Late huge thrombus formation after percutaneous closure of an atrial septal defect with an Amplatzer septal occluder: Implications of Kounis syndrome

To the Editor,

Common causes of thrombus formation following implantation of cardiac devices include incorrect device placement, device size, device instability, hypersensitivity to device components, foreign body reaction, anticoagulation, and antiplatelet therapy monitoring. In the very important paper entitled "Huge thrombus formation 1 year after percutaneous closure of an atrial septal defect with an Amplatzer septal occluder" published in the Anatolian Journal of Cardiology (1), a 17-year-old boy who was diagnosed with an atria septal defect (ASD) developed a huge mobile thrombus one year after an Amplatzer septal occluder device implantation. The thrombus and device were surgically removed, and examination of the thrombus revealed the presence of peripheral blood elements and fibrin but not acute or granulomatous inflammation. Although the authors did not describe any symptomatology or electrocardiographic findings, it is presumed that the peripheral blood elements in the removed thrombus were red cells, lymphocytes, monocytes, and multinucleated leukocytes including neutrophils, basophils and eosinophils.

This case raises important questions concerning the etiology of thrombus formation.

The Amplatzer septal occluder contains nitinol, an alloy composed of 45% titanium and 55% nickel. These two metals can release metal ions while they are embedded in the atrial septal defect and are directly in touch with the blood stream. Such an-

ions can react with high- and low-affinity IgE antibody receptors, the known FCγRI, FCγTII, FCεRI, and FCεRII receptors, situated on platelet surface and trigger the thrombotic cascade (2). Implanted devices, therefore, constitute an ideal surrounding for endothelial damage and dysfunction together with hemorheologic changes and turbulence as well as platelet dysfunction, coagulation, and fibrinolytic disturbances. Metals and polymers are great sensitizers that are able to produce corresponding IgE antibodies. Nickel, chromium, and cobalt induced hypersensitivity reactions in 14%, 4%, and 9% patients in the United stated and in approximately 20%, 4%, and 7% patients, respectively, in Europe (3).

In a report of patients who were allergic to nickel, as evidenced by cutaneous patch skin tests and suffering from interatrial shunts and having full nitinol Amplatzer occluder device and the low nitinol Premere closure implanted, a Kounis syndrome-like disease was developed in eight of nine patients (4). The symptoms these patients experienced were chest discomfort, exertional dyspnea, asthenia, palpitations, worsening of migraine headaches, and mild leukocytosis between postoperative days 2 and 3. All symptoms were resolved within one week with prednisone and clopidogrel administration. Interestingly, in the same report, two patients with negative skin patch testing who had occluder system implantation had postoperative atrial fibrillation that was resolved with antiarrhythmic treatment.

Thrombus formation can occur up to 5 years after Amplatzer device implantation, but this is rare. This can be explained by the fact that hypersensitivity inflammation goes through three phases: the early phase that lasts minutes; the late phase that lasts from 2 h to 2 days; and the chronic phase that follows a continuous, persistent, and repetitive allergen exposure and lasts as long as the allergen is present.

Thrombus formation on the Amplatzer device has emphasized the need for critical attitude in decision making in percutaneous closure of patent ovale (5). We therefore believe that careful history of contraindications and hypersensitivity with monitoring of inflammatory mediators and lymphocyte transformation studies would be helpful before such device implantation.

Nicholas G. Kounis, Dimitrios Lianas[1], George N. Kounis[2], George D. Soufras[1]
Medical Sciences Western Greece Highest Institute of Education and Technology, Achaia-*Greece*
[1]Patras State General Hospita, Patras, Achaia-*Greece*
[2]University Hospital of Patras, Achaia-*Greece*

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Address for Correspondence: Nicholas G. Kounis, MD
Queen Olgas Square, 7 Aratou Street,
Patras 26221-*Greece*
E-mail: ngkounis@otenet.gr

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