A Rare Side Effect of Hydroxycholoroqine: Acute Generalised Exanthematous Pustulosis Hydroxycholoroqine Induced Cutaneous Lesions

Hidroksiklorokinin Nadir Bir Yan Etkisi: Akut Jeneralize Egzantamatöz Pustulozis

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Abstract: Hydroxycholoroqine (HCQ) is a widely used drug in treatment of various rheumatic disease. Even, it is commonly used in treatment of cuteneus manifestations of lupus sometimes the drug it self can cause cutaneus adverse effects. Acute generalised exanthematous pustulosis (AGEP) is a rare kind of dermatosis and herein we report a case who developed AGEP after HCQ usage for treatment of rheumatoid arthritis.
Keywords: Acute generalized exanthematous pustulosis, adverse effect, hydroxycholoroqine, dermatosis

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Öz: Hidroksiklorokin (HCQ) pek çok romatizmal hastalığın tedavisinde yaygın olarak kullanılan bir ilaçtır. Her ne kadar kendisi lupusun cilt tutulumunda kullanılsa da bazen kendisi kutanöz yan etkilere sebep olabilir. Akut jeneralize egzantamatöz püstülozis (AGEP) nadir bir dermatoz türüdür ve burada RA tedavisi için HCQ kullanan ve AGEP gelişen bir olgudan bahsedilecektir.
Anahtar Kelimeler: Akut jeneralize egzantamatöz püstülozis, yan etki, hidroksiklorokin, dermatoz

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1. Introduction

Hydroxycholoroqine (HCQ) is a commonly used immunomodulatory drug in treatment of various autoimmune rheumatic disease. Even generally well tolareted, it has well known side effects such as ocular toxicity, hypoglisemia and hyperpigmentation. Acute generalised exanthematous pustulosis (AGEP) is a rare kind of dermatosis with suddenly onset fever and extensive pustular rash (1). More than 90% of the patients have the history of drugs, especially antibiotic usage (2).

Herein, we report a case who developed AGEP after HCQ usage for treatment of rheumatoid arthritis.

2. Case Report

On December 2014, a female patient at 58 years old has recoursed to rheumatology department with pain in bilateral wrists for 8 months. She had a history of sinovitis in her left knee 8 years ago and she was having pain and swelling in wrists and ankles since then. Her complaints were responding to non-steroidal anti-inflammatory drugs (NSAIDs). She had Graves disease and panic attack and was recieving ramipril, metoprolol ve essitalopram. On physical examination she had sinovitis in her left knee and pain in both wrists. On laboratory examination, she had mild anemia (Hgb 10.1 mg/dL), leucocyte levels was $13x10^3$/uL ,thrombocyte levels was $370x10^{3,}$ erythrocyte sedimentation rate was 80 mm/h (0-20), C-reactive protein level was 42.8 mg/L (0-8), rheumatoid factor level was 12 IU/mL (0-20) and antiCCP antibody level was 60.8 U/mL (0-20), respectively. Her biochemical tests were within normal ranges.

Arthrocentesis was performed to her left knee, and intraarticular steroid was injected. White blood cell count of the sinovial fluid was $4x10^3$/u L and evaluated as inflammatory.

She was diagnosed with rheumatoid arthritis and as having mild symptoms hydroxychloloroquine(HCQ) and NSAIDs was started. After 40 days, she recoursed with hyperemia and pustular lesions. All the drugs were stopped and she was consultated with Allergy Department. The lesions were revealed as drug eruption. Prednisolon 20 mg/day and desloratadine 5 mg/day were started. After using treatment she again recoursed with progressing symptoms. She was hospitalized and methylprednisolone iv 80mg/day(3 days), 60 mg/day (3 days), 40 mg/day (4 days) and 20 mg/day, pheniramine iv and fexofenadine oral, moisturisers locally were started. She developed new lesions on her legs 10 days after the begining of the therapy.(Figure 1) Skin biopsy was performed and subcorneal pustuls, low grade vascular injury was detected in pathology report. The pathological diagnosis was acute generalized exanthematous pustulosis (AGEP). Methylprednisolone restarted with 80 mg/day and tapered slowly. After one month, lesions were recovered with desquamation without leaving scar.

3. Discussion

HCQ is an antimalarial drug and has immunomodulatuar effects. It is widely used in rheumatologic diseases and AGEP is a rarely seen adverse drug erruption (1). The incidence of AGEP 1-5 patients/million/year (2). More then 90% of the cases with AGEP is trigerred by drugs. Antibiotics, calcium channel blockers, anticonvulsants, NSAIDs, proton pump inhibitors, corticosteroids and HCQ are the most common causes (3). However we rarely encounter in rheumatology practise.

AGEP is chracterised with disseminated sterile pustules but does not involve mucous membranes (2). In pathogenesis, CD8 cytotoxic T-cells are increased in epidermis and causes apoptosis of keratinocytes and formation of vesicles. Then CXCL-8-producing and granulocyte macrophage-colony stimulating factor-producing CD4 cells causes neutrophil mediated inflammation and pustul formation. AGEP is often diagnosed clinically. Supportive investigations may include biopsy and patch testing to confirm allergy to an agent causing AGEP.The classical histological findings are intraepidermal, usually subcorneal, pustules and with neutrophilic and lymphocytic infiltrate (2). Barbaud *et al*., in a multicenter study to determine the value and safety of drug patch tests, have reported positive results in 58% of AGEP cases (4).

In most cases, clinical findings are resolves within 15 days after cessation of the drug and with supportive treatment. But rarely like our patient, it takes long time to resolve and needs more agressive treatment such as oral

corticosteroids and cyclosporine (5). Also, the latent period of HCQ-induced AGEP was longer(40 days) in our patient ,similar with literature (5).

4. Conclusion

HCQ is known as an innocent drug among rheumatologists. But in such conditions it can cause late and severe si advers effects which clinicians must be aware in clinical practice.

5. Conflicts of Interest

None

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