



## When it is not an infection: metal allergy after the Nuss procedure for repair of pectus excavatum

Gregory D. Rushing<sup>a</sup>, Michael J. Goretsky<sup>a,b,\*</sup>, Tina Gustin<sup>b</sup>,  
Maripaz Morales<sup>c</sup>, Robert E. Kelly Jr<sup>a,b</sup>, Donald Nuss<sup>a,b</sup>

<sup>a</sup>Department of Surgery, Eastern Virginia Medical School, Norfolk, VA 23507, USA

<sup>b</sup>Division of Pediatric Surgery, Children's Hospital of the Kings Daughters, Norfolk, VA 23507, USA

<sup>c</sup>Division of Allergy and Immunology, Department of Pediatrics, Norfolk, VA 23507, USA

### Index words:

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Atopy;  
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### Abstract

**Purpose:** Increasing use of implantable bars for minimally invasive pectus excavatum repair has introduced metal allergy (nickel and chromium) to pediatric surgeons. Metal allergy is a well-recognized entity in neurologic, orthopedic, and craniofacial surgery. This study was performed to evaluate metal allergy and its effects on treatment with the Nuss procedure in 862 patients.

**Methods:** After institutional review board approval, we undertook a retrospective review of a prospectively gathered database of patients undergoing the Nuss procedure. Metal allergy was diagnosed either with the use of dermal patch or clinically, based on rash, fever, elevated erythrocyte sedimentation rate, cultures, and pathology specimens. Data collection included demographics, an allergy to jewelry, and history of atopy. Clinical outcomes including need for reoperation, removal of stainless steel bar, and replacement with titanium bar were evaluated.

**Results:** Over an 18-year period (1987-2005), 862 patients underwent the Nuss procedure. Nineteen (2.2%) were diagnosed with metal allergy, with an average age of 14.7 years (9-23 years). Eighteen (95%) were males. A history of atopy was present in 9 (56%) patients. Ten (63%) patients presented with rash and erythema, 1 (6%) with granuloma, 5 (32%) with pleural effusion, and 3 (15%) were diagnosed on preoperative screening. Stainless steel bars were removed because of allergic skin breakdown in 3 patients, with 2 patients requiring replacement titanium bars. In all 3 of these patients, symptoms resolved after removal of stainless steel bars. Titanium bars were placed in the 3 patients who were diagnosed preoperatively with metal allergy, without event.

**Conclusions:** Allergy symptoms often are misdiagnosed as infection, but require different treatment. If a history of metal allergy or atopy is suggested preoperatively, the patient should be tested for metal allergy, and if positive, a titanium bar used. Because the consequences of metal allergy may include the need to replace the bar, pediatric surgeons should be aware of this occurrence.

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\* Corresponding author. Department of Surgery, Eastern Virginia Medical School, Children's Hospital of the Kings Daughters, Norfolk, VA 23507, USA. Tel.: +1 757 668 7703; fax: +1 757 668 8860.

E-mail address: michael.goretsky@chkd.org (M.J. Goretsky).

Increasing use of implantable devices for surgical corrective procedures has led to a new awareness of metal allergies. Jewelry and dental procedures are no longer the sole cause of metal implants. Craniofacial, neurosurgical, orthopedic, and other surgeons often perform corrective

procedures with metal devices. Implants occasionally cause metal allergies. As many as 13% of patients are sensitive to nickel, cobalt, or chromium [1-3]. Physicians who care for patients who undergo these procedures need to be aware of this potential complication.

Metal allergy (specifically nickel) is the most common contact allergy in the United States and Europe [4,5]. The use of nickel jewelry in these populations is thought to be the main cause of allergen exposure. This is typically a delayed type IV hypersensitivity reaction, and T lymphocytes are the key to a patient's reaction. Both CD8<sup>+</sup> and CD4<sup>+</sup> T cells are responsible for the cytotoxic and inflammatory aspects of tissue damage, respectively [6-8]. In healthy people whose skin test is negative for nickel allergy, nickel-reactive CD4<sup>+</sup> T cells are present, but the corresponding specific CD8<sup>+</sup> T cells are absent [9]. This finding supports the theory that nickel allergen-specific CD8<sup>+</sup> T cells are required to develop an allergic reaction after exposure to nickel. More recent evidence suggests that some CD4<sup>+</sup> T cells actually are regulatory and help suppress nickel antigen stimulation [10,11].

The link between metal allergies and history of atopy has been described in the literature, although the exact association has not been fully elucidated. Atopy consists of allergic rhinitis, asthma, and eczema with varied clinical manifestations. Rash can present as urticarial or eczematous. Symptoms of inflammation such as pain, warmth, erythema, and swelling over the implant can be seen. Thoracic placement can cause symptoms of pericarditis or pleural effusion.

