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NEUTROPENIA AND THROMBOCYTOPENIA IN A PATIENT USED ISOTRETINOIN FOR ACNE VULGARIS

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To the Editor,

Isotretinoin is a drug which frequently used for the treatment of moderate to severe acne. However, it has a lot of side effects, and most of them are related in skin findings. In this case report bicytopenia development in a 15 year old male patient due to isotretinoin presented. The patient had been brought to the pediatric outpatient clinic suffering from weakness, dizziness, headache and an abdominal pain complaint for 5 days. In a private hospital antibiotics and analgesic therapy had been applied, however the patient has been referred to our hospital due to bicytopenia establishment. On his physical examination, he had fever, cheilitis and oropharyngeal hyperemia. From his medical history, we have learned that he had been taking pills containing 40 mg/d isotretinoin for 45 days for his acne, and he denied other medications. On his laboratory investigation, his white blood cell count was 2500/mm³, absolute neutrophil count was 1200/mm³ and his thrombocyte was 81000/mm³. In addition to these his AST was 114 IU/L, ALT was 119 IU/L, ferritin levels was above 1500 ng/dl, CPK was 450, LDH 576, CRP 125 mg/dL and erythrocyte sedimentation rate was 18 mm/h. On the bone marrow examination, no malignancy finding but it was hypocellular and myeloid, megakaryocytic precursors were diminished. However, the eosinophilic cell precursor and erythroid precursor relatively has been increased. The viral (Ebstein-Barr virus, Cytomegalovirus, Parvovirus, HIV, Hepatitis A, B, and C), bacterial (Salmonella, Brucella), and parasitic investigation results were normal. Patient's complaints may be due to the use isotretinoin was evaluated and the medication has been stopped and after four days the bicytopenia improved to normal limits. However, the other laboratory findings (liver function, LDH, ferritin, CPK) improved at the end of second week of medication interruption.

Isotretinoin is effective against all of the etiopathological factors of acne.¹ The drug act as an anti-inflammatory drug and inhibit the motility of neutrophils and eosinophils and their migration into the epidermis, decrease DNA synthesis of human lymphocytes by blocking their response to lectins and stimulate Langerhans cells, monocytes and macrophages.² However, it has multiple side effects. The most common known isotretinoin complications are dryness of skin, lips and mucous membranes, cheilitis, itch, skin fragility, skin peeling, rash, epistaxis, dry eyes, diffuse alopecia, hyperlipidemia, raised liver enzymes, headaches, myalgia and/or arthralgia, back pain. In addition to these, the rarely reported side effects are impaired night vision, cataracts, optic neuritis, menstrual disturbances, inflammatory bowel

disease, pancreatitis, hepatitis, corneal opacity, idiopathic intracranial hypertension, skeletal hyperostosis, extraosseous calcification, psychosis, raised blood glucose level, increased erythrocyte sedimentation rate and fatigue.³⁻⁵ In our patient has cheilitis, myalgia, arthralgia, hepatitis and all complaints were improved after medication stopped. However, our patient has bicytopenia related findings.

Retinoids are commonly using for cancer therapy and we thought our patient's findings due to isotretinoin use. Because, retinoids are derivatives of vitamin A and high levels of vitamin A derivatives can cause arrest of cell growth and morphologic differentiation of human cell lines.^{6,7} In Norris study,⁸ the effect of oral isotretinoin on in vivo chemotactic responses was studied longitudinally in 7 patients with cystic acne. As measured in a microchamber chemotaxis assay, both monocyte and neutrophil chemotaxis were inhibited 98% during isotretinoin treatment. Moreover, they showed that in vivo chemotactic responses returned to normal within 2 months of cessation of treatment. In addition, in vitro chemotactic responses of neutrophils and monocytes from patients on isotretinoin were not diminished. So, they claim that isotretinoin produces significant anti-inflammatory effects by inhibition of monocyte and neutrophil chemotaxis across intact biologic barriers in vivo. In our case, we believed that isotretinoin use caused of both myeloid and thrombocytic cell differentiation interruption. In literature, agranulocytosis has been described due to isotretinoin use by idiosyncratic reaction, but two cell line affecting was not reported.⁹⁻¹¹

In conclusion, isotretinoin is an effective agent to acne therapy and patient who use topical, oral or systemic retinoids should be monitored for its bone marrow effects.

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