were observed. Thus, when treating patients with eyelid eczema, the investigation with patch tests is essential.

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Authors' contributions

Mariana de Figueiredo Silva Hafner: Design and planning of the study; drafting and editing of the manuscript; collection, analysis, and interpretation of data; effective participation in research orientation; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the literature; critical review of the manuscript; approval of the final version of the manuscript.

Victoria Cerqueira Elia: Drafting and editing of the manuscript; collection, analysis, and interpretation of data; approval of the final version of the manuscript.

Rosana Lazzarini: Drafting and editing of the manuscript; collection, analysis, and interpretation of data; effective participation in research orientation; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the literature; critical review of the manuscript; approval of the final version of the manuscript.

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Conflicts of interest

None declared.

References

1. Amin KA, Belsito DV. The aetiology of eyelid dermatitis: a 10-year retrospective analysis. Contact Dermatitis. 2006;55:280–5.
2. Lewallen R, Clark A, Feldman SR. Clinical Handbook of Contact Dermatitis – Diagnosis and Management by Body Region. Boca Raton FL: Taylor e Francis Group; 2015.
3. Landeck L, John SM, Geier J. Periorbital dermatitis in 4779 patients - patch test results during a 10-year period. Contact Dermatitis. 2014;70:205–12.
4. Feser A, Plaza T, Vogelgsang L, Mahler V. Periorbital dermatitis – a recalcitrant disease: causes and differential diagnoses. Br J Dermatol. 2008;159:858–63.
5. Guin JD. Eyelid dermatitis: a report of 215 patients. Contact Dermatitis. 2004;50:87–90.
6. Wolf R, Orion E, Tüzün Y. Periorbital (eyelid) dermatides. Clin Dermatol. 2014;32:131–40.
7. Assier H, Tetart F, Avenel-Audran M, Barbaud A, Ferrier-le Bouëdec MC, Giordano-Labadie F, et al. Is a specific eyelid patch test series useful? Results of a French prospective study. Contact Dermatitis. 2018;79:157–61.
8. Rietschel RL, Warshaw EM, Sasseville D, Fowler JF, DeLeo VA, Belsito DV, et al. Common contact allergens associated with eyelid dermatitis: data from the North American Contact Dermatitis Group 2003-2004 study period. Dermatitis. 2007;18:78–81.
9. Herro EM, Elsaie ML, Nijhawan RI, Jacob SE. Recommendations for a screening series for allergic contact eyelid dermatitis. Dermatitis. 2012;23:17–21.
10. Ojo EO, Gowda A, Nedorost S. Scalp Dermatitis in Patients Sensitized to Components of Hair Products. Dermatitis. 2019;30:264–7.

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Effectiveness of dupilumab for chronic prurigo in elderly patients with atopic dermatitis☆

Dear Editor,

Chronic prurigo (CPG), such as prurigo nodularis, is often a complication of atopic dermatitis (AD).[1] CPG is a common and distinct skin disease characterized by multiple pruriginous skin lesions,[2] and its pathophysiological mechanisms remain unknown; however, the involvement of an atopic predisposition has been suggested.[2] CPG in AD is highly intractable to traditional treatments. Herein, we present the cases of four elderly patients with AD complicated by CPG in whom traditional treatments had failed previously and describe their successful treatment with dupilumab within the last 2 years.

The clinical characteristics of the four patients are shown in Table 1. The AD in the four patients was complicated by CPG (Fig. 1A). None of the patients had a history of childhood AD, but the onset of AD was noted in old age. As previous tra-

☆ Study conducted at the Department of Dermatology, Sakura Medical Center, School of Medicine, Toho University, Chiba, Japan.

Table 1 Clinical characteristics of four elderly patients with atopic dermatitis complicated by chronic prurigo.

