

Grover's Disease Associated with Waldenström's Macroglobulinemia and Neutrophilic Dermatitis

Sir,

We report herein an original case of transient acantholytic dermatosis (Grover's disease) remarkable by its association with both Waldenström's macroglobulinemia and neutrophilic dermatosis.

CASE REPORT

A 52-year-old man who had had Waldenström's disease for 5 years presented to our department with clinical manifestations of hyperviscosity syndrome including headaches and paresthesias of the extremities. All treatments for the haemopathy had been withdrawn 6 months earlier because of drug resistance. Besides splenomegaly, physical examination showed 2 types of cutaneous lesions: non-follicular and papular lesions, non-pruriginous, some slightly crusted, localized at the upper part of the trunk that developed during previous weeks (Fig. 1) and purplish isolated papules on the lower limbs surrounded by an erythematous halo (Fig. 2), which had appeared recently together with fever.

Several skin biopsy specimens were taken. Histological examination of the skin biopsy specimens from the lesions on the back showed focal acantholysis associated with "corps ronds" compatible with a diagnosis of transient acantholytic dermatosis (TAD). Direct immunofluorescence was negative. Biopsy specimens of skin lesions



Fig. 1. Papules on the upper part of the trunk.



Fig. 2. Purplish papule on the lower limb, bordered by an erythematous halo.

of the leg showed a dense dermal and epidermal neutrophilic infiltrate without acantholysis or vasculitis suggestive of a neutrophilic dermatosis. Bacterial cultures performed on both lesions were sterile. Blood investigations showed pancytopenia (WBC: 1500/mm³, haemoglobin level: 8.1 g/dl, platelet count: 29000/mm³), elevated sedimentation rate (150/h), high level of total serum proteins (107 g/l) and of gamma globulins (60 g/l). IgA and IgG levels were normal. Circulating anti-intercellular substance antibodies were positive (titre: 1/640) as anti-smooth muscle antibodies (titre: 1/1280, identified as anti-actine antibodies). A bone marrow biopsy showed a high-grade polymorphous lymphoplasmocytic lymphoma. The patient died a few weeks later despite a treatment including chemotherapy (cyclophosphamide, adriamycin, prednisone) and plasmapheresis. During that period, the cutaneous lesions remained unchanged.

DISCUSSION

Since the first description by Grover in 1970, 545 cases have been reported (1–3). TAD is characterized by a polymorphous eruption with papules or papulovesicles at the upper part of the trunk, which are usually pruriginous. It mostly affects white men over the age of 40 years and seems to be favoured by exposure to the sun, sweating and fever (4). Some cases have been induced by radiotherapy (5) or human interleukin 4 (6). Histologically, there is a focal acantholysis that may mimic Darier's disease, as in our observation. TAD may be associated with other dermatosis, particularly with eczema and other malignancies (3, 7). To date, no case of TAD associated with Waldenström's disease or neutrophilic dermatosis has been reported. Furthermore, the simultaneous occurrence of pyoderma gangrenosum and Waldenström's macroglobulinemia is quite uncommon (8). Neutrophilic dermatoses are often associated with paraproteinemia, mostly of the IgA type. Pyoderma gangrenosum has been observed frequently with hematologic malignancy and inflammatory bowel disease. In the literature, there is only 1 case similar to our observation, exhibiting an association of TAD, pyoderma gangrenosum and IgA paraproteinemia (9). The link between these 3 diseases may be fortuitous as we report herein only the second case since 1980. The high level of anti-intercellular substance antibodies was probably the consequence of Waldenström's disease. We suppose this IgM paraproteinemia had a specificity against intercellular substance. Furthermore, Bystrin reported 3 positive indirect immunofluorescence among 11 cases of TAD (10) and these antibodies are not specific for pemphigus. In our case, histological findings and negative direct immunofluorescence permitted us to exclude a diagnosis of pemphigus. Neutrophilic infiltrate, negative bacterial cultures and direct immunofluorescence were suggestive of neutrophilic dermatosis. Because of the clinical aspect of the lesion on the leg and the localization of the infiltrate, we suppose this neutrophilic dermatosis probably corresponded with a pyoderma gangrenosum. Some authors consider Grover's disease may be a paraneoplastic syndrome (7), though TAD and malignancies occurred together more often in elderly patients. They recommend a complete clinical examination of all patients with TAD (2). In our observation, TAD occurred at the time of a worsening of the Waldenström's disease (drug

resistance, high grade of malignancy), suggesting its possible paraneoplastic nature even if all the criteria were not gathered. We therefore recommend that a complete physical examination be carried out, in addition to blood count, sedimentation rate and serum electrophoresis, in the search for haemopathy or dysglobulinemia.

