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Nickel Allergic Reaction post-Transcatheter Atrial Septal Defect Device Closure: A Case Report

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ABSTRACT

Background: Although transcatheter device closure of atrial septal defect (ASD) is a common, safe, and effective interventional cardiac procedure, some adverse effects have been reported including device migration, cardiac erosion, and nickel allergic hypersensitivity reaction.

Objective: Here we report on an eleven-year-old boy who experienced a nickel allergic reaction after transcatheter ASD device closure, and we report on how we managed this critical situation.

Case Report: Here we report on an eleven-year-old boy who experienced a nickel allergic reaction after transcatheter device closure of a large ostium secundum ASD with a 34-mm Hyperion™ ASD occluder (Comed, Netherlands). Ten days post-procedure, the patient complained of fever, severe allergic reaction; dermatitis, and pruritic rash on his face, arms, trunk, and genital area. Dug allergic reaction and infective endocarditis was excluded. Immediately the patient was managed as a case of device-induced nickel allergic reaction. All manifestations were resolved completely after one week with high doses of dexamethasone and clopidogrel 75 mg orally for 6 months. Subsequent follow-up for 6-month post-procedure showed that the device was properly seated with no recurrence of the nickel allergic symptoms.

Conclusions: Nickel allergy and device allergic syndrome must be considered during transcatheter device closure. Despite still controversial, confirmation of a nickel allergy pre-procedure with the patch testing or with the device itself may be useful. Nickel-avoidance strategies using modified devices could be considered a treatment option for patients with nickel allergy.

Keywords: Nickel allergy, Nickel allergic reaction, Atrial septal defect, Occluder devices, Transcatheter atrial septal defect device closure.

INTRODUCTION

In patients with adequate anatomy, transcatheter closure of atrial septal defects (ASDs) is a common, safe, and successful interventional cardiac catheterization technique. Although device closure is safe and successful, there have been reports of device migration, embolization, cardiac erosion, and allergic hypersensitivity reactions [(1,2)].

The main component of the most often used ASD occlusion devices is nitinol, a nickel-titanium alloy. Nickel is the most allergenic of the nitinol alloys, followed by titanium. Nickel allergy affects up to 30% of the general population, with the greatest rates seen in young females under the age of 30. Nickel allergy causes a pruritic rash and dermatitis at the site of nickel contact, and it can happen even after occlusion devices have been implanted [(3,4)].

Here we report on an eleven-year-old boy who experienced a nickel allergic reaction after transcatheter ASD device closure, and we report on how we managed this critical situation.

CASE REPORT

An eleven years old boy, weighing 31 Kg, with a body surface area (BSA) of 1.3, presented with grade II dyspnea, with a systolic ejection murmur on the left upper sternal border. Transthoracic and transesophageal echocardiograms were performed and revealed a large ostium secundum ASD that measured 32 x 30 x 29 mm in diameters, with a left to right shunt, a sufficient atrioventricular rim of 8 mm, a sufficient inferior vena cava rim of 9 mm, a deficient flimsy posterior rim of 3 mm, and a deficient superior-posterior rim of 4 mm, with a total septum of 58 mm (Figure 1).

The right side was dilated with a right ventricular diastolic diameter (RVDD) of 35 mm with mild tricuspid valve regurgitation (TR) and with normal right ventricular systolic pressure (RVSP) of 19 mmHg.