Clinical characteristic	Case 1	Case 2	Case 3	Case 4
Age of first visit	71-year-old	65-year-old	84-year-old	69-year-old
Sex	Male	Male	Male	Female
Age of onset of AD	67	65	84	67
Age of patient when dupilimab was initiated	73	66	85	70
History of childhood atopic dermatitis	No	No	No	No
Complication	Allergic rhinitis, Allergic conjunctivitis, Type 2 diabetes, Diabetic nephropathy, previous Myocardial Infarction	Allergic rhinitis, Bronchial asthma, Cerebral infarction	Hypertension, Dyslipidemia, Sleep apnea syndrome, Bilateral osteoarthritis of the hip	Bronchial asthma, Allergic bronchopulmonary aspergillosis, Eosinophilic pneumonia, Hypertension, Type 1 diabetes mellitus, Hashimoto's thyroiditis, Ulcerative colitis
Previously failed therapies	H1 antihistamines, Topical corticosteroids, NB-UVB phototherapy, Prednisolone	H1 antihistamines, Topical corticosteroids, NB-UVB phototherapy, Prednisolone, Cyclosporine A	H1 antihistamines, Topical corticosteroids, NB-UVB phototherapy, Prednisolone	H1 antihistamines, Topical corticosteroids, NB-UVB phototherapy, Prednisolone
Histological findings	Spongiosis, Perivascular infiltration of lymphocytes and eosinophils in the upper dermis	Spongiosis, Perivascular infiltration of lymphocytes and eosinophils in the upper dermis	Epidermal hyperplasia, Spongiosis, Perivascular infiltration of lymphocytes and eosinophils in the upper dermis	Hyperkeratosis, Epidermal hyperplasia, Spongiosis, Perivascular infiltration of lymphocytes and eosinophils in the upper dermis
Percent BSA affedted when dupilimab was initiated (%)	17	52	56	57
EASI score when dupilimab was initiated	16.3	29	20.7	17.3
Total IgE (IU/mL)	3,100	4,300	190	7,900
TARC (pg/mL)	1,050	5,500	12,800	4,050
Absolute eosinophil count (/μL)	678	1,410	1,782	1,335a

AD, Atopic Dermatitis; BSA, Body Surface Area; EASI, Eczema Area and Severity Index; H1, Histamine 1; NB-UVB, Narrow-Band Ultraviolet B; TARC, Thymus and Activation-Regulated Chemokine.

ditional treatments had failed in all the patients, dupilumab treatment was initiated at standard doses of 600 mg subcutaneously at week 0 and then at 300 mg every other week. All the patients showed significant improvement in pruritus 2–4 weeks after initiation of dupilumab treatment. In all cases, treatment with dupilumab was very effective, and the Eczema Area and Severity Index (EASI)-90 was achieved 4–8 weeks after initiating dupilumab treatment (Fig. 1B). Although all the patients had various medical diseases, no side effects were observed in any patient.

Dupilumab is a fully human monoclonal antibody directed against the α subunit of the Interleukin (IL)-4 receptor; it inhibits the signaling of IL-4 and IL-13 pathways, which play pivotal roles in the pathogenesis of Th2 inflammation and AD. Dupilumab is reportedly effective for CPG in patients with AD.[3,4]

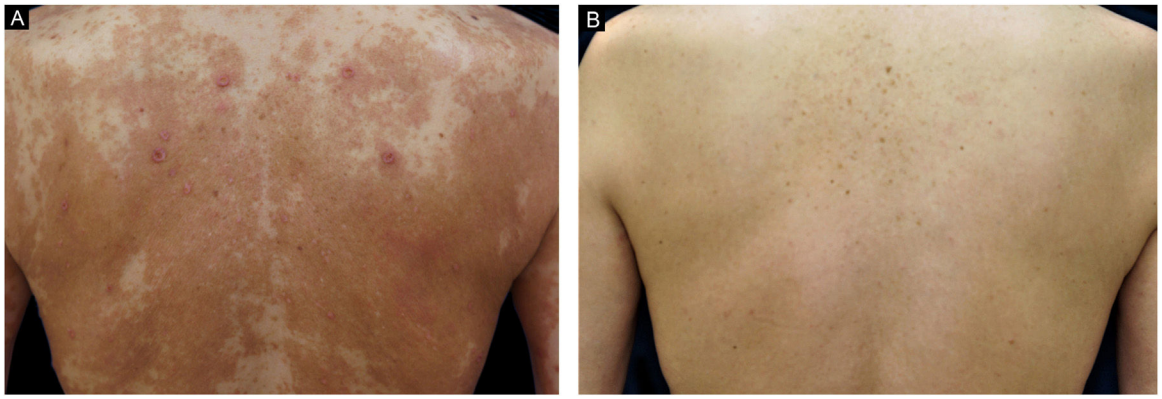

Figure 1 Clinical presentation of the upper back in a 65-year-old Japanese man (Case 2). (A) Pruritic lichenified plaques, papules, and prurigo nodules were present before dupilumab treatment. (B) Complete clearance of the cutaneous manifestations was achieved by 24 months after the initiation of dupilumab.

