LATE LEFT ATRIAL THROMBOSIS OF AN AMPLATZER PATENT FORAMEN OVALE OCCLUDER MAY BE THE RESULT OF KOUNIS HYPERSENSITIVITY-ASSOCIATED SYNDROME

To the Editor:

In the very interesting report by Klotz and colleagues published in this Journal, a patient with a patent foramen ovale that was successfully occluded with an Amplatzer occluder had a large thrombosis develop on the atrial disk of the device 33 months after the initial implantation. Although Klotz and colleagues did not refer to the etiology of thrombus formation, several such causes have been reported, including incorrect device placement, device size, device instability, anticoagulation, and antiplatelet therapy monitoring.

The Amplatzer closure device is made from nitinol, which is a nickel-titanium alloy. Nickel allergy is quite common, and in a recent report the overall prevalence was found to be 24.6%. Titanium hypersensitivity, although low, has been seen in dental procedures and induces implant failure. The described patient received aspirin and warfarin on several occasions, both of which are well-known antigenic compounds. It is known that mast cells bring, on their surface, 500,000 to 1 million IgE molecules, and to degranulate they need 2000 of these molecules, which is a critical number, to make 1000 bridges with antigens. These bridges can be made by antigens of different specificities, as happens in patients with metal device implantation. It looks likely that the more antigens to which a patient with metal device implantation is exposed, the more easily and quickly the degranulation occurs.

Nickel and titanium ions acting as antigens can activate platelets to release proinflammatory, prothrombotic, adhesive, and aggregatory mediators to induce thrombus formation. Platelet activation is taking place through stimulation of some known receptors in the platelet surface, such as receptors for adenosine diphosphate, for thrombocyte, for thrombin, for serotonin, and for epinephrine, and through some less-known receptors, such as receptors for platelet activating factor, for histamine, and for high-affinity low-affinity IgE receptors FcεRI and FcεRII. Thrombus formation after left atrial appendage occlusion with an Amplatzer cardiac plug device can occur months after the procedure. Nickel allergy to intracardiac devices has caused systemic allergic reactions confirmed by patch tests to nitinol, which necessitated the removal of those devices. A device syndrome resembling Kounis syndrome and consisting of chest discomfort, exertional dyspnea, palpitations, asthenia, atrial fibrillation was reported in 8 of 9 patients in a series after Amplatzer implantation. Those patients had positive patch skin test reactions to nickel.

Although the rate of thrombosis complicating such devices might be low, we are still in the learning curve, and additional research is needed to prevent and treat such consequences. We recommend avoidance of metal device implantation in patients with known hypersensitivity or contraindication to any structurally related compound and to drugs these patients would need to take after implantation.

References

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Reply to the Editor:

My coauthors and I read with great interest the Letter to the Editor by Kounis and colleagues regarding our case report of a left atrial thrombosis of an Amplatzer patent foramen ovale (PFO) occluder (St Jude Medical, St Paul, Minn) 33 months after implantation. Kounis and colleagues hypothesized that this thrombosis could the result of the Kounis hypersensitivity-associated syndrome. This syndrome describes, among others, an allergic reaction to intracardiac metal devices (such as PFO occluders and stents) containing nickel or other metals. We appreciate the input from Kounis and colleagues, which might give