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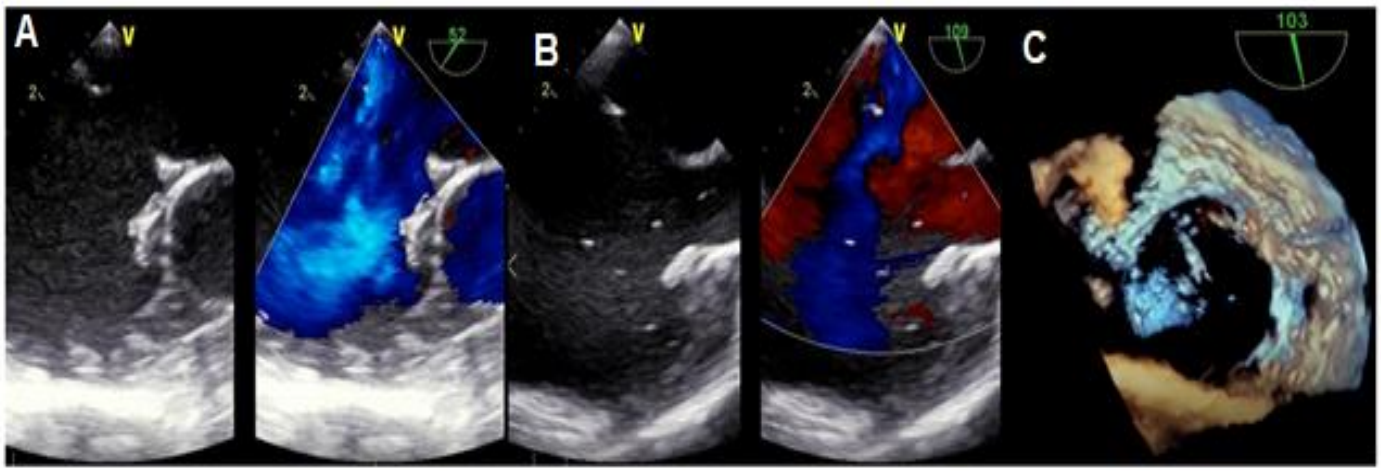

Figure (1): Transesophageal echocardiography of a large ostium secundum atrial septal defect (ASD), measuring 32 x 30 x 29 mm in diameters, with a left to right shunt. A: Short axis view. B: Bicaval view. C: Three-dimensional transesophageal echocardiography right atrial perspective.

The patient was admitted for closure of this large secundum ASD. Firstly, the patient underwent an invasive hemodynamic assessment that revealed an increased pulmonary to systemic flow (QP/QS) ratio of 2.3 with a normal mean pulmonary artery pressure (mPAP) of 12 mmHg. Therefore, the patient experienced successful transcatheter-transesophageal-guided closure of the large ASD using the right upper pulmonary vein (RUPV) technique with a 34-mm Hyperion™ ASD Occluder (Comed, Netherlands). The procedure was uneventful, with no residual shunt, or device encroachment on any of the cardiac structures (Figure 2).

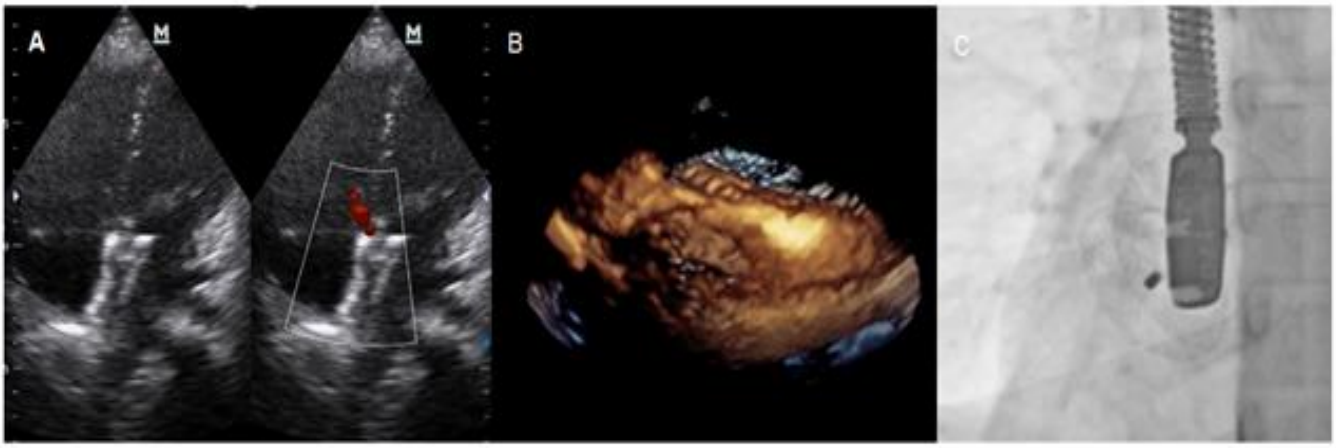

Figure (2): Secundum atrial septal defect closure (ASD) that closed with a 34-mm Hyperion™ ASD Occluder (Comed) with no residual shunt or device encroachment on any of the cardiac structures. A: Transthoracic echocardiography. B: Three-dimensional transesophageal echocardiography. C: Fluoroscopy.

