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Letter to the Editor

Senile erythroderma with hyper IgE: an independent and novel disease form

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To the editor,

Erythroderma is a rare exfoliative dermatitis with various causes [1, 2]. The exact pathophysiology of this disease has not received much attention. Moreover, while it has been reviewed many times [1, 2], there is little mention of senile erythroderma. The accumulated findings [1, 2] reveal 3 factors involved in its etiology: drugs such as carbamazepine, pre-existing skin diseases such as psoriasis [1], and stages of malignancies such as cutaneous T-cell lymphomas. Li and Zheng [2] reported the most prevalent causative factors—pre-existing dermatoses (70.77%), followed by idiopathic causes (14.23%), drug-induced reactions (12.69%), and malignancies (2.31%). Among the pre-existing dermatoses, psoriasis was the most common etiology (55%). Several case analyses show that males are 4 times more likely to be affected by erythroderma than females [1, 2]. The average age is 52 to 57 years, including those in 80s [1, 2]. One study reported a unique case of erythroderma caused by propolis [3]—a food product produced by honeybees. Steroid withdrawal erythroderma [4] has been reported; as it is caused by medical care, it is called iatrogenic. Patients with systemic eczema have received steroids for external use at various medical institutions for many years due to the intractability of their conditions. In cases of steroid withdrawal, erythroderma occasionally occurs. As the cases caused by an underlying disease are diverse, dermatologists and clinicians should first determine the possible cause in patients with erythroderma.

We have focused on this disease, erythroderma, that occurs as an exacerbation of eczema in senile patients [5] in the Kitasato University clinic. Patients were also predisposed to atopic reactions with high serum IgE [5]. We hypothesized that there is a form of erythroderma secondary to eczema, owing to the atopic predisposition, which occurs in elderly patients and manifests as atopic dermatitis (AD). Erythroderma of unknown cause and protracted course may be secondary to senile AD. In addition, AD occurring in patients in their 30s and in the elderly has been reported [6]. It seems that this disease is an exacerbated form that can be said to be senile AD. It has been proposed that elderly patients are a subgroup of patients with distinct AD manifestation [6]. It's a shame that the number of patients is so small that it cannot be said, but it has been advocated for over 30 years since this disease form, senile erythrodema with hyper IgE [5], was proposed. The possibility of a drug was initially denied, so far, this advocacy was made because of our finding aggregation of senile erythroderma patients.

Nakano-Tahara et al. [7] analyzed 68 patients over 65 years of age who presented with erythroderma and identified 2 subgroups: idiopathic and secondary senile erythroderma. In both of them, serum IgE and TARC (thymus and activation-regulated chemokine) levels were elevated. They reported only 4 patients clearly categorized as having senile erythroderma with hyper IgE as a distinct form of senile type AD. Although we have confirmed that there are no abnormalities in the IgE gene [8] in patients with this disease, it seems that there is Th1 and Th2 dysregulation with aging [9]. Recently, Ohga et al. [10] also proposed the presence of idiopathic senile type erythroderma with hyper IgE which is likely to occur in elderly men, in whom immunity is shifted toward Th2; however, the mechanism may differ from that of AD. Deficiency in immune response due to aging [11, 12] has been seen in those with cancer and various infectious diseases, and side effects of drugs [13] are often observed in the elderly. Thus, imbalance in the Th1/Th2 response [9] due to aging is likely to occur. Even though both conditions are extremely rare and difficult to analyse, the differences between atopy and idiopathic type senile erythroderma with hyper IgE should be further clarified. The mechanism of decline of imunoregulatory function and inflammatory mediators is possibly due to dysregulation of the innate immune system, and skewing of adaptive immunity to a type 2 T helper cell response [9, 12], which is likely to occur in elderly men. Moreover, a natural progression of mitochondrial dysfunction [14] with aging has also been suggested. And the mechanism of immune dysfunction due to aging is still only theoretical.

It is unclear if hyper IgE syndrome (HIgES) [15] overlaps with senile erythroderma with hyper IgE, or whether it is another disease entirely. HIgES [15] has been observed in pneumonia, severely disseminated molluscum contagiosum and food allergies with a skewed T helper 1 (Th1) cell/Th2 cell ratio, but not erythroderma in clinical studies. Although HIgES is a disease based on a very clear genetic immune deficiency [16], we believe senile erythroderma with hyper IgE should be considered as an immune regulation disorder associated with aging. Further analysis is required to determine the mechanism of senile erythroderma with hyper IgE as a form of senile AD.

Countries, including Japan, have entered an era of longevity, and people worldwide are affected by various diseases associated with aging [11, 12] as well as cancer. An age-related decline in immune regulation [11] can influence response to infectious pathogens, and environmental irritants, and advanced age leads to more frequent side effects from drugs [13], probably due to a decrease in cell-mediated immune function such as in macrophages and natural killer T cells [12]. Unfortunately, senile erythroderma with hyper IgE has not been thoroughly investigated due to its rarity. We eagerly anticipate studies that will elucidate the pathological mechanism by which aging leads to abnormal Th2 regulation and immune hypersensitivity to environmental substances. In the meantime, senile erythroderma may become a frequent encounter in the clinic due to the aging population.

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