

## Circumstances that Led to the Definition of Papuloerythroderma (Ofuji) as an Individual Entity

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### Abstract

Papuloerythroderma is a unique and somewhat curious skin disease which was reported by Shigeo Ofuji, Japanese Dermatologist in 1984. This review introduces circumstances that led to the definition of papuloerythroderma as an individual entity.

**Keywords:** Papuloerythroderma; Erythroderma; Eczema

### Introduction

Papuloerythroderma (Ofuji) was initially reported in a Japanese academic paper in 1979, entitled: Two cases of diffuse erythroderma-like skin changes which developed with the onset of a lichenoid papular eruption [1]. This skin condition has at least two aspects of eczema and erythroderma, which has attracted many dermatologists. This will describe the circumstances that led to the introduction and definition of papuloerythroderma (Ofuji) as an individual entity.

### Characteristics of the Skin Eruption

At present, the diagnosis of papuloerythroderma tends to start with the examination of the disorder-specific distribution of the skin eruption. In fact, the skin eruption distribution is markedly characteristic in papuloerythroderma. The skin eruption develops over the entire body, particularly on the trunk. It is distributed along with wrinkle lines. In intertriginous areas, such as axillary, cubital, and popliteal fossas and the inguinal region, as well as the abdomen, the eruption is absent, showing a clear boundary in accordance with major wrinkle lines (Figures 1a and 1b). Such a zebra or belt-shaped skin eruption distribution is called a 'deckchair sign' in Western countries [2].



**Figure 1:** In intertriginous areas, such as axillary, cubital, and popliteal fossas and the inguinal region, as well as the abdomen, the eruption is absent, showing a clear boundary in accordance with major wrinkle lines.

The skin eruption does not appear, or it is mild, if any, on the face. It occasionally involves palmoplantar hyperkeratosis with mild or without scales. Itching is also present to various degrees.

### Onset of the Initial Eruption

However, on examining reports on this case by Ofuji et al., it is clear that the clinical individuality of the disorder was not based on such a completed systemic eruption distribution. At the 285th Kyoto Dermatological Society Meeting held in October 21, 1978, Papuloerythroderma was presented as a case presentation of unusual and/or unidentified dermatoses. When published in *Acta Dermatol-Kyoto journal* (74:129, 1979), the abstract title of this report was revised as follows: A case of extensive and systemic skin changes which developed with the onset of a lichenoid papular eruption.

In papuloerythroderma, a solid, red, papular eruption without a tendency toward weeping, which differs from secondary eruptions in the onset mechanism, initially appears. Such a papular eruption is sparsely or densely manifested, and it is repeatedly alleviated and aggravated in the early stages. Subsequently, the number of papulas increases, and, after several weeks or months, they become flat. Fusing together in a valvate manner, they become diffuse, and the condition progresses to a state of erythroderma.

### Dermatopathological findings

In papuloerythroderma, papular and erythrodermic lesions show essentially identical symptoms. In the epidermis, partial parakeratosis, mild acanthosis, and a slight mononucleosis invasion are observed. Mild spongiosis may also be present, but intraepidermal blisters rarely develop. In the papillary to reticular layer of the dermis, inflammatory cell infiltration occurs around blood vessels. Lymphocytes and histiocytes play a central role, involving or not involving eosinophils.

### Blood examination and other findings

The pathological condition is characterized by an increased peripheral eosinophil count (10-20% higher). The IgE level also increases in some cases; however, this is not correlated with the pathological condition. Lymph nodes at lesional sites are enlarged as a manifestation of dermatopathic lymphadenopathy.

## Change of nomenclature

Based on the results of such a case study, a report was published in Japanese in the *Acta Dermatol-Kyoto* journal [1]. It was entitled: Two cases of diffuse erythroderma-like skin changes which developed with the onset of a lichenoid papular eruption, with a brief opening paragraph, explaining that this paper reports 2 cases, which had not previously been reported, and recently treated with by the authors. On comparison with the title of the presentation made at the academic meeting, the term 'lichenoid' remained, while skin changes were newly described as 'erythroderma-like'. Furthermore, when the report was published in the practical dermatology journal in 1980, its title was revised again: Case of erythroderma-like skin changes which developed with the onset of a solid papular eruption, with the term "lichenoid" removed, possibly based on findings of additional case studies [3-5].

