

Severe Allergic Dermatitis After Closure of Foramen Ovale With Amplatzer Occluder

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Allergic reaction to nitinol is rarely reported, and its incidence, symptoms, and course have not been clearly defined. We report an occurrence of severe progressive generalized exanthema 3 days after the implantation of an Amplatzer occluder for a patent foramen ovale, with symptoms disappearing immediately after surgical removal of the device 3 months later. The risks and possible prevention of allergic reaction to nickel and especially to titanium are discussed.

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Metal allergy, particularly to nickel, is a frequent cause of allergic contact dermatitis. Nickel allergy was even a subject of European Union regulatory intervention [1]. Allergic reaction to nitinol has been described rarely, and its incidence, symptoms, and course have not been clearly defined. The development of a generalized allergic dermatitis after insertion of an Amplatzer occluder and stabilization after systemic corticosteroid administration has been described [2]. Other symptoms of allergic reaction to nitinol include severe chest pain immediately after device insertion, resistant to any treatment and subsiding after removal of the occluder [3]. Increasing numbers of reports have been published describing migraine episodes and palpitations in patients with inserted Amplatzer occluder, potentially related to contact hypersensitivity to nickel [4]. In a published case series of 9 patients with proven symptomatic and instrumental allergies to nickel (as evidenced by cutaneous patch skin tests), the symptoms evolving on the second and third postoperative days tended to resolve within 2 week of prednisone therapy [5]. Cases of allergic reactions to titanium have also been documented, specifically, reactions to titanium coating of pacemakers, repeatedly implanted because of sterile wound necrosis, which

subsided after the insertion of a gold-coated pacemaker [6]. Similar symptoms referred to as Kounis syndrome have been described after intracoronary stent implantation [7].

We report here an occurrence of severe progressive generalized exanthema after the implantation of an Amplatzer occluder for a patent foramen ovale, which later had to be removed surgically because of intractable symptoms. The patient provided written informed consent with publication.

A 40-year-old woman with a history of moderately dry skin in the cubital regions during childhood, who had never experienced any contact allergy to metals or cosmetic products, underwent a minor gynecologic operation complicated by ischemic stroke and left-sided symptoms that resolved completely. She had undergone a thorough clinical examination, which revealed a patent foramen ovale as the only possible cause of her stroke. The patient was eligible for occluder insertion through a transcatheter approach. On October 11, 2010, an Amplatzer occluder was implanted, and the patent foramen ovale was successfully closed. Three days after the implantation, a generalized exanthema developed, beginning at sites typical for atopic dermatitis but spreading progressively, being most pronounced on the trunk. The exanthema was bright red, itching, felt like a burn or sunburn, and worsened with movement, physical activity, and in cold (Fig 1). The patient had undergone epicutaneous tests revealing a strongly positive reaction to nickel sulfate (vesicular lesions spreading beyond the test area). Unfortunately, epicutaneous testing for titanium allergy was not performed. With respect to the severity of her symptoms, a combination of local and systemic corticosteroids and antihistamines was prescribed, but the patient's problems did not resolve. Finally, a Melisa test [8] revealed

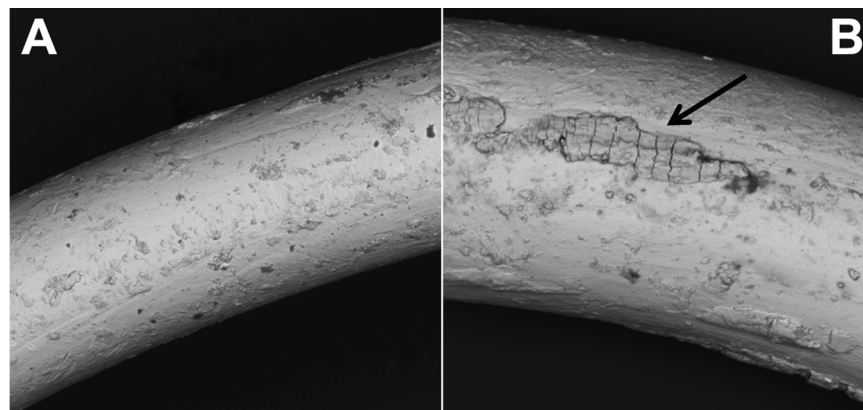


Fig 1. Severe generalized allergic skin reaction, detail of abdomen.

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Fig 2. Electron microscope (VEGA-SEM, TESCAN, a.s., Brno, Czech Republic) imaging of explanted occluder demonstrating (A) damage to the struts of the device with (B) detail of eroded part (black arrow).



a hypersensitive reaction to a wide range of metals, the strongest response being to inorganic mercury (stimulation index of 58.3), titanium trichloride (30.9), titanium dioxide (11.2), and nickel (3.5); a positive reaction is considered to be above 2.0. At that time, removal of the occluder had to be considered because of the patient's worsening skin problems, fatigue, and stress associated with the debilitating symptoms. The patient also started to report sensitivity (contact dermatitis) to titanium earrings and described having burning sensations in the oral cavity after consumption of certain foods (probably resulting from nickel or titanium contained therein). Owing to the progressive nature of the patient's problems, the operation was performed in January 2011, and the Amplatzer occluder was successfully removed without any complications. Three days after the removal, the patient's skin lesions resolved completely without any relapse. She remained completely asymptomatic more than 1 year after explantation of the occluder.

Comment

With respect to the straightforward relationship between the rash development and nitinol occluder insertion and resolution of all symptoms after the occluder removal, we conclude that the patient's problems were most likely attributable to an allergic reaction to nitinol. As per our results, the patient was simultaneously hypersensitive to nickel and titanium. Analogous results with positive Melisa test reactions to titanium have been observed in patients with hypersensitive reactions to titanium pacemaker coating or titanium joint replacements. After titanium removal, Melisa test results can normalize (6). The case described here, of a confirmed allergy to titanium in relation to the Amplatzer occluder, is the first case described in the literature as far as we know.

Although the manufacturer of the Amplatzer occluder claims that it is safe to use in patients with allergies to metals, experimental studies have confirmed that nickel serum levels rise with maximum values reached approximately within 1 month after implantation, and during the following 2 months they gradually drop again [9]. Therefore, the safety of the occluder in

sensitive patients remains questionable. Moreover, the implanted material inevitably undergoes a breakdown, leading to increased exposure to released metal ions, as demonstrated by an electron microscope imaging of the removed occluder in our case (Fig 2).

Owing to the severity of the allergic reaction in the case described here, it was necessary to remove the nitinol occluder through an open-heart procedure with extracorporeal circulation, a procedure with considerable risks. This raises the question of how to prevent similar cases. Allergy to metals is currently being assessed in some patients before the implantation of teeth in dentistry and before joint replacement in and orthopedics. Nevertheless, the patient in our case had no history of contact allergy to metals. Sensitization of the patient to nickel, titanium, or both could occur after previous encounters with food or environmental aggressors. Therefore, an allergic reaction might have been activated after the insertion of the nitinol occluder in the bloodstream. Unfortunately, it is not possible to resolve whether testing for allergies before insertion of the occluder could have detected the risk of subsequent allergic reaction.

Addendum

The case had been presented as an oral abstract at the 2011 meeting of the Czech Society of Allergy and Clinical Immunology and reported in Czech language with an English abstract [10].

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