Do you know this syndrome?*
Você conhece esta síndrome? *

Roberto Rheingantz da Cunha Filho [1] Roberto Lopes Gervini [2] André Cartell [3]

CASE REPORT

Seventy-year-old male patient, who, from the third decade of life, had assymptomatic dome-shaped papullae, skin-colored or whitish, of non-uniform sizes, located at face, neck and upper trunk (Figure 1). In the axillae and dorsum there were light brown or skin-colored pedicled papullae – acrochordons (Figure 2). Morbid history: basocellular carcinomas treated by exeresis with safety margins. Smoker from 18 to 32 years of age, 10 cigarettes a day. History of "emphysema bubbles" and spontaneous pneumothorax 38 years ago. There were no other findings in history or clinical examination. Seven biopsies were performed, with the findings of two types of tumors at histopathological examination: fibrofolliculomas – a tumor with dilated follicle and proliferation of the epithelial wall, formation of strings of cells anastomosed in a soft stroma (Figure 3). The other tumor was a perifollicular fibroma – follicular epithelium within a prominent stroma (Figure 4). The axillary lesion was excised – histology of acrochordon.

Computarized tomography from the thyroid cleavage plan to the pelvic floor showed: cysts and multiple emphysema bubbles in both lungs, pleural calcification and a nodular lesion to the right – the side where pneumothorax is referred – with calcified content (Figure 5), and diverticular disease at the sigmoid. Laboratory tests without any particularities. Patient refused to undergo colonoscopy or contrast-

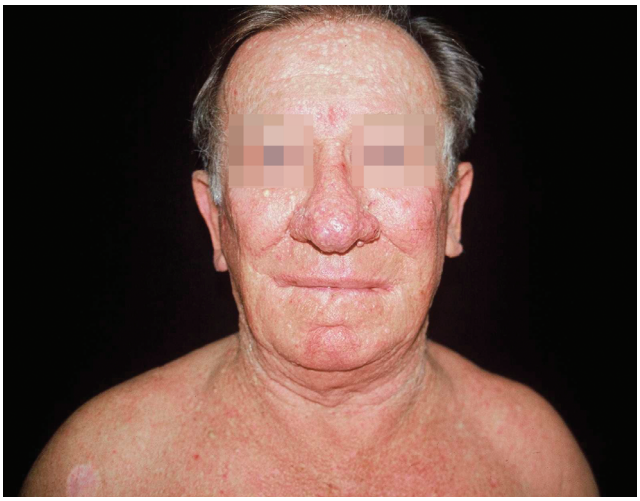

FIGURE 1: Multiple whitish or skin-colored papular lesions in the upper third of the body: head, neck and upper trunk.

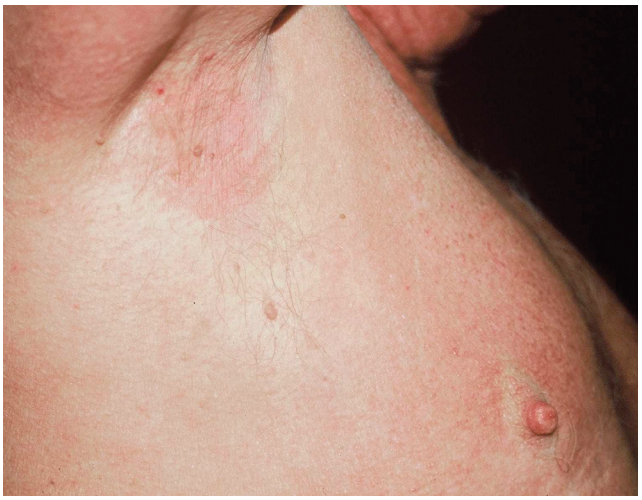

FIGURE 2: Presence of acrochordons in the axilllary region.

Received on January 16, 2004.
Approved by the Editorial Council and accepted for publication on March 2, 2005.
* Work carried out at the Dermatology Service at Universidade Federal do Rio Grande do Sul - UFRGS – Santa Casa de Porto Alegre Hospital Complex - Porto Alegre (RS), Brazil.

