An unknown side effect of isotretinoin: Pericardial effusion with atrial tachycardia

To the Editor,

Isotretinoin is a synthetic vitamin A derivative used in the treatment of acne vulgaris and other dermatologic disorders. Systemic isotretinoin therapy may cause some cardiac side effects, like atrial tachycardia (1), congenital heart disease, and cardiac remodeling (2), reported as case reports. A 26-year-old female presented to the emergency unit of with syncope after a long palpitation episode. Her physical examination was normal except for tachycardia. A 12-lead electrocardiogram revealed atrial tachycardia, and the heart rate was 149 beats/min. After a 25-mg intravenous injection of diltiazem hydrochloride bolus, the atrial tachycardia terminated and normal sinus rhythm was sustained. Her laboratory tests and chest X-ray were normal. Echocardiography revealed normal left ventricular function and pericardial effusion of 0.8 cm at posterior side, 0.9 cm at the right atrial side and 1.3 cm at the right ventricle side. Several atrial tachycardia episodes were detected on rhythm Holter. During the longest episode of atrial tachycardia, the heart rate was 149 beats/min. The patient had been on oral isotretinoin therapy of 0.5 mg/kg/day for the previous 4 months because of nodular acne and was not using any other medication. After consulting with a dermatology physician, isotretinoin was stopped. Holter analysis revealed whole-day sinus rhythm 2 months after the drug therapy was interrupted. Echocardiography revealed gradual regression of pericardial effusion at the follow-up.

Isotretinoin is the most effective treatment options for severe nodular acne, and it belongs to the first generation of synthetic 13-cis reti-

noic acid compounds. Although cheilitis, dry skin, and transient worsening of acne are the most common side effects, adverse effects associated with the nervous, musculoskeletal, ocular, gastrointestinal, hematological, psychiatric, and cardiac systems were also reported.

Cardiac side effects, such as congenital heart disease (3) and arrhythmias, which are frequently atrial arrhythmia, and a case right bundle branch block were reported due to isotretinoin use. Limited reports about adverse cardiac effects are controversial or insufficient to understand the underlying pathology. The therapeutic mechanism of retinoids or their side effects are not well defined. The most common adverse musculoskeletal system events associated with isotretinoin use are calcifications of the tendon and ligaments and myalgias. Isotretinoin was supposed to stimulate degeneration in the synovial cells by influencing the lysosomal membranes of the cells. Therefore, the cells were damaged by becoming vulnerable.

Large doses of retinol result in tissue damage due to the release of certain acid hydrolases and lysosomal enzymes into circulation (4). On the other hand, it was shown that with excess retinol, resting heart rate is increased and action potentials are affected (increased systole duration and decreased diastole duration) because of altered myocardial cell permeability (5). The cell membrane fragility for both myocardial and pericardial cells may be convincing to explain the mechanism of atrial tachycardia and pericardial effusion. Structural changes in the cell membrane affect action potentials, and this may cause atrial tachycardia. Alterations in pericardial cell permeability might also have led to extravasation of fluid to the pericardial space.

It might be useful to question isotretinoin use in cases of pericardial effusion or atrial tachycardia, especially in young patients with dermatological problems, in our daily practice.

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