

Urticaria pigmentosa: Report of seven cases in three families

*Elias O. da-Silva^{1,2}, Aline C. Alexandrino¹, Valter Kozmhinsky^{3,4},
Valdir Bandeira⁴ and Andréa R. Duarte²*

ABSTRACT

We report seven cases of urticaria pigmentosa (UP) in three sibships belonging to separate families. The affected persons had normal parents. UP probably is an etiologically heterogeneous disorder. In familial cases, the usual pattern of inheritance is autosomal dominant but here UP appears to be an autosomal recessive entity.

INTRODUCTION

Urticaria pigmentosa (UP) is the cutaneous manifestation of mast cell disease. According to Gross and Hashimoto (1964), the first case was reported by Nettleship in 1869, but Anstey *et al.* (1991) emphasized that only in 1949 was it recognized as a systemic disease. The skin lesions vary in color from yellowish to tan or brown, and in shape from papule to macule, nodule and plaque, with or without vesiculous or bullous components (Klaus and Winkelmann, 1962; Caplan, 1964). Diagnosis can be made through Darier's sign (urtication of the lesion by mild trauma) and skin histological examination, which shows an increased number of mast cells. The course of the disease is usually of benign nature (Klaus and Winkelmann, 1962), but generalized involvement may occur and it can be fatal (McKusick, 1992).

The first familial cases were reported four decades ago (de Auster and Bonafina, 1953). In this paper, we report seven familial cases of UP, and discuss the probable genetic heterogeneity of the disease.

CLINICAL REPORTS

The pedigrees of the families are shown in Figure 1. In each case, the parents of the affected children were normal and nonconsanguineous. In family 3, child II-1 died on the first day of unknown cause and II-3 was an eight-month stillborn girl, who presented oligodactyly (right hand and foot).

The patients varied in age from five to 14 years. With the exception of the cutaneous manifestations, their physical examination was normal. The skin lesions were almost identical in all the cases, consisting of several hyperchromic (brown) macules and papules, elliptical or rounded in shape, about 5 mm in diameter, located mainly on the upper trunk and neck (Figure 2). Darier's sign was positive in all cases. The onset of the symptoms ranged from eight months to four years of age.

¹ Departamento de Genética, Universidade Federal de Pernambuco, Recife, PE, Brasil.

² Serviço de Genética Médica, Instituto Materno-Infantil de Pernambuco (IMIP), Rua dos Coelhos 300, Boa Vista, 50070-550 Recife, PE, Brasil. Send correspondence to E.O. da-S.

³ Serviço de Dermatologia, IMIP, Recife, PE, Brasil.

⁴ Departamento de Dermatologia, Universidade Estadual de Pernambuco, Recife, PE, Brasil.

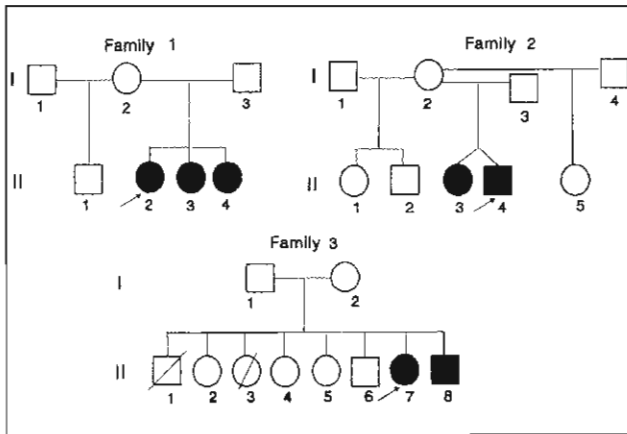


Figure 1 - Pedigrees of families showing probable autosomal recessive inheritance. Arrows point to the probands.

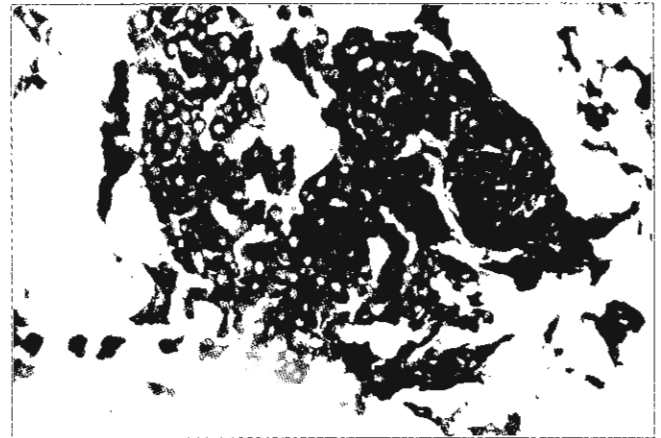


Figure 3 - Skin histopathological examination showing infiltration of cuboidal mast cells into the dermis (hematoxylin-eosin stain; magnification X40).



Figure 2 - Clinical appearance of the skin in two patients belonging to families 1 (top) and 2 (bottom).

The skin histopathological examination is shown in Figure 3. In all patients we found a dense infiltrate of mast cells together with metachromatic granulations. The mast cells were confluent in the papular lesions.