[1] Dermatologist. Master in Health and Behavior at Universidade Católica de Pelotas - UCPel - Pelotas - (RS), Brazil.
[2] Professor of Dermatology at Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.
[3] Professor of Pathology at Universidade Federal do Rio Grande do Sul - UFRGS - Porto Alegre (RS), Brazil.

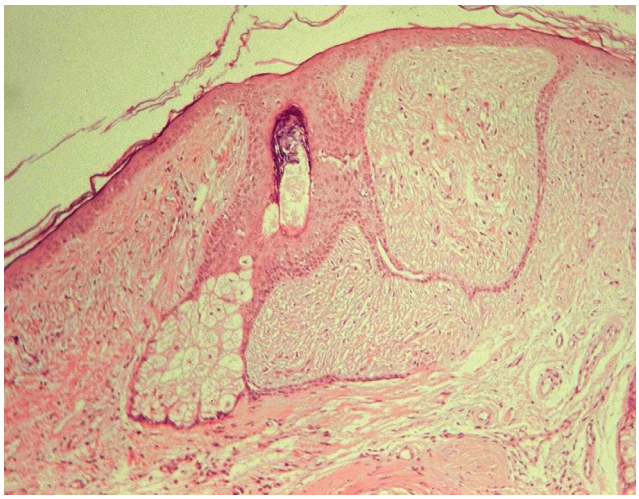

Figure 3: Hyperplastic, dilated follicle, with keratin plugging and epithelial wall proliferation, forming cell strings within a relatively well-delineated proliferation of soft connective tissue. The strings anastomose, and are also located by the sebaceous gland (HE, 100x)

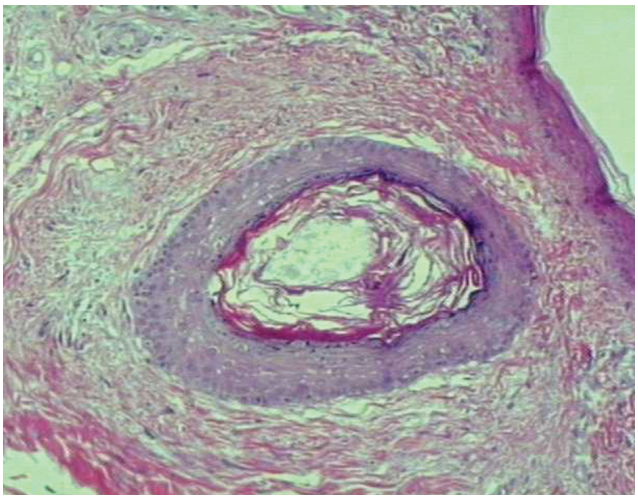

Figure 4: Perifollicular fibroma: dilated central follicle and concentric proliferation of collagen fibers (HE, 160x).

ed study of the intestine.

The patient reported that his father, three brothers and a sister also had similar lesions in the face, being the father and himself the most affected. He had 11 brothers and sisters, one had passed away because of disseminated non-pigmented skin tumors, which he could not specify. The affected sister was 80 and had similar lesions that had begun at 30 years of age (Figure 6). Anatomopathologic exams demonstrated perifollicular fibromas. There were no other clinical, laboratorial or imaging alterations. Management has been guidance and medical follow-up with emphasis on possible associated diseases.

COMMENTS

In 1977, dermatologist Birt, pathologist Hogg and intern physician Dubé described the syndrome that has their names, characterized by an eruption of face, neck and upper trunk tumors, with dominant autossomic inheritance.[1] Lesions are fibrofolliculomas, trichodiscomas and acrochodons. Throughout the last 28 years, new and more frequent associations, histopathological features and gene mutations have been discovered.

