To the Editor,

Acute generalized exanthematous pustulosis is a rare drug eruption that affects 1-5 in a million individuals mainly females characterized by a sudden occurrence of pinhead sized non follicular sterile pustules on erythematous areas, accompanied by fever and pruritus. Visceral organ involvement may also occur. Medicines that induce acute generalized exanthematous pustulosis (AGEP) include antibiotics- ampicillin, macrolides, quinolones, sulfonamides-chloroquine, hydroxychloroquine, terbinafine and diltiazem. It is currently uncertain whether AGEP is strictly human leukocyte antigen (HLA) restricted. In 1995 Bernard et al. showed a statistically significant augmentation of frequency of the alleles HLA-B51, DR11 and DQ3 associated with acute generalized exanthematous pustulosis although an association with a specific drug has not been reported. We present a case of acute generalized exanthematous pustulosis AGEP - induced by hydroxychloroquine associated with HLA-B51, DR11Q1, Q4, DQ3Q5 and for the first time in the literature with HLA-B15.

A 72-year old woman of Caucasian origin was admitted for fever, pruritus and rash of one day duration. She was treated for hypothyroidism with thyroxine 75 μgr daily. For the last two weeks she had been taking hydroxychloroquine 200 mgr twice daily for joint pains although a definite diagnosis had not been made. Clinical examination revealed good general condition, fever 38.2 C and an eruption of erythematous patches on the back, - between the mammary glands- and lower limbs covered with non-follicular pustules forming at certain areas lakes of pus. Mucous membranes were intact. Figure 1. Full blood count showed leucocytosis with neutrophilia, liver tests were normal. Histology showed a subcorneal pustule with neutrophils, perivascular neutrophilic infiltrate in the dermis, compatible with acute generalized exanthematous pustulosis - AGEP Figure 2. The eruption regressed following withdrawal of hydroxychloroquine and

Keywords: Pustulosis, hydroxychloroquine, HLA

Anahtar Kelimeler: Püstüloz, hidroksiklorokin, HLA

©Copyright 2020 by Turkish Society of Dermatology and Venereology
Turkderm - Turkish Archives of Dermatology and Venereology published by Galenos Yaynevi.
administration of oral steroids 3 weeks later. Thorax Radiography and abdomen tomography were normal. Serum titers for cytomegalovirus, Epstein-Barr virus, Parvovirus B19, Coxsackie, Echo Herpes 6 and 7 viruses, anti-nuclear antibody and rheumatoid factor were negative. The HLA typing was performed for the HLA-A, B and C antigens using the sequence specific oligonucleotide-polymerase chain reaction (PCR) and for the HLA-DR, DQ the sequence specific primer PCR based assay. The patient proved to be positive for the alleles HLA-B51, HLA-B15, HLA-DR1101,04 and HLA-DQ03,05.

HLA genetic testing for B1502 is recommended prior to initiation of carbamazepine therapy because this anti-epileptic may induce Stevens Johnson and or toxic epidermal necrolysis. HLA-B allele is the most common determinant of the most severe types of drug hypersensitivity reactions, including SJS, TEN, HSS and rashes. AGEP is a very rare drug induced condition with very few cases HLA investigated. Although not associated with severe mortality (4%), AGEP may provoke considerable morbidity, the reported patient has been hospitalized for a month. Furthermore the HLA-B15 positivity reported is an interesting finding because HLA-B15 is rare in Caucasians-carrier frequency <1%. After review of the literature the reported case seems to be the first case of confirmed AGEP in a Caucasian associated with HLA-B51, HLA-DR1101,04, HLA-DQ03,05 and with HLA-B15, an HLA-B allele, which although rare in Caucasians, is related-such as HLA-B5701, HLA-B5801 (carbamazepine induced AGEP) to cutaneous adverse drug reactions in Asian populations. Informed consent was obtained.

**Ethics**

**Informed Consent:** It was obtained.
**Peer-review:** Externally peer-reviewed.
**Financial Disclosure:** The authors declared that this study received no financial support.

**References**