REFERENCES

1. Grover RW. Transient acantholytic dermatosis. *Arch Dermatol* 1970; 101: 426–434.
2. Maghraoui S, Crickx B, Grossin M, Belaïch S. Dermatose acantholytique transitoire (maladie de Grover). *Ann Dermatol Venereol* 1995; 122: 801–806.
3. Grover RW, Rosenbaum R. The association of transient acantholytic dermatosis with other skin diseases. *J Am Acad Dermatol* 1984; 11: 253–256.
4. Horn TD, Groleau GE. Transient acantholytic dermatosis in immunocompromised febrile patients with cancer. *Arch Dermatol* 1987; 123: 238–240.
5. Pasolini G, Lonati A, Manganoni AM, De Panfilis G. Grover's like disease associated with radiotherapy. *Eur J Dermatol* 1992; 2: 91–92.
6. Malher SJ, De Villez R, Pulitzer DR. Transient acantholytic dermatosis induced by recombinant human interleukin 4. *J Am Acad Dermatol* 1993; 29: 206–209.
7. Schneider I, Mojzes J. La maladie de Grover: une maladie faiblement corrélée à des tumeurs malignes viscérales. *Ann Dermatol Venereol* 1993; 120: 65–71.
8. Chevrant-Breton J, Logeais B, Pibouin M. Pyoderma gangrenosum (pyodermite phagédénique). *Ann Dermatol Venereol* 1989; 116: 577–589.
9. Andersen BL. Pyoderma gangrenosum associated with transient acantholytic dermatosis and paraproteinemia. *Acta Derm Venereol* 1981; 61: 77–79.
10. Bystrin JC. Immunofluorescence studies in transient acantholytic dermatosis. *Am J Dermatopath* 1979; 1: 325–327.

Accepted October 13, 1999.

M Roger^{1,2}, C Valence³, J.M Bressieux¹, P Bernard⁴ and A Fur²
 Departments of , ¹Dermatology, ²Internal Medicine, ³Histopathology, Centre Hospitalier des Hauts Clos, 101 Avenue Anatole France, F-10003, Troyes and ⁴Department of Dermatology, Centre Hospitalier Robert Debré, Reims, France.

BOOK REVIEW

Epidermolysis Bullosa: Clinical, Epidemiologic and Laboratory Advances and the Findings of the National Epidermolysis Bullosa Registry by J.-D. Fine, E.A. Bauer, J. McGuire and A. Moshell. Hardcover. 490 pages. ISBN 0-8018-6024-5. Price \$90. John Hopkins University Press. 1999.

The rapidly advancing knowledge about epidermolysis bullosa (EB) means that there is a constant need for up-dated comprehensive reviews on the subject. The new textbook on EB, edited and co-authored by some of the leading scientists and physicians in the field of EB management in the States, is somewhat different compared to previous ones. It gives both an overview of recent advances in EB research and a detailed account for the vast amount of data collected over the last 10 years in the US national EB registry (NEBR) headed by one of the editors, Dr. Jo-David Fine, University of North Carolina, Chapel Hill. The registry comprises nearly 2600 patients suffering from one of almost 20 different forms of EB, which are traditionally subdivided into three main groups: EB simplex, junctional EB and dystrophic EB. To date, the predominating diagnosis in the registry is non-surprisingly EB simplex accounting for nearly 1200 of registered patients, a figure which probably underestimates the true, since many patients with the Weber-Cockayne subtype have mild symptoms and are unlikely ever to be correctly diagnosed. The more severe forms of EB, dystrophic and junctional EB, accounted for 30 and 8%, respectively, of the registered patients.

The book starts with an historical description and makes a clinical classification of EB that is somewhat difficult to read in the absence of recent data concerning the underlying molecular defects of the various forms of EB. However, this is well compensated in later chapters of the book giving a very detailed and up-to-date picture of the molecular pathology of EB. These chapters are written by some of the world leading scientists in skin biology, viz, Drs E. Fuchs, J. Uitto and A. Christiano.

Much space is devoted to detailed descriptions of the demography, symptomatology and disease-associations of the various forms of EB as derived from the NEBR data base. Some figures in the numerous Tables are of direct use for a doctor handling EB patients. For example, it is important to know that 80% of patients with recessive dystrophic EB will develop squamous cell carcinoma before the age of 60 and 75% of the patients with junctional EB will have at least one episode of sepsis during a lifetime.

Although, there are no color pictures in the book, many good black-and-whites illustrate the typical skin and mucousal signs in EB. By and large the book is well written and interesting to read. For someone who wants to get a first grasp of EB and its many facets the book is probably not ideal. But for departments specialized in the care of EB patients, it will be a very valuable addition to the literature.

The Editor-in-Chief