CASE REPORT

FAMILIAL BENIGN CHRONIC PEMPHIGUS (HAILEY & HAILEY)

(A report of recurrent herpetiform dermatitis repens in a family)

By

T. K. MEHTA* L. MERQUIS** & S. M. MATHUR***

This disease is a rare familial chronic benign vesiculobullous eruption. Since the publication by Hailey & Hailey (1939)[1] more than 110 cases have been reported. In India, Rajam[2] reported a case in 1956, Kandhari & Gurmohan Singh[3] reported a case in a child in 1963 and subsequently Kandhari et al[4] in 1969 reported two cases in adults. Besides Ramarao[5] et al also repoted a case in an adult.

Lesions may first appear at puberty or be delayed to middle age. The disease runs an intermittent course, being much worse in the summer and improving or disappearing in winter. Sometimes, the patient may be free of lesions for several years. Recurrence usually involves the same sites. As a rule, the attacks are milder and less frequent as the patient grows older. Itching varies from mild to intense.

The primary lesion is a superficial vesicle which appears on normal skin. It grows to become a flaccid bulla, which soon ruptures leaving a raw denuded area.

The sites of predilection are the nape, sides of the neck, axillae and groins. Less frequently involved are the perianal region, umbilicus, scrotum, cubital and popliteal fossae, thighs, back and rarely the scalp. Keratoconjunctivitis involving the bulbar and palpebral conjunctiva as well as the cornea occurs and heals without scarring. In a few instances, involvement of the oral mucosa has been noted. In no instance does the general health of the patient seem affected.

There is usually a history of familial involvement among patients. It appears to be an inborn abnormality of the skin, transmitted as an irregular dominant trait. Clinically it resembles impetigo contagiosa. Older lesions suggest disseminate neurodermaitis. Rare instances may be confused with dermatitis herpetiformis, herpes simplex and dermatitis repens. Histologic sections may suggest keratosis follicularis or epidermolysis bullosa, but clinically the similarity is not striking.

Pathology–The most prominent feature is the formation of intraepidermal vesicles and bullae located chiefly in the midepidermis. The basal cell layer remains attached to the cutis. The roof of the vesicle or bullae is composed of 2–3 layers of epidermal cells covered by a hyperkeratotic stratum corneum. The lacunae are lined by cells in various stages of dyskeratosis. The prickle cells show a pronounced spongiosis. Corps ronds are not found and grains are rare. A moderate lymphocytic infiltration is seen in the cutis but the elastic tissue is present and normal[7].

Case Reports

Case 1. Name K. M. P. 36 H Age 36 years. Sex-Male. Attended the out-patient of the hospital with history of skin lesions of vesiculo-bullous nature for the last 12

*Hon. Chief, **Hon. Assist, ***Registrar.

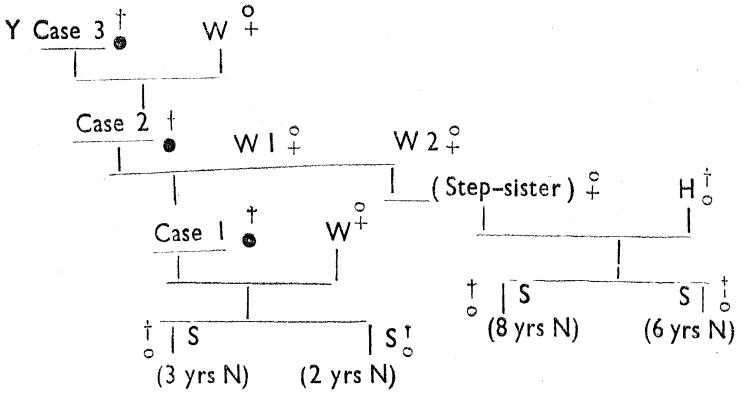
Dept. of Dermatology & Venereology, T. N. Medical College & Nair Hospital Bombay 8.

Received for publication on 18-9-69.

years. The lesions were situated over the forehead, sides of the neck, axillae, cubital fossae, sides of the abdomen and umbilical region and popliteal fossae. These lesions would subside in 1½ to 2 months with fresh recurrences, more in the summer months with relief in the cooler months. Itching moderate. Patient had tried various topical applications, but felt that the lesions healed spontaneously. History of similar lesions in his father. No brothers; one step-sister has no skin disease; she is married and has 2 sons aged 8 yrs, and 6 yrs, both normal. Patient is married and has 2 sons aged 8 yrs and 2 yrs both normal. H/O similar lesions in his grand-father.

Chart Showing the Family of Patient

(Showing involvement in three generations)



Local Examination–Vesicular lesions with erythematous base and a few bullae were seen over the forehead, sides of the neck (Photo 1) axillae, cubital fossae sides of the abdomen and umbilical region (Photo 2) and popiiteal fossa (Photo 3). A few of the lesions were pustular with central crust formation and peripheral flaccid bullae with sharply defined advancing margins. The central lesions showed maceration, crusting and gyrate patches of eczematization. Scattered small crusted lesions were seen. Nikolsky's sign was negative. The initial impression appeared to be one of an acute disseminated neurodermatitis.