Professor Ofuji temporarily named the disorder 'papuloerythroderma syndrome' (introduced in reference 4,5), but it was presented as Papuloerythroderma in *Dermatologica* (currently, *Dermatology*) in 1984 (Table 1) [6].

History of diagnosis	Year
A case presentation of unusual and/or unidentified dermatoses	1978
Extensive and systemic skin changes which developed with the onset of a lichenoid papular eruption	1979
Diffuse erythroderma-like skin changes which developed with the onset of a lichenoid papular eruption	1976
Erythroderma-like skin changes which developed with the onset of a solid papular eruption	1980
Papulo-erythroderma syndrome	1983
Papuloerythroderma	1984

**Table 1:** Showing history diagnosis chronically.

When such reporting began to be made from Europe [2,7], the clinical individuality of this disorder was established [6,8].

## Association with malignant tumors, particularly hematopoietic neoplasms

The disorder is prevalent among elderly males. It is also characterized by a higher incidence of complicating organ cancers, compared with that in the known erythroderma. According to a summary of the 31 cases examined by Ofuji, the condition was complicated by cancer and hematopoietic neoplasms in 31.2 and 3.1%, respectively [4]. However, Danno [5] conducted additional case studies, and noted a higher incidence of hematopoietic neoplasms among 68 Japanese patients, as it developed in 10 (14.7%), while organ cancer occurred in 16 (23.5%). In the latter, gastric cancer was the most prevalent, developing in [9-12]. Complications by pulmonary, renal, hepatic, laryngeal, and prostate cancers, squamous cell carcinoma, and angiosarcoma were also reported. It was also clarified that there is no temporal association between the onset of a skin eruption and the identification of cancer.

In other countries, although the number of reports on organ cancer complicating papuloerythroderma has been limited, an association of hematopoietic neoplasms, including cutaneous T-cell lymphoma, has

been suggested in some case studies. Professor Ofuji had highlighted the differentiation from cutaneous T-cell lymphoma as the most important point, since he initially introduced papuloerythroderma [1,7,8]. While some researchers regarded the disorder as a type of cutaneous T-cell lymphoma, he focused on its individuality. For example, he offered a counterargument against a report by Grob et al., entitled: Ofuji papuloerythroderma - report of a case with T-cell skin lymphoma and discussion of the nature of this disease [9], by emphasizing that the disorder is an individual entity [10].

## Factors inducing the specific skin eruption

The influences of the long-term use of topical steroids on the development of such a specific skin eruption have also been noted. The absence of eruptions in accordance with major wrinkle lines in joint flexion areas and the abdomen may be a result of the high absorbability of topical steroids. On the other hand, they have been reported to develop even in individuals without a history of steroid use. Ofuji ruled out a causal relationship between the development of papuloerythroderma and topical steroid, considering that the absence of eruptions showing a clear boundary cannot be completely explained only by the influences of the latter [4,6]. Furthermore, as the disorder is prevalent among elderly males, some researchers suspect an association of a decreased sweat gland function in dry skin, although this theory has not been established.

The causes of papuloerythroderma have remained unclear. Recently, a papuloerythroderma-type drug eruption associated with Th2 cells as drug-reactive T cells is drawing attention [11]. There have also been reports discussing the up-regulation of activation markers on basophils [12], as well as the relationship between the thymus and activation-regulated chemokine levels [13,14].

In short, types of papuloerythroderma may be classified into 2 categories: those associated with inflammatory cutaneous disorders, hematopoietic neoplasms, malignant tumours of organs, or drug eruptions, similarly to erythroderma; and those developing spontaneously and independently of other disorders. In the latter, it is necessary to elucidate the mechanism of specific eruption development as a future challenge.

This paper summarizes an educational lecture given at the 115th Annual Meeting of the Japanese Dermatological Association (in Kyoto in 2016). Only Japanese abstract was published at a quarter part of page 755 of *The Japanese Journal of Dermatology* Vol. 126, No.5, 2016. No other publications are there except this program.

## Conflict of Interest

The author has no conflicts of interests.

## Acknowledgment

This paper will be dedicated to the late Shigeo Ofuji (1917-2012).

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