When a cutaneous lesion reveals an underlying disease...

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Case 1: clinical data

• 43 y old woman
• Multiple small white papules (1-4mm)
• Cheeks, nose, neck, chest
Case 1

- Clinical exam: nothing
- Anamnese: nothing
- 4 brothers and sisters without any pathology
- 2 sons alive and well (13 and 19 y old)
- Mother (59 Y old): bilateral renal carcinoma
Case 1: Histology of a papule

- Concentric perifollicular fibrosis, fibroblasts
- Proliferation of cords of epithelial cells emanating from the hair follicle
- Dilated hyperkeratotic infundibulum
Case 1

- Histological diagnosis: fibrofolliculoma
Case 1: pedunculated lesion of the chest

Histological diagnosis: fibrofolliculoma / acrochordon
Case 1: papule of the nose

Diagnosis: Trichodiscoma
Case 1: Diagnosis

Association of multiple pilar tumors and notion of renal carcinoma (mother)

*Birt-Hogg-Dubé syndrome*

Rare inherited disease (1977) predisposing to visceral tumors associated with cutaneous signs
Case 1: Birt-Hogg-Dubé syndrome
Cutaneous signs

- Multiple (10-100) firm **papules** of face, neck and/or trunk sometimes pseudo comedon
- Soft **pedonculated lesions** (acrochordons / skin tags) skin folds
- 20-40 y ;fast constant;
- **More than 10 skin lesions** (more with age)
- Minimum 1 lesion confirmed as a **Fibrofolliculoma**
Case 1: Birt-Hogg-Dube syndrome
Histological classification of cutaneous lesions

- Previously:
  - papules: Fibrofolliculoma (FF) or trichodiscoma
  - Pedonculated lesions: acrochordons

- Now:
  Trichodiscoma and acrochordon-like lesions considered as variants of FF

*benign proliferation of ectodermal and mesodermal component of pilar apparatus*
Case 1 : Birt-Hogg-Dube syndrome
FIBROFOLLICULOMA

- Predominance of epithelial component
- Papule:
- Pedonculated lesion
Case 1: Birt-Hogg-Dube syndrome
Histology of cutaneous lesions

- TRICHODISCOMA
- Papule
- Predominance of connective component
- CD34+
Case 1: Birt-Hogg-Dubé syndrome
Associated internal diseases

- **Pulmonary manifestations:**
  - Recurrent spontaneous pneumothorax
  - Lung cysts
  - Bullous emphysema
  Risk of spontaneous pneumothorax x 50

- **Renal tumors**: bilateral, multifocal
  - Hybrid tumors: chromophobe carcinoma/oncocytoma (67%), Chromophobe Carcinoma (23%), Oncocytoma (3%) papillary/clear cell carcinoma
  - Risk of renal tumors x 6.9
Case 1: Birt-Hogg-Dube syndrome
Other rarely associated disease

- Medullary thyroid cancer/thyroid adenoma
- Parotid oncocyctoma
- Multiple lipoma /angiolipoma
- Intestinal polyposis
- Neural tissue tumor
- Large connective tissue nevus
Case 1: Birt-Hogg-Dube syndrome
Genetic data

- Rare Autosomal dominant
- related to mutations of gene of folliculin on chromosome band 17p11.2
- tumor suppressive gene
- Depressed expression of Folliculin: protein expressed in follicules and pleura
- Variable phenotypic expression for the same genotype in the same family.
Case 1: Birt-Hogg-Dube syndrome

TO REMEMBER

• Recognize Cutaneous lesions
  – clinically multiple
  – histologically fibrofolliculoma with variants
  – Can precede renal tumors

• Clinical and radiological screening for
  – Renal tumors
  – Lung manifestations

• Clinical examination, interrogation, familial examination, genetic counseling