Our patients with CPG in AD showed highly elevated total IgE and thymus and activation-regulated chemokine levels and peripheral blood eosinophil counts. Histological findings revealed superficial, perivascular, and interstitial eosinophil infiltration in the skin lesions in all the patients, which corresponds with the characteristic histological findings reported in CPG – a superficial perivascular and interstitial inflammatory infiltration composed mainly of lymphocytes and eosinophils identified in the skin lesions.[5] According to the literature, dupilumab is also effective for eosinophilic diseases, such as eosinophilic pneumonia,[6] eosinophilic chronic rhinosinusitis,[7] and eosinophilic esophagitis.[8] Eosinophilic pneumonia in the 69-year-old female patient was improved by dupilumab treatment. We presume that our cases pathologically involved both Th2 response and eosinophilic inflammation and that dupilumab was effective in managing both these conditions.

In elderly patients with AD, systemic therapy with immunosuppressive agents is difficult due to various complications. Additionally, topical steroid treatment is difficult due to skin atrophy caused by aging. Generally, dupilumab is well tolerated, with few adverse effects. Therefore, dupilumab is a useful treatment option for CPG in elderly patients with AD.[3] Because our patients were elderly, it was difficult to continue systemic therapy and topical steroids due to various complications and skin atrophy. Therefore, we initiated dupilumab treatment with successful in treating the patients.

Our study suggests the usefulness of dupilumab for CPG in elderly patients with AD.

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Authors' contributions

Shinji Mitsuyama: Approval of the final version of the manuscript; Study conception and planning; Critical literature review; Data collection, analysis, and interpretation; Preparation and writing of the manuscript.

Tetsuya Higuchi: Approval of the final version of the manuscript; Critical literature review; Manuscript critical review.

Conflicts of interest

None declared.

References

1. Huang AH, Canner JK, Khanna R, Kang S, Kwatra SG. Real-World Prevalence of Prurigo Nodularis and Burden of Associated Diseases. J Invest Dermatol. 2020;140:480–3.
2. Pereira MP, Steinke S, Zeidler C, Forner C, Riepe C, Augustin M, et al. European academy of dermatology and venereology European prurigo project: expert consensus on the definition, classification, and terminology of chronic prurigo. J Eur Acad Dermatol Venereol. 2018;32:1059–65.
3. Liu T, Bai J, Wang S, Ying S, Li S, Qiao J, et al. Effectiveness of Dupilumab for an Elderly Patient with Prurigo Nodularis Who Was Refractory and Contradicted to Traditional Therapy. J Asthma Allergy. 2021;14:175–8.
4. Calugareanu A, Jachiet M, Tauber M, Nosbaum A, Aubin A, Misery L, et al. Effectiveness and safety of dupilumab for the treatment of prurigo nodularis in a French multicenter adult cohort of 16 patients. J Eur Acad Dermatol Venereol. 2020;34:e74–6.
5. Weigelt N, Metze D, Ständer S. Prurigo nodularis: systematic analysis of 58 histological criteria in 136 patients. J Cutan Pathol. 2010;37:578–86.
6. Menzella F, Montanari G, Patricelli G, Cavazza A, Galeone C, Ruggiero P, et al. A case of chronic eosinophilic pneumonia in a patient treated with dupilumab. Ther Clin Risk Manag. 2019;15:869–75.
7. Suzaki I, Tanaka A, Hirano K, Arai S, Kobayashi H. Successful management of eosinophilic chronic rhinosinusitis complicated by severe asthma using dupilumab, following negative initial results with benralizumab. Allergol Int. 2021;70:150–2.
8. Hirano I, Dellon ES, Hamilto JD, Collins MH, Peterson K, Chehade M, et al. Efficacy of Dupilumab in a Phase 2 Randomized Trial of Adults With Active Eosinophilic Esophagitis. Gastroenterology. 2020;158:111–22.

