHD patients or their relatives but recommendations include magnetic resonance or ultrasound for renal cancer screening every 3-5 years from the age of 20 years and a baseline chest X-ray or CT scan and follow-up every 3-5 years to detect asymptomatic pulmonary cysts.[4]

In our patient, gene sequence analysis of FLCN on peripheral blood revealed a heterozygous c.1285 deletion confirming the diagnosis of Birth-Hogg-Dubé syndrome. Screening chest X-ray and abdominal ultrasonography were performed in our patient and both were unremarkable. Follow-up tests have not shown any abnormalities.

REFERENCES

1. Gupta N, Sunwoo BY, Kotloff RM. Birt-Hogg-Dubé Syndrome. Clin Chest Med. 2016;37:475-86.
2. López V, Jordá E, Monteagudo C. [Birt-Hogg-Dubé syndrome: an update]. Actas Dermosifiliogr. 2012;103:198-206.
3. Aivaz O, Berkman S, Middelton L, Linehan WM, DiGiovanna JJ, Cowen EW. Comedonal and Cystic Fibrofolliculomas in Birt-Hogg-Dube Syndrome. JAMA Dermatol. 2015;151:770-4.
4. Lencastre A, Ponte P, Apetato M, Nunes L, Lestre S. Birt-Hogg-Dubé syndrome. An Bras Dermatol. 2013;88 (6 Suppl 1):203-5.