Investigations: 1) Blood countW.B.C.–10,800/cmm. P–76 L–20 E–4 Hb, 9.5 Gms. Stool & Urine–N. A. D. Bl. V. D. R. L.–negative scrapings for fungus negative. 2) Culture and sensitivity testing with antibiotics from the Bullae material–Stap. aureus–resistant to sulpha, sensitive to broad spectrum antibiotics. 3) Skin biopsy–Section showed a supra basal separation with lacunae formation, villous elongated papillae lined by single layer of basal cells were seen protruding into the bullae The cells of the stratum malphigi showed loss of their inter, cellular bridges-acantholysis. The epidermis appeared like " dilapidated brick wall " (Photo 4).

Treatment: Patient was put on sulphonamides for 10 days with no response, Cortico steroids-20 mgm daily gradually reduced over 1½ month showed no appreciable change. Penicillin and other broad spectrum antibiotics were administered, with control of secondary infection and topical antibiotic and steroidal creams showed

reduction in the oozing and eczematous phase. However fresh crops of lesions would come up with subsequent gradual subsidence of lesions. The warmer months showed increased activity of the disease, with remissions in the cooler months. The patient has been under our observation for the last 2 years.

Case 2 Name M. P. Age 65 years Sex-Male. Father of Case I-was subsequently examined and investigated after Case I was diagnosed as a case of chronic benign familial pemphigus. Patient presented with vesiculo-bullous lesions over the sides of the abdomen, right cubital and right popliteal fossae.-for last 25 years. Itching was minimal. H/o recurrent attacks, more in summer, with the advancing of years, patient states that the severity of the disease has diminished. H/o similar lesions in his father i.e. grand father of Case I.

Local Examination: Vesiculo-bullous lesions over the sides of abdomen, right cubital fossa (photo 5) and over the right popliteal region (photo 6). A comparison of the lesions in the father and son, show severe lesions in Case I as compared to (Photo 7) Case 2. The lesions gave an initial appearence to be one of acute disseminated neurodermatitis.

Investigations: Idential to those of Case I. The skin biopsy showing an identical picture.

Discussion : Butterworth et al[6] believer, that familial chronic benign pemphigus is a diseases sui generis in no way related to Davier's disease or epidermolysis bullosa inspite of the confusing histology.

Familial chronic benign pemphigus histologically share features common with darier's disease and pemphigus. In all 3 diseases, seperation of the epidermis caused by acantholysis is seen, with upward proliferation of papillae, so called villi extending into the lacunae or bullae. Familial chronic benign pemphigus differs from Darier's disease by the lesser degree or even absence of dyskeratosis[7]. If dyskeratosis is absent, differention from pemphigus may be difficult or even impossible[7]. However two findings help in differentiation. First in familial chronic benign pemphigus acantholysis is more marked than in pemphigus, in pemphigus acantholysis is limited to the lower portion of the epidermis *(Jablonska & Chorzelski)*[7] Secondly in familial chronic benign pemphigus acantholytic cells show less evidence of degeneration than in pemphigus vulgaris, their nuclei appear normal, even showing mitotic activity *(Winer & Leeb, Herzberg,)*[7] and their cytoplasm does not appear condensed at the periphery. *Dupont*[7], concluds in pemphigus vulgaris cellular degeneration is the primary change, while in familial chronic benign pemphigus the basic change consists of loss of intercellular bridges due to premature aging of cells[7].

The nosologic position of the disease is uncertain, The presence of dyskeratotic change in some cases of familial chronic benign pemphigus has led some observers to regard this disease as a bullous variant of Darier's disease (Ellis, Finnerued & Szy-

manski, Winer & Leeb)[7] However, until more is known about the cause of the disease, it may be well to regard it as an independent entity. (Hailey & Hailey, Pinkus & Epstein, Dupont, Herzberg, Jablonskas & Chorzelski, Butterworth et al)[6],[7].

The disease usually manifests after puberty and most cases are young adults (Palmer & Perry 1962[8] Cullan[9] 1965), cases reported in the 6th (Jewell & Key [10] 1957), and 7th decade (Hurley & Cornelius[11] 1967) The first case reported by Rajam et al (1956) was a middleaged female and Kandharl et al reported 3 cases, one a boy of 2½ yrs, the other two with a late onset of the disease, being 49 yrs. and 52 years respectively, with no familial involvement. Ramarao et al reported a male case of 35 yrs. with no familial involvement.