The patient was discharged the day next to the procedure day after a thorough transthoracic echocardiography evaluation of the proper positioning of the device, the absence of any residual shunt, the exclusion of encroachment on any of the cardiac structures, and the exclusion of pericardial effusion. Acetylsalicylic acid 75 mg oral was started the night before the procedure and was prescribed for 6 months after the procedure.

Three days post-procedure, the patient was cleared clinically and showed no abnormality in physical examination. Ten days later, the patient complained of fever, and allergic reaction (severe dermatitis and pruritic rash) on his face, arms, trunk, and genital area (Figure 3).

Figure (3): Allergic reaction (severe dermatitis and pruritic rash) on the patient face, arms, and trunk.

A detailed history of the previously taken medications with any previous allergic reactions was completely negative. Additionally, the patient was not previously known to have a nickel allergy. Physical examination unless pruritic rash was unremarkable. All laboratory tests were performed and were within normal ranges except for a slightly elevated estimated sedimentation rate (ESR) and a mild eosinophilia. All septic workup has been carried out and revealed negative aerobic and anaerobic blood cultures. Multiple chest X-rays and electrocardiograms did not display any abnormality. Repeat echocardiography revealed a well-seated device with no residual shunt, erosion, pericardial effusion, masses, or any other complications.

Three differential diagnoses have been proposed; device (Nickel) allergic reaction, dug (Acetylsalicylic acid) allergic reaction, and infective endocarditis. The drug allergic reaction was ruled out because the patient had not received any drugs before, except the acetylsalicylic acid which had been safely administered in other previous situations, and the dermatological consultation cleared any doubt for drug allergy. Additionally, infective endocarditis was excluded because the patient had insufficient Duke's criteria, negative aerobic and anaerobic blood cultures, with the subsiding of the fever only one day after intravenous (IV) injections of antibiotics with the ordinary doses (amoxicillin/clavulanate: 30 mg/kg/day IV divided q12hr and gentamicin 3-5 mg/kg/day IV divided q8hr).

Since the device (Nickel) allergic reaction was the first and the most serious possibility, the patient has initially managed as a case of device-induced nickel allergic reaction. The patient was admitted immediately to the cardiac care unit (CCU), the cardiac surgery team was informed, and the operating theater was on hold. All medications for anaphylaxis (Adrenaline, corticosteroid, antihistaminic) were also prepared. Cutaneous testing was performed using a 25-mm Amplatzer™ PFO Occluder that was applied to a clear area of the patient's chest and revealed a positive test with an increase in the pruritic rash (Figure 4).

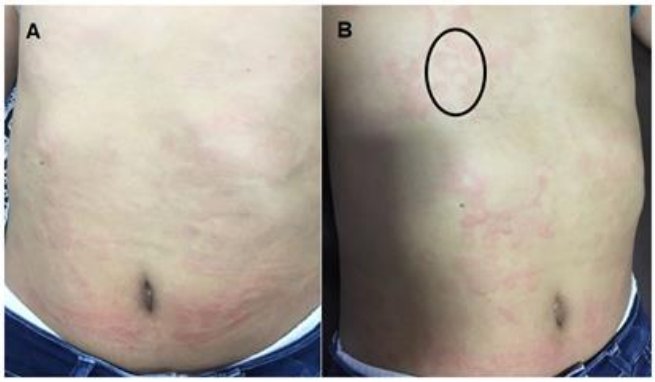

Figure (4): Positive cutaneous testing using a 25-mm Amplatzer™ PFO Occluder.