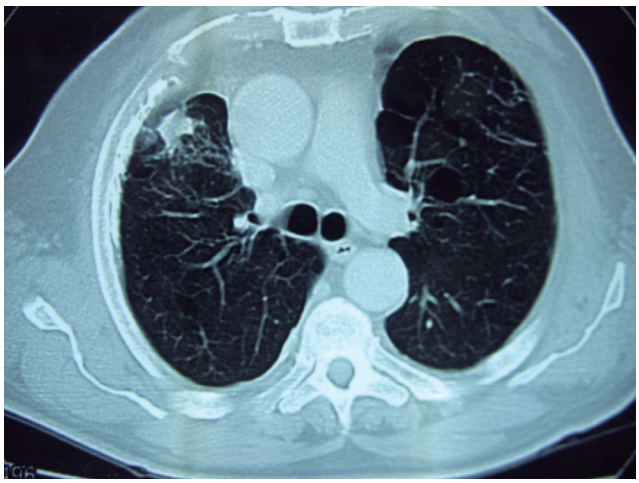

Figure 5: Tomography: cysts, emphysema bubbles and pleural thickening with rough residual calcification on the right lung.

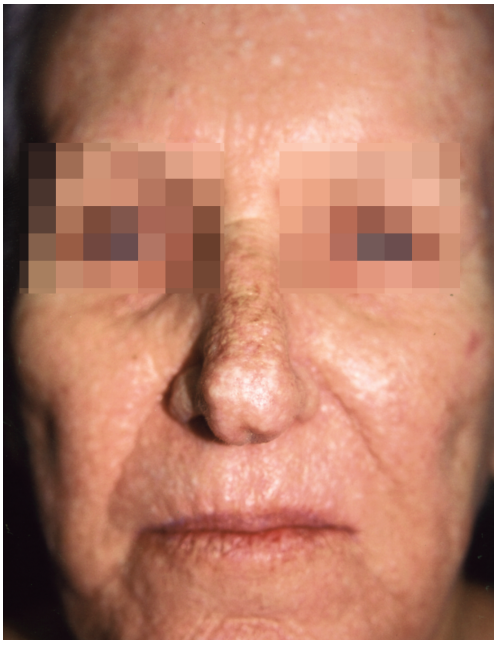

Figure 6: Patient 2: multiple skin-colored or whitish papulae on the face.

These three tumors of the perifollicular connective tissue are clinically undistinguishable, present as smooth, skin-colored or pink papulae and almost always are assymptomatic.[2] Regarding histological aspects, there are two considerations: fibrofolliculoma is the most frequent tumor, according to available evidence; there is still controversy as to the existence of these three types of tumors, for there is a possibility that they are only different interpretations for the same lesion, according to the adopted histological slicing. Schulz and Hartschuh[3] demonstrated that fibrofolliculomas and perifollicular fibromas represented the same lesion, albeit with different section plans. A horizontal section yields the interpretation of perifollicular fibroma, and a vertical section, fibrofolliculoma. Collins et al.[4] demonstrated, by means of immunohistochemical techniques, that fibrofolliculoma and trichodiscoma share the same origin, and that morphologic differences are subtle.

Multiple familial tricodiscomas,[5] multiple familial fibrofolliculomas,[6] familial perifollicular fibromas,[7] and the association of fibrofolliculoma, trichodiscoma and perifollicular fibroma8 have already been described.

Initial association with thyroid carcinoma has been described only in the original paper of Birt, Hogg and Dubé. More consistent associations are those with kidney neoplasia and spontaneous pneumothorax.[9,10] A recent study has indicated a relative risk of nine times for kidney neoplasia and up to 50 times for spontaneous pneumothorax, which was influenced by a more advanced age of the patient.[11] There are reports with association with type II multiple endocrine neoplasia,[9] basocellular carcinoma,[9] intestinal poliposis,[5,7,9] emphysema bubbles,[10] pulmonary cysts,[10] parotid oncocytoma,[12] connective tissue nevus, lipoma, angiolipoma and parotid adenoma.[13] The patient described here has association which are already described in the literature: pneumothorax, cysts and emphysema bubbles, and basocellular carcinoma.

