Small Plaque (Digitate) Parapsoriasis Is an 'Abortive Cutaneous T-Cell Lymphoma' and Is Not Mycosis Fungoides

ABOUT 100 YEARS ago, Unna et al[1] described two cases of so-called parakeratosis variegata. Brocq,[2] 7 years later, saw one of Unna and colleagues' cases, as well as some similar cases, and described it as "érythrodermies pityriasiques en plaques disséminées."

In a 1902 article, Brocq[3] reviewed the German, French, and American literature and reported 10 cases of his own, for which he created the term *parapsoriasis* because of their similarities to psoriasis, seborrheic eczema, and lichen ("paralichen"[3]).

Brocq[3] describes three major subgroups, the common features of which are (1) the long duration of the disease; (2) no reduction of general health; (3) absence of pruritus; (4) superficial localization of the process involving the upper dermis and the epidermis, leading to erythema and pityriasiform scaling; (5) resistance to topical treatment modalities; and (6) histologically round cellular infiltrate around dilated blood vessels of the papillary dermis, edema in the papillary dermis, spots of spongiosis, and parakeratosis. Based mainly on clinical manifestations, Brocq[3] differentiates the following subgroups:

1. "Parapsoriasis en gouttes," showing small papules and papulosquamous lesions resembling papular syphilis or guttate psoriasis. Today, this form is usually referred to as *pityriasis lichenoides chronica* (synonymous with parapsoriasis guttata of Jadassohn and Juliusberg). Pityriasis lichenoides et varioliformis acuta (Mucha-Habermann disease) and lymphomatoid papulosis are more acute and proliferative variants of this form.

2. "Parapsoriasis lichenoide," consisting of a network of "pseudopapular"[3] lesions with atrophy exhibiting a poikilodermic appearance. Unna and colleagues'[1] cases of parakeratosis variegata[1] and the poikilodermia vasculare atrophicans of Jacobi[4] have to be included in this group.

3. "Parapsoriais en plaques," formerly referred to by Brocq[2] as "érythrodermies pityriasiques en plaques disséminées," is characterized by round or oval well-circumscribed macules ("plaques"[2]), the diameter of which does not exceed 2 to 6 cm. Today, this variant, which is the subject of an article by Haeffner et al[5] in this issue of the ARCHIVES, is referred to as *Brocq's disease; parapsoriasis, small-patch (digitiform) type; digitate dermatosis; xanthoerythroderma perstans;* and *chronic superficial dermatitis.*[6]

Several other classifications of parapsoriasis have been described,[7-10] and various aspects of the topic have been critically reviewed[11-13] and discussed.[14]

A classification needs to be simple and reproducible and should fulfill clinical requirements by dissecting various nosologic entities that have to be differentiated with respect to differences in clinical manifestation, biological behavior, and routine diagnostic techniques: histopathologic features, staging procedures, and laboratory findings, as well as treatment approaches, follow-up requirements, and others.

Each entity is characterized by a spectrum of criteria typical for the disease. The presence of one criterion in two diseases does not prove these conditions to be nosologically identical.

Brocq's[2] group of parapsoriasis en gouttes no longer should be referred to as *parapsoriasis.* The two remaining forms of parapsoriasis exhibit clear-cut differences in clinical manifestations that are usually not reflected in the histologic features:

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1. Large plaque parapsoriasis with the macular form of parakeratosis variegata of Unna et al,[1] with poikilodermia vasculare atrophicans of Jacobi.[4] These cases most probably are premycotic stages of cutaneous T-cell lymphoma (CTCL) and may be referred to as such.

2. Small plaque (digitate) parapsoriasis (SPP), referred to as *parapsoriasis en plaque*[3] or as *érythrodermie pityriasique en plaque disséminée*[2] by Brocq. Other conditions that do not fulfill the specific clinical and biological criteria of this nosologic entity should not be included. It has to be made clear that this condition is not identical with the historical term *parapsoriasis en gouttes*[2] (also known as *pityriasis lichenoides*), as implicated in the title of one of the recent aricles on this topic.[15]

Haeffner et al[5] have analyzed the differentiation and clonality of lesional lymphocytes in SPP using immunohistologic and molecular biological methods and have come to the conclusion that SPP is a clinically indolent, histopathologically nonspecific, predominantly $CD4^+$ T-cell–mediated disease that, at least in some cases, contains a dominant T-cell clone. They ask whether dominant T-cell clones in some cases of SPP can ever be the direct precursors of overt CTCL.

None of the five cases that Haeffner and colleagues studied and followed up over periods ranging from 3 months to 18 years showed evidence of deterioration of skin lesions or development toward overt CTCL. However, this does not exclude the possibility that SPP is a potential precursor of CTCL that is kept in a biologically silent stage between control and derailment of lymphocyte turnover and/or apoptosis.