High doses of dexamethasone were started immediately and were tapered gradually over 5 days (Days 1 and 2: 8 mg IV divided q12hr, Day 3: 3 mg/day IV divided q12hr, Day 4: 1.5 mg/day IV divided q12hr, Day 5: 0.75 mg/day single dose in the morning). Aspirin was replaced by clopidogrel 75 mg orally for 6 months. In addition, an antihistamine treatment (Pheniramine maleate) was administered. Intravenous antibiotics at regular doses (amoxicillin/clavulanate: 30 mg/kg/day IV divided q12hr and gentamicin 3-5 mg/kg/day IV divided q8hr) were started after blood culture specimen collection. Also, an intravenous infusion of fluids at a rate of 5 mL/kg/day was administered by the patient.

Fortunately, two days later, symptoms and signs started disappearing and the skin rash was completely dissolved after one week. The patient was discharged after the complete resolution of all symptoms and signs (Figure 5). A subsequent follow-up for 6 months post-procedure showed that the device was properly seated without recurrence of the nickel allergic symptoms.

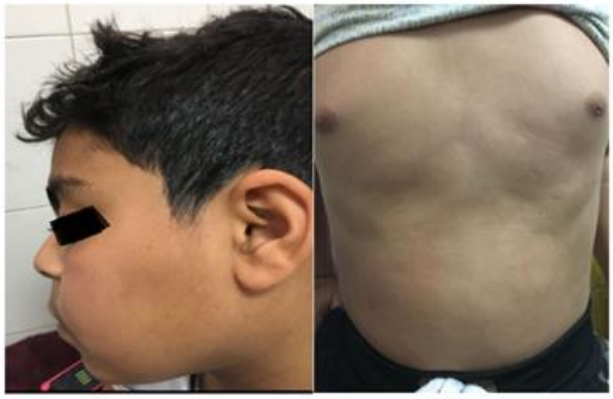

Figure (5): Resolving of the skin rash after medical management.

Ethical consent:

Approval of the study was obtained from Tanta University Academic and Ethical Committee. Informed written consent was obtained from the parents of the patient for publication. This work has been carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

DISCUSSION

The incidence of cutaneous nickel allergy has been more recorded likely due to the increase in body piercings, jewelry, and electronic devices [5,6]. Likewise, the implanted metal devices for multiple medical/surgical indications have increased the interest in the biocompatibility of adverse metal reactions.

Most devices used in atrial septal defect (ASD) and patent foramen ovale (PFO) occlusion are made of a nitinol frame or mesh. It is a metal alloy of mostly equal atomic percentages of nickel and titanium (Mostly 55% nickel, 45% titanium). In physiological solution, nitinol develops a titanium oxide coating with a surface layer of calcium phosphate. This coating encourages epithelization and reduces the chance of thrombus formation. The Manufacturer and User Facility Device Experience database reported that the allergic reaction rate post-implantation of atrial septal occluders (ASOs) was 1.4% (10 of 705 ASO implantations) [7]. Correspondingly, the Congenital Cardiovascular Interventional Study Consortium (CCISC), recorded that the nickel allergy incidence after congenital cardiac defects closure with nitinol-containing devices was 2.06% (33 of 1600 device implantations) [8]. In the 3 randomized trials on PFO closure published in 2017, only 1 of 2,000 patients had a device-related allergic reaction without the need to explant the device in any of the three trials [9-11]. It remains a rare and poorly defined phenomenon.

Despite the paucity of literature describing the immunologic mechanism in device hypersensitivity, it is suggested to be a predominantly type IV hypersensitivity with delayed T-cell type reaction [12]. Specific to ASD and PFO devices, while the mechanism remains unknown, elution of nickel was observed to be related to the slow and transient release of nickel into the systemic circulation with an elevation of blood nickel levels to reach 2-5 folds within 4-6 weeks after insertion of nickel-containing devices, with a gradual decline to baseline within 4-6 months as well [13-16].