Mutations on gene 17p11.2 have been identified. They result in the production of an abnormal protein, folliculin, found in the skin, lungs and kidneys. This may explain the observed alterations. [10]

Treatment can be done with YAG laser, CO_2 laser and electrocauterization, with irregular results.[14] Genetic counseling and clinical control of the parents are essential. ❑

REFERENCES

1. Birt AR, Hogg GR, Dubé WJ. Hereditary multiple fibrofolliculomas with tridiscomas and acrochordons. Arch Dermatol. 1977;113:1674-7.
2. Elder D, Elenitsas R, Jaworsky C, Johson B, editors. Lever´s Histopathology of the skin. 8th ed. Philadelphia: Lippicontt-Raven Publishers; 1997.
3. Schulz T, Harstchuh W. Birt Hogg Dubé Syndrome and Horntein Knickenberg Syndrome are the same. Different sectioning technique as the cause of different histology. J Cutan Pathol. 1999;26:55-61.
4. Collins GL, Somach S, Morgan MB. Histomorphogic and immunophenotypic analysis of fibrofolliculomas and trichodiscomas in Birt Hogg Dubé Syndrome and sporadic disease. J Cutan Pathol. 2002;29:529-33.
5. Le Guyadec T, Dufau JP, Pulain JF, Vaylet F, Grossin M, Lanternier G. Multiple trichodiscomas associated with colonic polyposis. Ann Dermatol Venereol. 1998;125:717-9.
6. Starink TM, Brownstein MH. Fibrofolliculoma: Solitary and multiple types. J Am Acad Dermatol. 1987;17:493-6.
7. Binet O, Robin J, Vicart M, Ventura G, Beltzer-Garelly E. Fibromes périfolliculaires polypose colique familiale pneumothorax spontanés familiaux. Ann Dermatol Venereol. 1986;113:928-30.
8. Korge BP, Smola H, Schulze HJ. Multiple perifollicular fibromas, fibrofolliculomas, trichodiscomas and association with scars of chorioretinitis and colon polyp (Hornstein-Birt-Hogg-Dubé-syndrome). Hautarzt. 1996; 47:129-31.
9. Toro JR, Glenn G, Duray P, Darling T, Weirich G, Zbar B, et al. Birt Hogg Dubé Syndrome. A novel marker of kidney neoplasia. Arch Dermatol. 1999;135:1195-202.
10. Schmidt LS, Warren MB, Nickerson ML, Weirich G, Matrosova V, Toro JR, et al. Birt Hogg Dubé Syndrome, a genodermatosis associated with spontaneous pneumothorax and Kidney neoplasia, maps to chromossome 17p11-2. Am J Hum Genet. 2001;69:876-82.
11. Zbar B, Alvord WG, Glenn G, Turner M, Pavlovich CP, Schmidt L, et al. Risk of renal and colonic neoplasms and spontaneous pneumothorax in the Birt-Hogg-Dubé syndrome. Cancer Epidemiol Biomarkers Prev. 2002;11:393-400.

12. Liu V, Kwan T, Page EH. Parotid oncocytoma in the Birt-Hogg-Dubé syndrome. J Am Acad Dermatol. 2000; 43: 1120-2.
13. Chung JY, Ramos-Caso FA, Beers B, Ford MJ, Flowers F. Multiple lipomas, angiolipomas and parathyroid adenomas in a patient with Birt Hogg Dubé Syndrome. Int J Dermatol. 1996;35:365-8.
14. Jacob CI, Dover JS. Birt-Hogg-Dubé syndrome: treatment of cutaneous manifestations with laser skin resurfacing. Arch Dermatol. 2001;137:98-9.

MAILING ADDRESS:
Roberto Rheingantz da Cunha Filho
Bela Pele Clínica Dermatológica®
Rua Dr Luiz de Freitas Melro, 395 / 604 – Ed Columbia Center - Centro
89010-310 Blumenau SC
Tel.: (47) 3035-4053
E-mail: robertodermatologista@yahoo.com.br