Letter to the Editor — Editöre Mektup

Hypersensitivity to corticosteroids, Kounis syndrome, myocardial infarction with normal coronary arteries, and triamcinolone

Dear Editor,

We read the article published in the Turk Kardiyoloji Dernegi Arsivi[1] concerning a 52-year-old female patient without a previous history of any illness who developed severe retrosternal pain and an electrocardiographic ST depression on the DII, DIII, aVF, and V3-V6 leads 15 minutes after the intramuscular injection of 40 mg/mL of triamcinolone acetonide (Kenacort-A Retard ampule; Bristol-Myers Squibb, New York, NY, USA) for a rash and itching on the scalp with interest. The troponin level was elevated (0.98 ng/mL), but her coronary arteries were observed to be normal on coronary angiography, and she recovered with antihistaminic therapy. The final diagnosis was variant type I Kounis syndrome.

This report raises the following issues as far as hypersensitivity to corticosteroids, myocardial infarction with non-obstructive coronary arteries (MINOCA)-type Kounis syndrome, and triamcinolone allergy.

1. Corticosteroids are potent anti-inflammatory agents and immunomodulators used in the treatment of allergic manifestations, but they can induce immediate or delayed allergic hypersensitivity reactions. The mechanism of their anti-allergic and anti-inflammatory action includes:[2]

a. Suppression of the release of arachidonic acid from mast cell membranes via the inhibition of phospholipase A2, and the inhibition of eicosanoid biosynthesis,

b. Promotion of cell apoptosis via an autocrine or paracrine pathway involving the up-regulation of the death receptor CD95 and its ligand CD95L on cell membranes that reduce inflammation, and

c. Induction of the synthesis of a family of proteins, such as annexins, also called lipocortins, which have a pivotal role in modulating inflammatory cell activation, adhesion molecule expression, transmigratory, and phagocytic functions.

However, paradoxically, topical corticosteroid-induced delayed reactions are more common (0.5%–5%), whereas immediate reactions to systemic steroids are rare (0.1%–0.3%).[3]

Historically, in the first published report on corticosteroid allergy, 16 patients developed itching, macular rash, paresthesia, tremor of the arms and legs, and nausea and vomiting following intravenous administration of 200mg of hydrocortisone sodium phosphate for the treatment of status asthmaticus.[4]

2. The described patient developed a non-ST elevation myocardial infarction (MI) accompanied by rash and itching of her scalp following triamcinolone administration but angiography demonstrated normal coronary arteries. MINOCA constitutes a new cardiological entity of various causality and pathogenetic mechanisms. Coronary artery spasm, coronary artery dissection, coronary embolism, Takotsubo syndrome, myocarditis, arrhythmias, mild plaque disruption, hypercoagulable status, type 2 MI, and amyloid light-chain amyloidosis are some of the causes. The prevalence of MINOCA in MI patients ranges between 5% and 25%, according to the registries.[5] In a recent report that studied 199,163 MI admissions, 9092 consecutive unique patients had MINOCA. A total of 2147 experienced a new major adverse cardiovascular event and 1254 patients (14%) died during the mean follow-up of 4.5 years.[6]

The report of Yılmaz and Korkmaz[1] adds Kounis hypersensitivity-associated type I variant syndrome, which is a manifestation of endothelial dysfunction or microvascular angina in patients with normal or nearly normal coronary arteries, as another cause of MINOCA. This was omitted in the European Society of Cardiology working group position paper on MINOCA.[7]

3. Triamcinolone is a synthetic pregnane corticosteroid and derivative of cortisol (hydrocortisone) that has been suspected of inducing hypersensitivity and anaphylactic reactions during local, intra-lesional, and intramuscular administration. Triamcinolone acetonide, which was given in the described case, is a more potent type of triamcinolone, about 8 times as effective as prednisone. However, in a recent report[8] concerning a 32-year-old woman suffering from atopic dermatitis, administration of intramuscular tri-

amcinolone induced an immediate hypersensitivity reaction of erythematous patches with a slight elevation and itching on the face, trunk, and both hands that worsened after a therapeutic intravenous injection of dexamethasone.

Therefore, we agree with the authors of this report: extreme care should be applied when this drug is used for treatment and in the event of any reaction, additional tests, such as serum-specific immunoglobulin E tests, radioallergosorbent testing, an enzyme-linked immunosorbent assay, or an fluoroenzyme immunoassay would be helpful in diagnosing the cause of the reaction.

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