LETTERS TO THE EDITOR

Cutaneous Paraneoplastic Syndromes and Genodermatoses with Malignant Potential

Sir,

The review article by Politi et al. (1) on mucosal and skin conditions that may be associated with cancer summarizes the salient features of several of the cutaneous paraneoplastic syndromes. The authors also discuss some of the genodermatoses with malignant potential: keratosis palmaris et plantaris (Howell-Evans syndrome or tylosis), Cowden’s disease, nevoid basal cell carcinoma syndrome, Gardner’s syndrome, mucosal neuroma syndrome and Peutz-Jeghers syndrome. The importance of differentiating these two groups of mucocutaneous disorders is more than merely semantics.

Cutaneous paraneoplastic syndromes are a group of conditions in which the mucosal or skin lesions may precede, occur concurrent with, or follow the diagnosis of an associated malignancy; hence, they may be the initial manifestation of an unsuspected neoplasm in a previously cancer-free individual or herald the recurrence of malignancy in an oncology patient. Individuals with these disorders are not genetically predisposed to develop neoplasms and the cancer-related appearance of these syndromes does not occur in other family members. Although the pathogenesis for many of these syndromes remains to be determined, the release or the induction of cytokines by the tumor has been postulated to have an etiologic role in these conditions (2, 3).

Genodermatoses with malignant potential are inherited disorders with dermatologic manifestations in which disease-associated malignancies may subsequently develop. An individual in whom one of these conditions is diagnosed requires an initial evaluation and periodic follow-up examinations for cancer. Also, since these disorders are familial, screening of the patient’s family for the genodermatosis and genetic counseling should be performed (4, 5).

In conclusion, disease-associated internal malignancies occur in both patients with cutaneous paraneoplastic syndromes and genodermatoses with malignant potential. Whereas individuals with either of these conditions should receive an appropriate work-up for cancer, evaluation of the family members is only necessary for those patients who have a genodermatosis with malignant potential. Therefore, differentiating these two groups of cancer-related conditions is essential.

REFERENCES


Received October 20, 1993.

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In response to the Letter by Cohen

We appreciate the comments of Dr. Cohen in regard to our review article “Cutaneous Paraneoplastic Syndromes” (1).

Concerning the differentiation between cutaneous paraneoplastic syndromes and cancer-associated genodermatoses, we would like to emphasize the following:

Paraneoplastic syndromes are defined as cancer-associated phenomena. This means that although they are not a direct constituent of the malignancy or metastases, they appear associated with cancer in a frequency that makes their presence significant. Hence, cancer-associated genodermatoses, even if they are to be treated as a special group both clinically and theoretically, still meet the criteria of paraneoplastic syndromes.

In practice, the finding of a cutaneous paraneoplastic marker and the diagnosis of such genodermatoses herald the possible association of an underlying neoplasia, even if specific clinical steps should be taken, e.g. genetic counseling and family screening.

Unfortunately, the classification of paraneoplastic conditions still poses significant problems, especially since many of these conditions also appear without any underlying malignancy or are not specific enough and therefore associated with a wide range of cancer types.

Furthermore, the pathogenesis of many of these syndromes is still obscure, although several mechanisms have been proposed for explaining these syndromes. These include the activity of various cytokines, oncogenes, hormones, the association of bacterial superantigens that may directly bind with the major histocompatibility complex (MHC) receptors and tumor-induced depletion of specific substances (1).

Finally, recent studies point to an inherited susceptibility to
some cancer types, associated with the inheritance of a gene conferring high risk for cancer.

For example, 5–10% of breast cancer (2, 3) and ovarian cancer (4) cases can now be attributed to such a pattern of inheritance.

Hence, it is likely that such genetic links will be found in the future in some patients with cutaneous paraneoplastic syndromes, which are present are not yet genetically determined. We conclude that cancer-associated genodermatoses are to be classified as paraneoplastic syndromes. Furthermore, this group should be defined as a subclass of cutaneous paraneoplastic syndromes, which indeed it is.

REFERENCES

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Milia during Treatment of Mycosis Fungoides: Follicular Mycosis Fungoides?

Sir,

We read with interest the letter from Chang et al., reporting the occurrence of multiple milia on the head of a patient after treatment of mycosis fungoides (MF) with acitretin (1). The authors question whether milia could be due to an unexpected side-effect of acitretin treatment or to MF itself. It is of interest to note that they describe milia as being connected to hair follicles at clinical examination. Although no histological picture is shown, they state that the follicular origin of milia had been confirmed histologically. They do not specify, however, if the follicles were surrounded or not by a lymphocytic infiltrate. We think that their patient had what we call “follicular MF”, a clinical and histological variant of MF.

We recently reported two cases of MF with marked, pleomorphic follicular manifestations (2). Follicular hyperkeratosis, comedo-like lesions, acquired epidermal cysts and patchy alopecia developed simultaneously or successively in various locations in both patients. Histopathological and immunohistochemical studies showed atypical CD4+ T lymphocytes infiltrating the follicles, without follicular mucinosis. Focal expression of ICAM-1 was observed within the cyst walls. These findings suggested that the follicular lesions were specific and represent a distinct clinical and histological form of mycosis fungoides. This variant probably accounts for cases of mycosis fungoides with clinically suspected alopecia mucinosa, in which follicular mucinosis cannot be histologically proved. Such cases have already been reported in the literature (for review see ref. 2) and should be grouped under the name follicular MF. The lesions usually predominate on the head, probably because it is a region where a great number of hair follicles is found. As to the case reported by Chang et al. we would be cautious in the interpretation of these clinical lesions, since they could be markers of the development of MF rather than sequelae observed after remission. Biopsies with immunophenotyping of the follicular infiltrate should be carried out. If serial examination does not show any specific involvement, we would interpret these milia as sequelae of follicular MF rather than a side-effect of acitretin treatment.

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Received October 13, 1992.

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