Our two cases, father and son, showed manifestations of familial chronic benign pemphigus, one at the age of 40 yrs and the other at an earlier age of 24 yrs with a possibility in the grand father. These patients clinically resembled very much acute disseminated neurodermatitis with lesions in the cubital and popliteal fossae, hence the importance of recognising this entity as possibly, though 110 cases have been recorded, many others may have passed undiagnosed. The typical histological appearence of the epidermis "dilapidated brick wall" appearence (Haber & Russell)[7] is however diagnostic.

Case 2 showed a milder form of the disease as opposed to *Case*[1], this is in conformity with the behaviour of the disease, in that the severity is reduced with the advance of age. No ocular or mucous membrane lesions were seen in both cases.

The absense of family history in some patients of benign familial pemphigus is explained on the basis of it being an autosomal dominant trait with in complete (Cram et al[12] 1966) Patients without family history have been reported by Rajam etal penetrance (1956) Jewel & Key (1963), Hurley and Cornelius (1967), Kandhari etal (1969) and Ramarao etal (1969). The two cases presented by us were in father and son.

The disease, though inhereted, is precipitated by various factors. Lowenthal[13] (1959) demonstrated acantholysis after inoculation with staph, aureus, Burns et al[14] (1967) produced the same by topical application of candida albicans. Chorzelks unrelated (1962)[15] induced typical lesions also by freezing, mild burns, chemical insults and allergy to adhesive tape, while Cram et al (1967) could induce acantholysis by ultraviolet. These facts imply that diverse forms of trauma could precipitate acantholysis in a genetically predisposed individual.

Summary (1) Two cases of familial chronic benign pemphigus are reported in a family, with a possiblity of the grand father also having been a similar case.

(2) Case 1 showed earlier onset as opposed to Case 2. while the severity was less in Case 2 as compared to Casel[1].

(3) The initial suspicion of disseminated neurodermatitis in these cases was proved wrong by the skin biopsy, which was diagnostic of familial benign chronic pemphigus–"dilapidated brick well" appearence.

Acknowledgement

Our thanks are due to Dr. T. H. Rindani, Dean Topiwala National Medical College and B. Y. L. Nair Hospital, Bombay. for his kind permission to utilise the Hospital record for publication.

REFERENCE

1. Hailey H and Hailey H : Familial benign chronic pemphigus. Arch. Dermatology & Syphilogy 39:679, 1939.

2. Rajam R. V., Rangiah P. N., Thambiah, A. S. and Anguli V. C.—Chronic benign pemphigus of Hailey and Hailey-Indi J. of Derm & Ven. 22:71, 1956.

3. Kandhari K.C. & Gurmohan Singh; Chronic benign pemphigus of Hailey and Hailey in an Indian child. Brit. J. Derm. 75: 212, 1963.

4. Kandhari K. C., Butani L. K., Hajini G. H. and Malhotra Y. K. : Familial Benign chronic pemphigus of Hailey & Hailey. Ind. J. of Derm & Ven. Vol, 35 No. 5 235-237, 1969.

5. Ramarao K. M, Siddappa K., & Patil R. S. : Chronic benign pemphigus of Hailey & Hailey. Ind. J. Derm. & Ven. Vol. 35. No. 1. 18-20, 1969.

6. T. Butterworth, & L. Strean : Clinical genodermatology. Williams & Wilking Co. Baltimore 1962

7. Lever. W. F. : Histopathology of the Skin, Philadephia, London. Montreal. J. B. Lippincott Company, 1961.

8. Palmer, D. D. & Perry H O. : Ben gn familial chronic pemphigus. Acta Dermato-venereol. 39 : 280, 1959.

9. Cullen D. R. : Genetic features of familial benign pemphigus Brit. J. Derm. 77:20, 1965.

10. Jewell, R. W. & Key M, M. Familial benign chronic pemphigus in negroes A M. Arch. Dermat. 75 : 715, 1957.

11. Hurley H. T. & Cornelius C. Familial benign chronic pemphigus. Arch Dermat. 95:235, 1967.

12. Cram. D. L. Muller S. A. & Winkleamn B. K. : Ultra-violet induced acantholysis in familial benign chronic pemphigus. Arch. Derm. 96;636, 1967.

13. Loewenthal L. J. A. Familial benign chronic pemphigus, A. M. A Arch. Dermat. 80: 318, 1959.

14. Burns, R. A. : Reed, W B. Swatek F. E & Omleczynskic, D. T. Familial benign chronic Pemphigus, Arch. Dermat. 96, S54, 1967.

15. Chorzelski T. : Experimentally induced acantholysis in Hailey's benign pemphigus. Dermatologica 124: 21, 1962.

16. Gougerot H : Ann. Dermat. & Syph. 10: 361. 1950. Quoted by Rasschou Nielsen and Raynann 19.9.

17. Rassehou-Nielsen and Raymann F. Familial bengn chronic pemphigus. Acta Dermat. Venereol, 39. 280. 1959.

18. Lyles. T. W; Knox J. M. & Richardson J. B. Atypical features in familial benign chronic pemphigus. A. M. A. Arch. Dermat. 78: 446, 1958.