Some Differences Between Typical Features of Small Plaque Parapsoriasis (SPP) and Mycosis Fungoides (MF)

	SPP	MF
Clinical features of skin lesions	<6 cm in diameter, no progression	Often >6 cm in diameter, progression
Extracutaneous spread	Never occurs	Occurs frequently
Staging procedures	Not necessary	Mandatory
Histologic features	No edema, no plasma cells, no eosinophils	Edema, plasma cells, and eosinophils regularly found (T-helper-2–cytokine pattern)
Clonal T-cell receptor gene rearrangement	Usually absent	Usually present
Treatment	Topical	Topical and/or systemic
Potential transformation into high-grade malignant lymphoma	Never	Frequently seen in late phases
Life threatening	Never	Typical feature
Combination with other lymphomas	Not reported	Occurs

Some questions that should be considered follow:

1. Does clonality necessarily reflect neoplasia? Obviously not, since clonal T-cell populations also have been demonstrated in pityriasis lichenoides et varioliformis acuta (Mucha-Habermann disease),[16] which is a self-limiting inflammatory process, and in some eczematous processes (eg, "clonal dermatitis"[17]). On the other hand, clonality of T cells is inconsistently detectable in some cases of SPP.

2. Is SPP mycosis fungoides (MF)? That it is has been stated in retrospective studies of 216 specimens removed from 210 patients.[15] The long list of clinical diagnoses (12) listed on the biopsy request slips indicates heterogeneity of the material sent for histologic evaluation. The size of the lesions, which is a distinct crucial criterion of SPP (diameter not exceeding 5 to 6 cm), unfortunately is not reported. On the other hand, an early lesion in an otherwise clear-cut patch of plaque-stage MF may have the size of a lesion in SPP. In 23 (27%) of 84 specimens of guttate parapsoriasis and digitate dermatosis, the diagnosis of MF was made. This diagnosis was based on histologic criteria alone, which are known not to be sufficiently reliable in the early stages of MF,[18] and was not confirmed by clinical follow-up information.[15] In its early stage, MF, to some extent, may simulate SPP, which exhibits distinct small patches (plaques) as an unmistakable hallmark. There is no report that convincingly demonstrates the transformation of clear-cut SPP into MF or any other form of CTCL.

Phenotypically, the infiltrate in SPP is composed of $CD4^+$ T cells intermingled with a few $CD8^+$ cells and cannot be differentiated from eczematous actions. Early lesions of CTCL do not show the immunophenotypic aberrancies seen in the advanced stages but are indistinguishable from benign inflammatory cutaneous conditions by immunophenotypic criteria.[19]

Cytoanalytic investigations, including DNA cytometric and morphometric studies (nuclear contour index), also have provided some differences between parapsoriasis and MF.[20]

3. Is there clinical evidence of SPP transforming into CTCL? In the literature, figures reported on incidences of transformation of SPP into CTCL range from 0% (N=180 patients; follow-up, 8 to 20 years)[8] to 46% (N=13 patients; follow-up, 8 to 25 years).[21]

Among 84 of our own cases, which were followed up for 5 to 35 years, potential manifestation of CTCL was seen in two cases; however, on retrospective analysis, these two cases initially showed poikilodermatous features and probably were CTCL from the very beginning, simulating SPP. The degree of epidermotropism of lymphocytes seen in these cases ranged from weak (one to 10 lymphocytes per 2-mm length of epidermis) to strong (>50 lymphocytes per 2-mm length of epidermis). There was no correlation between degree of epidermotropism and clinical features on the natural course of the disease (H. T. Thailmair, unpublished data, 1978).

In conclusion, there is not sufficiently convincing evidence that SPP can transform into MF, or even that it is MF, since the biological behavior of SPP is completely different from MF.

4. What is SPP? Besides the male germinative system, the hematopoietic and the epithelial systems are the only cell systems with permanent turnover and renewing. Homing of a clonal T-cell population into the skin in SPP may result from an early step in cancer promotion. There is no mitosis or increased cell proliferation.

Small plaque parapsoriasis is not simple reactive inflammation, since skin lesions—which are different from inflammatory reactions such as secondary syphilis, eczema, and psoriasis—do not show spontaneous regression but do persist. Treatment with nonaggressive modalities (eg, topical steroids and oral psoralen with UV-A radiation therapy) may lead to temporary remission and control of the disease; however, skin lesions usually recur after cessation of therapy, and clonality of the lymphoid cell population can be demonstrated in some cases of SPP.[5]

On the other hand, SPP is not MF: MF is a nosologic defined entity that progressively develops through stages reflected in changes of the clinical as well as the histologic features, and systemic spread can be demonstrated even if routine staging procedures do not yet show extracutaneous involvement.[22]

Small plaque parapsoriasis is a process in which an initial DNA defect is followed by weak promotional stimuli leading to the generation of a T-cell clone, which homes exclusively to the skin. However, this cell clone does not undergo the further mutations that are necessary for the development of overt CTCL: it is the dead end of tumor promotion that does not reach the biological level of a steadily progressive disease, such as malignant lymphoma, and therefore may be referred to as *abortive CTCL*.

5. Why is it important to recognize SPP as an entity? Isolate clinical, histologic, or molecular biological criteria that often present similarly in various lymphoproliferative skin conditions erroneously may simulate identity between different nosologic entities.

If two conditions behave differently from one another biologically (**Table**), they should be recognized as separate nosologic entities. A disease that is fatal in most cases (MF) cannot be identical to a disease (SPP) that results in nothing more than some cosmetic trouble with a little itching in some cases.

As long as physicians have to evaluate and treat patients to the best of their knowledge, the intellectually and ethically appropriate approach is to differentiate entities rather than to lump them together.

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