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Epidemiological transition of primary cutaneous melanoma in a public hospital in Brazil (1999–2019)☆

Dear Editor,

Despite accounting for only about 1% of all skin cancers, melanoma accounts for 90% of mortality from cutaneous malignancies, and the treatment of the advanced forms inflicts a significant budgetary impact on the health system.[1] In recent decades, there has been a consistent increase in its incidence worldwide; however, its specific mortality has remained stable or has slightly decreased in most historical series.[2]

In the 2020-2022 triennium, INCA (Brazilian National Cancer Institute) estimated the diagnosis of 8,400 melanomas in Brazil (4 cases/100,000 inhabitants). As Brazilian longitudinal epidemiological data are scarce, this study aimed to verify the transition in the epidemiology of primary cutaneous melanomas diagnosed in a public university service in the hinterland of Brazil over a 21-year period.

A retrospective and analytical study of patients diagnosed with *in situ* or invasive melanoma was conducted between January 1999 and December 2019, in the Pathology Laboratory of Hospital das Clínicas, Medical School, Botucatu (FMB-Unesp). Demographic and histopathological data of the patients were collected, related to the characteristics of the neoplasm. The subgroups were compared by logistic models (binary or ordinal), the effect size was estimated by the odds ratio with its 95% confidence interval (95%CI), and the significance level was defined at $p < 0.05$. The project was approved by the Research Ethics Committee of the institution.

During this period, 615 primary cutaneous melanomas were diagnosed in 590 patients, of which 300 (50.8%) were female, and 24 (4.1%) had more than one melanoma during the period. The mean age (standard deviation) at diagnosis was 61.3 (15.8) years, ranging from 12 to 92 years. The incidence of primary cutaneous melanoma showed an average annual growth of 4.0% (95%CI 2.0% to 5.7%) at the institution per year, in the last 21 years. There was no difference in the proportion of elderly individuals or regarding sex, as a function of age ($p > 0.68$).

Table 1 shows the main characteristics of melanomas and their association with sex and age group. There was a predominance of cases occurring in the thoracic and cephalic regions. Tumors in the limbs were more frequent in women, while cephalic tumors were more frequent in the elderly and in men. The superficial spreading histopathological subtype was the most common, in addition to being associated with the female sex and ages under 60. Nodular melanomas predominated in men. Patients under 60 also had higher levels of histopathological invasion (1–3 mm).

When comparing melanomas grouped into three seven-year periods (Table 2), adjusted for sex and age using ordinal logistic regression, acral and thoracic tumors increased in frequency, as did superficial spreading and acral lentiginous histopathological subtypes. On the other hand, tumors located on the head and neck, as well as lentigo maligna, had their frequency decreased during the periods. There was no change in tumor proportions according to histopathological invasion levels, and about 35% of the diagnosed melanomas measured > 1 mm.

Fig. 1 depicts the perceptual map, estimated by the multivariate technique of multiple correspondence analysis, which simultaneously adjusts for sex, age group, histopathological type, and Breslow thickness. The multivariate model consisting of two dimensions explained 62% of the total variation (32% and 29% inertia), allowing the identification of close relationships between variables and continuity between the categories. Melanomas of intermediate thickness (1–3 mm), acral, superficial spreading subtype, and age under 60, were closer to the most recent period (2013-2019) of follow-up. While the most remote period (1999-2005) was closer to the elderly, lentigo maligna and tumors < 1 mm. The nodular subtype was associated with higher levels of invasion, without approaching the time of follow-up, sex, or age group.

In this series, the increased percentage seen in melanomas diagnosed at the institution was greater than the population growth in the region, suggesting an increase in incidence. However, despite awareness campaigns, invasive melanomas still comprise an important fraction of the tumors diagnosed in the institution, and the results do not show a reversal of this scenario. In fact, there is multifactorial evidence for the transition in the epidemiology of melanomas in different international series, with justification ranging from overdiagnosis to photoexposure profiles, population aging, racial miscegenation, and prevention campaigns.[3,4]

In this population, despite increasing aging, the reduction in the proportion of melanomas in the elderly, and in the lentiginous subtypes prevalent in the head/neck region, may reflect a better occupational photoprotection pattern, in addition to the urbanization process that Brazil has been experiencing since the 1970s.[5] This melanoma profile is asso-

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