Birt-Hogg-Dubé Syndrome

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Synonym: fibrofolliculomas with trichodiscomas and acrochordons

Birt-Hogg-Dubé syndrome is named after the three authors of a paper that described family members with papular skin lesions on their face, forehead, scalp and neck.\(^1\)

When these lesions were examined, the following were found:\(^2\)

- Fibrofolliculomas (benign tumours of the hair follicle).
- Trichodiscomas (hamartomatous tumours of the hair disc).
- Acrochordons (‘wart with a thin neck’ skin tags).

This triad of features became known as Birt-Hogg-Dubé syndrome. It is now thought that these may all just be part of the spectrum of fibrofolliculomas.\(^3\)

Genetics

- Birt-Hogg-Dubé syndrome is a rare inherited genodermatosis.\(^2\)
- The condition is caused by mutation in the gene encoding folliculin which may have a role as a tumour suppressor gene.
- The mutation is at gene map locus 17p11.2.
- An autosomal dominant inheritance pattern has been identified.\(^4\)

Epidemiology

- The actual incidence is unknown, but it is likely to be underdiagnosed.\(^5\)

Presentation

- Onset tends to be in adulthood with skin lesions:\(^2\)
  - These develop in the 20s or 30s and remain throughout life.
  - They are typically small, dome-shaped, papular skin lesions, about 2 mm to 4 mm in diameter, that develop over the scalp, face, neck and upper trunk. They may also be seen in the mouth.
  - They cause no symptoms and the reason for presentation is usually cosmetic.
  - Acrochordons are warty-like skin tags that may be found on the eyelids, neck, axilla and upper half of the trunk.\(^3\)

  - Presentation may also be with renal carcinoma, spontaneous pneumothorax or other possible associated condition - see below.

Associations

There are a number of conditions associated with Birt-Hogg-Dubé syndrome including:\(^3\)

- Renal carcinomas (may be multifocal or bilateral; most commonly chromophobe renal carcinoma and oncocytic hybrid tumours).\(^6\)
- Pulmonary cysts.
- Spontaneous pneumothorax.

These are thought to result from a mutation in the FLCN gene. The conditions below are other possible associations.

- Connective tissue naevi.
- Parathyroid adenomas.
- Flecked chorioretinopathy.
- Bullous emphysema.
- Lipomas and angiolipomas.
- Parotid oncocytomas.
- Multiple oral mucosal papules.
Neural tissue tumours.
Multiple facial angiofibromas.
Colonic polyps and colonic adenocarcinoma.
Medullary thyroid carcinoma.

Investigations

Birt-Hogg-Dubé syndrome should be looked for in any patient with multiple bilateral kidney tumours, especially if the predominant histological type is chromophobe renal cell carcinoma or hybrid oncocytic tumour.[7]

- Skin biopsy will confirm the nature of the lesions.
- Molecular genetic testing is available.
- CXR (may show pulmonary cysts, bullous emphysema or pneumothorax).
- Renal ultrasound and CT scan of the abdomen/pelvis should be performed to screen for renal tumours. Relatives should also be screened for renal cancer.
- Consider colonoscopy because of the possible association with colonic polyps/carcinoma, although this is debated.[8, 9]

Management

- There is no specific therapy.
- Skin lesions may be treated by surgical removal. Dermabrasion, electrodesiccation and laser treatment have been used but the lesions may recur.[3]
- There should be long-term follow-up for malignant change, especially renal carcinoma and possibly colonic carcinoma.
- Monitoring and screening for associated chest conditions should be carried out.
- Associated conditions should be managed appropriately.
- Genetic counselling should be offered.

Prognosis

- This depends on the development of associated conditions, especially renal carcinoma.
- The tendency for associated malignancy seems variable between families.
- Specific mutations in the folliculin gene may predispose to cancer development in Birt-Hogg-Dubé syndrome.[10]
- Malignancy is not an invariable part of the disease.

Prevention

- Encourage patients to stop smoking because of the additive risk factor for lung disease and renal carcinoma.
- Avoidance of high ambient pressures may reduce the risk of spontaneous pneumothorax.[11]

Further reading & references

- Birt-Hogg-Dubé syndrome; DermNet NZ
- Buckley KK et al; Birt-Hogg-Dube Syndrome, Medscape, Genet Med 2009
- Schmidt LS; Birt-Hogg-Dubé syndrome, Online Mendelian Inheritance in Man (OMIM)
- Toro JR; Birt-Hogg-Dubé Syndrome, Gene Reviews, September 2008

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