Reactive manifestations can occur from 2 days to months after implantation. The most common manifestations of nickel hypersensitivity include rash/urticaria, dyspnea, atypical chest pain, fever, new or increased frequency of headaches/migraines, hypersensitivity pericarditis, pericardial effusion, cardiac tamponade, and device syndrome [7,8,13,17]. To diagnose an allergic reaction to nickel, cutaneous testing is used and relies on the principle of type IV hypersensitivity reaction. The patch test is used to detect whether a specific element causes skin allergic inflammatory reaction. The device test is a new method used also to determine the nickel allergy. Two studies found that a positive nickel patch test before device implantation was linked to the allergic symptoms after device implantation [16,18]. However, another study showed that the allergic symptoms after device implantation were similar between nickel allergic and non-allergic patients, but this trial was a retrospective one, and the number of patients was insufficient [19]. Unfortunately, pre-implant testing is neither recommended nor reliable; due to the uncertain relevance of the positive patch test and the limited alternatives for device materials. Additionally, the negative pre-implant testing only reflects the current state of allergy and does not predict the future hypersensitivity that may occur after device implantation [12].

In one cohort study that experienced ASDs and PFOs closure with Amplatzer™ (Abbott Vascular, IL, USA) occluders showed that nickel allergy symptoms were associated with a new-onset or aggravation of headache/migraine that was alleviated with clopidogrel. They explained the increased headaches/migraines by the local inflammatory response to the implanted device with the formation of platelet adhesions that could travel to the brain and supported this by the alleviation of headache by the usage of clopidogrel. The authors also noted that these events lasted for 6 months and then have been resolved [16]. Most allergic reactions can be relieved by medical therapy. However, patients who develop respiratory distress, severe refractory symptoms suggestive (device syndrome), or systemic hypersensitivity reaction that could not be relieved by medical therapy have been reported in some cases and the device had to be surgically removed [7,17,20,21]. In a retrospective analysis of explantation rates for PFO/ASD occluders, 38/13736 (0.28%) of patients underwent device removal [22].

Secondary allergies to the Amplatzer™ (Abbott Vascular, IL, USA) [7,23,24], PFOStar (Cardia Inc., Burnsville, Minnesota) [13], and Gore Helex (WL Gore & Associates, Inc.) [14] devices have been previously described. In vitro elution of nickel from 3 different devices; Amplatzer™, Gore Helix, and Gore Septal showed that the Amplatzer™ had the highest nickel levels [25]. A recent study suggested that both Amplatzer™ and Gore Helix devices are vulnerable to this complication [17]. Nickel-avoidance strategies using modified devices have been anticipated to be safe and effective; platinum-coated device (Cocoon septal occluder) [26], and expanded Polytetrafluoroethylene (PTFE) covered Gore Septal Occluder (GSO) (WL Gore & Associates, Inc.) [25].

In patients with previously known nickel allergy, **Rigatelli *et al.*** [18] described their experience with implantation of Amplatzer™ and Premere occluder devices in 9 patients with a proven allergy to nickel. Eight out of nine patients developed nickel allergic reactions. These symptoms lasted for a median duration of 11.5 days. All of them were treated with prednisone and clopidogrel [18]. Also, in a woman with a history of nickel allergy, successful use of Gore septal occluder for PFO closure has been experienced without undesirable reaction [27].

In 2016, a 28-year-old woman with a history of nickel allergy had an ASO device test for allergy using 2 different ASO devices: Amplatzer™ (Abbott

Vascular, IL, USA) and Lifetech CeraFlex ASD Occluder (Lifetech Scientific Corporation, Shenzen, China) ASO. After 48 hours, mild swelling and erythema appeared at the site of the Amplatzer™ ASO device only. ASD was closed with a 30-mm Lifetech Cera ASO device under steroid and antihistaminic therapy. The patient has continued on aspirin 100 mg and clopidogrel 75 mg for 6 months. At 1-year follow-up, the patient remained asymptomatic [28]. **Cammalleri *et al.*[29]** reported the successful use of the Atriasept II (Cardia, Eagan, MN, USA), a device with a lower content of nitinol, for closure of patent ductus arteriosus in 4 patients with severe nickel allergy.

CONCLUSIONS

Nickel allergy and device allergic syndrome must be considered during transcatheter device closure. Despite still controversial, confirmation of a nickel allergy pre-procedure with the patch testing or with the device itself may be useful. Management is difficult, starting from prednisone and clopidogrel therapy to surgical explantation in patients with respiratory distress, device allergic syndrome, and failed medical management. Nickel-avoidance strategies using modified devices could be considered a treatment option for patients with nickel allergy.

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