Nickel allergy has been extensively studied in European communities. On that continent, laws were enacted to reduce its occurrence. Significant decreases in nickel allergy were seen in Danish teenagers after nickel content in jewelry was limited [12,13]. The amount of nickel released was

limited to 0.5  $\mu\text{g}/\text{cm}^2$  per week from products such as earrings, bracelets, necklaces, wristwatches, and costume jewelry. The European Union adopted similar mandates in 1994 [14]. Exposure to nickel can also be seen in patients who work in manufacturing or industrial jobs. No such measures to limit nickel exposure have been adopted in the United States.

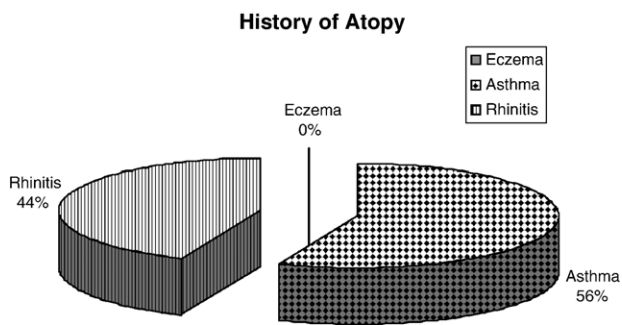
Our interest in metal allergy began with patients undergoing the minimally invasive Nuss procedure for repair of pectus excavatum. In this procedure a stainless steel bar is placed under the sternum for correction of the thoracic defect. A few patients developed complications during the postoperative period that we originally thought were either infectious or nonspecific. We discovered that these patients had a metal allergy. These patients made us question the optimal screening and treatment methods for metal allergy in the pediatric population undergoing minimally invasive repair of pectus excavatum with a metal bar.

## 1. Materials and methods

This study is a retrospective review of patients who presented with concerns for metal allergy after undergoing minimally invasive repair of pectus excavatum by the pediatric surgery service at Eastern Virginia Medical School, a tertiary referral center. Institutional review board approval was obtained for this study (01-05-EX-0175). All data collection complied with HIPAA regulations. Inclusion criteria were (1) repair of pectus excavatum with the minimally invasive Nuss procedure and (2) concern for metal allergy either on preoperative screening or postoperative follow-up. Concerns for metal allergy arose when symptoms of fever, rash, erythema, effusion, and granuloma



Fig. 1 The TRUE test skin patch system.



**Fig. 2** History of atopy in our patient population who were diagnosed with metal allergy.

formation were noted, without obtainable evidence of infection or positive cultures. Exclusion criteria included the following: (1) repair of pectus excavatum without use of metal implants, (2) preoperative screening revealed no metal allergy, (3) postoperative follow-up was uneventful for metal allergies, and (4) symptoms were found to have infectious or other causes by culture or pathology.

Epidemiologic information was collected including age and sex. History of metal or jewelry allergy was recorded. Atopic history (ie, eczema, Allergic rhinitis, or asthma) as well as food allergy were documented. The method of allergy diagnosis including thin-layer rapid use epicutaneous (TRUE) patch test (Fig. 1), metal sensitivity disc, pathology reports, and clinical outcomes were included. The need for reoperation, stainless steel bar removal, and replacement with titanium bars was evaluated.

Statistical analysis was performed using commercially available statistics software (MedCalc, Mariakerke, Belgium) with the  $\alpha$  value set at .05 for significance. Epidemiologic information was compared using a  $\chi^2$  analysis for comparison of proportions. The effects of a history of atopy, food allergy, and prior allergy to jewelry on current metal allergy diagnosis were analyzed using analysis of variance and regression analysis.

## 2. Results

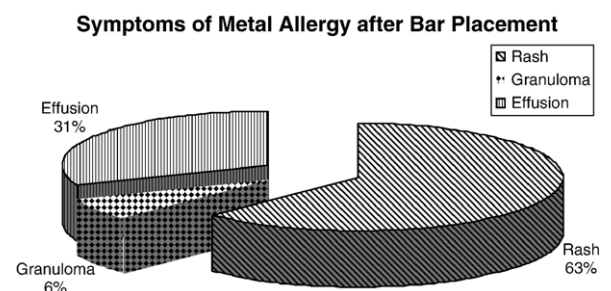
During an 18-year period (1987-2005), 862 patients underwent minimally invasive repair of pectus excavatum. Of these 862 patients, 19 had suspected metal allergy on preoperative screening or postoperative follow-up, resulting in a 2.2% incidence. The average follow-up time was 25 months (range, 1-67 months). Ninety-five percent (18) of patients diagnosed with metal allergy were males ( $P = .513$ ), with an average age of 14.7 years (range, 9-23 years) ( $P = .705$ ). Some history of atopy (eczema, rhinitis, or asthma) was present in 56% (9) of patients ( $P = .001$ ). Forty-four percent (7) had a history of rhinitis ( $P = .003$ ), 56% (9) had a history of asthma ( $P = .001$ ), and none had a history of eczema (Fig. 2). Sixteen percent (3) of the patients had an allergy to jewelry or braces ( $P = .003$ ), with 0.5% (1)

having food allergies ( $P = .146$ ). Sixty-three percent (10) presented with a rash and erythema ( $P = .001$ ), 6% (1) with a granuloma ( $P = .876$ ), and 32% (5) with a pleural effusion ( $P = .003$ ) (Fig. 3). Fifty-six percent (9) presented with more than one of the above symptoms ( $P = .001$ ). Time to presentation of symptoms averaged 40 days (range, 5-140 days). The average erythrocyte sedimentation rate was elevated at 34 mm/h; however, this laboratory value was only available for 6 patients. In patients with granulomas, effusions, or bar revisions in the operating room, tissue cultures were taken. No diagnostic organisms grew from any cultures taken.