DISCUSSION

Familial cases of UP are rare (Fowler *et al.*, 1986). By 1970 there were over 600 patients reported with UP, of which 40 were familial cases (Selmanowitz and Orentreich, 1970). Now, at least 50 families are documented (Anstey *et al.*, 1991). There is a general impression that UP is an autosomal dominant disorder (Gross and Hashimoto, 1964; Shaw, 1968; Clark *et al.*, 1990; Winship, 1990; Oku *et al.*, 1990; Anstey *et al.*, 1991; McKusick, 1992). The families studied by Gross and Hashimoto (1964), Shaw (1968) and Clark *et al.* (1990) presented an autosomal dominant pattern of inheritance with reduced penetrance.

Klaus and Winkelmann (1962) studied 37 patients with UP and reported that the ages of onset ranged from birth to eight years, with half of the patients showing evidence of the disorder in the first six months of life. Oku *et al.* (1990) described an affected mother and her three children (two girls and one boy). In the children, the first manifestations began before six months of age, but the onset in the mother occurred only in the third decade. As in most reported cases, the first symptoms in our patients appeared in early childhood.

The parents of the patients were normal and nonconsanguineous. In spite of the absence of consanguinity, the inheritance pattern is probably

autosomal recessive, but it is not possible to exclude autosomal dominant inheritance with reduced penetrance. The hypothesis of recessivity is supported by the results of the test with Haldane's classical method (Haldane, 1932):

$$q = \frac{7-3}{13-3} = 0.40$$

$$\sigma^2 = \frac{(0.40)(0.60)}{10} = 0.024$$

$$\chi^2_{(1)} = \frac{(0.40-0.25)^2}{0.024} = 0.938; P=0.333$$

the corrected frequency of affected persons in the three sibships (0.40) does not deviate significantly from the expected frequency of 0.25. Affected siblings of both sexes, with normal parents, were reported by Bureau *et al.* and Oliver (cited by Bazex *et al.*, 1971), James and Eady (1981) and Fowler *et al.* (1986), but no information on consanguinity was available. These data suggest that UP is probably a genetically heterogeneous disease and, for the purpose of genetic counselling, a probable autosomal recessive form may be taken into consideration.

ACKNOWLEDGMENTS

This work was supported in part by FACEPE (APQ. 0168-2.02/94).

The authors thank the families for their collaboration.

RESUMO

Relatamos sete casos de urticária pigmentosa (UP) em três irmandades pertencentes a diferentes famílias. Os pais dos afetados eram normais. A UP é uma doença que provavelmente apresenta heterogeneidade etiológica. Nos casos familiares, o padrão de herança é geralmente o autossômico dominante mas, aqui, a UP parece ser uma entidade autossômica recessiva.

REFERENCES

Anstey, A., Lowe, D.G., Kirby, J.D. and Horton, M.A. (1991). Familial mastocytosis; a clinical, immunophenotypic, light and electron microscopic study. *Br. J. Derm.* 125: 583-587.

- Bazex, A., Dupré, A., Christol, B. and Andrieu, H. (1971). Les mastocytoses familiales. Présentation de deux observations. *Revue general. Interêt Nosologique. Ann. Derm. Syph.* 98: 241-260.
- Caplan, R.M. (1964). The natural course of urticaria pigmentosa. *Arch. Derm.* 87: 146-157.
- Clark, D.P., Buescher, L. and Harvey, A. (1990). Familial urticaria pigmentosa. *Arch. Intern. Med.* 150: 1742-1744.
- de Auster, M.J.T. and Bonafina, O.A. (1953). Urticaria pigmentaria en gemelos univitelinos. *Rev. Arg. Dermatosisif.* 37: 75-85.
- Fowler Jr., J.F., Parsley, W.M. and Cotter, P.C. (1986). Familial urticaria pigmentosa. *Arch. Derm.* 122: 80-81.
- Gross, B.G. and Hashimoto, K. (1964). Hereditary urticaria pigmentosa. *Arch. Derm.* 90: 401-403.
- Haldane, J.B.S. (1932). A method for investigating recessive characters in man. *J. Genet.* 25: 251-255.
- James, M.P. and Eady, R.A.J. (1981). Familial urticaria pigmentosa with giants mast cell granules. A clinical light and electron microscopic study. *Arch. Derm.* 117: 713-718.
- Klaus, S.N. and Winkelmann, R.K. (1962). Course of urticaria pigmentosa in children. *Arch. Derm.* 86: 116-117.
- McKusick, V.A. (1992). *Mendelian Inheritance in Man. Catalogs of Autosomal Dominant, Autosomal Recessive, and X-Linked Phenotypes.* The Johns Hopkins University Press, Baltimore, pp. 700.
- Oku, T., Hashizume, H., Yokote, R., Sano, T. and Yamada, M. (1990). The familial occurrence of bullous mastocytosis (diffuse cutaneous mastocytosis). *Arch. Derm.* 126: 1478-1484.
- Selmanowitz, V.J. and Orentreich, N. (1970). Mastocytosis: a clinical genetic evaluation. *J. Hered.* 61: 91-94.
- Shaw, J.M. (1968). Genetic aspects of urticaria pigmentosa. *Arch. Derm.* 97: 137-138.
- Winship, I.M. (1990). Urticaria pigmentosa. In: *Birth Defects Encyclopedia* (Buyse, M.L., ed.). Blackwell Scientific Publications, Dover, pp. 1737-1738.

(Received February 7, 1995)