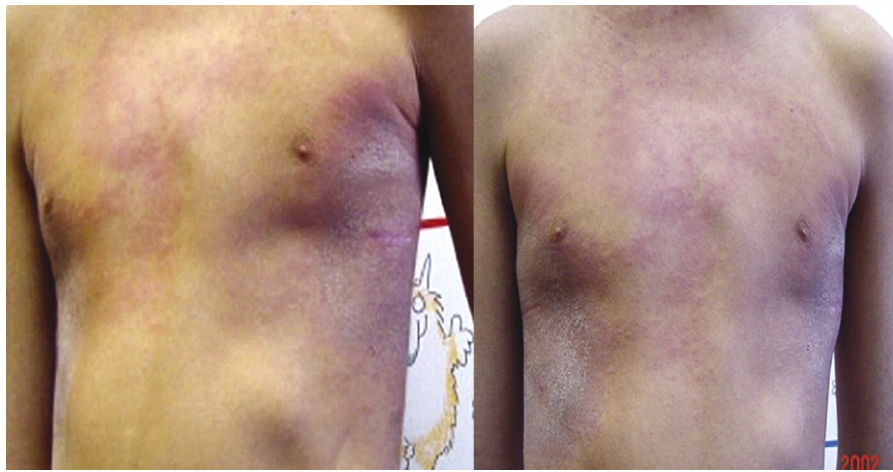
Titanium bars were placed in 3 patients who were diagnosed with metal allergy before surgery. Stainless steel bars were removed because of allergic skin breakdown in 3 patients and, in 2 of these patients, titanium bars were inserted instead. The third patient had no bar replacement with good resolution of his pectus excavatum and allergic manifestations. In all 3 of these patients, symptoms resolved after removal of the stainless steel bars.

## 3. Discussion

The 2.2% incidence of metal allergy seen in our patient population is far less than the 13% traditionally reported in the orthopedic literature [15-17]. However, those studies investigated metal hip joints, not static metal implants such as the pectus bar implant used for our patients. Ninety-five percent of the patients with allergies in our study population were males. Pectus excavatum affects males predominantly, which is why this might not have reached statistical significance. Overall, the 82% of patients we operate on for pectus excavatum are male. The most common symptoms presenting in allergic patients were erythema and rash (Fig. 4). Granuloma formation did not reach statistical significance in association with metal allergy in our study. However, when this symptom was combined with others, as was the case in 56% of our patients, these symptoms together were significantly associated with metal allergy. We also found that a history of atopy was significant for predicting metal allergy in our patient population.



**Fig. 3** Symptoms seen in patients in whom stainless steel bars were placed before knowledge of metal allergy.



**Fig. 4** A patient with erythema and rash after placement of stainless steel bar.

Although many of these symptoms are nonspecific, we discovered that what we thought were infections either did not grow anything in culture or had atypical skin manifestations. These patients had allergies to the bar, and a short course of steroids was sometimes helpful in confirming the diagnosis if their symptoms disappeared with steroid treatment.

Because of the above experience with metal allergy, we have implemented a screening program for our patients within the last year. On initial presentation to our office, a screening history and physical examination evaluate the patient for allergies to (1) jewelry, (2) orthodontic braces, (3) metal buttons/snaps on clothing, and (4) food. In addition, signs/symptoms of atopy are evaluated (allergic rhinitis, eczema, asthma). If any of these indications are found in the patient history, a dermal patch test is performed. The TRUE test contains 23 allergens and allergen mixes that have been reported to be responsible for up to 80% of allergic contact dermatitis [18] (Fig. 3). The most common metal allergies (nickel and cobalt) are components of this test, and it is the only patch currently available commercially in the United States. In addition, several patients have presented to us already diagnosed with some form of metal allergy, usually nickel.

Any patient diagnosed with metal allergy should have a custom-made titanium bar implanted because titanium does not produce allergic reactions. These bars are at times more expensive than stainless steel. Part of the expense of the titanium bars is caused by the need to bend them with a computer-assisted manufacturing technique, to fit the patient's computed tomography scan, because they are not malleable. In addition, the surface of the bar must be finished to a mirror-smooth surface to prevent tissue ingrowth, which is not necessary for stainless steel.

Metal allergies are frequently misdiagnosed as surgical infections. However, management of these complications is quite different. Because the consequences of metal allergy may include the need to replace the bar, pediatric surgeons

should be aware of this occurrence. Further prospective studies are warranted to assess the true incidence of metal allergy in patients undergoing surgical procedures to implant potential contact allergens.

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