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Клинический случай аллергии на титановое покрытие имплантированного кардиовертера-дефибриллятора у пациента 14 лет

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АННОТАЦИЯ

В настоящее время титан широко используется в имплантатах, в частности в таких кардиоресинхронизирующих устройствах, как кардиовертеры-дефибрилляторы, поскольку хорошо переносится пациентами и редко становится причиной аллергических реакций. Диагностика аллергии на титан крайне затруднительна в связи с низкой информативностью доступных аллергологических тестов к данному металлу. По мнению специалистов, ложноотрицательные результаты кожных аппликационных тестов с титаном могут быть связаны с использованием в аллерготестировании не чистого металла, а его соединения с хлором — тетрахлорида титана. Применение глюкокортикоидов в терапии аллергических реакций на компоненты имплантируемого кардиовертера-дефибриллятора носит временный характер и не исключает рецидивов воспаления. Основным лечением пациентов в таких случаях является замена имплантируемой системы на аппарат из максимально гипоаллергенных материалов.

В настоящей статье описывается клинический случай аллергии на кардиостимулятор с титановым покрытием, имплантированный 14-летнему пациенту. В ходе диагностики гиперчувствительности к титану впервые зафиксированы высокие уровни эозинофильного катионного протеина и триптазы непосредственно в очаге воспаления наряду с нормальными значениями данных показателей в сыворотке крови. Сделан вывод, что концентрация эозинофильного катионного протеина и триптазы в очаге воспаления представляется перспективным маркером при диагностике аллергии на металл и требует дальнейших исследований.

Своевременная диагностика аллергии на титан и реимплантация кардиостимулятора с золотым покрытием предотвращает развитие рецидивов воспалительных изменений в ложе кардиостимулятора, снижает риск инфекционных осложнений и существенно улучшает прогноз для пациента.

Ключевые слова: кардиостимулятор; титан; аллергия; триптаза; эозинофильный катионный протеин.

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A case of titanium-coated pacemaker allergy in a 14-year-old patient

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ABSTRACT

Currently, titanium is widely used in implants, particularly in cardioresynchronizing devices, such as pacemakers, because it is well tolerated by patients and rarely causes allergic reactions. The low informative value of the allergy testing for titanium makes its allergy diagnosis difficult. Experts reported that false negative results of skin application tests with titanium may be associated with the use of titanium tetrachloride in allergy testing, which is not pure metal. The use of glucocorticoids in treating pacemaker component-related allergy is temporary and does not exclude recurrence of inflammation. The main treatment for patients is the replacement of the implantable system with a device made of the most hypoallergenic materials.

The present paper describes a case of a 14-year-old patient with an allergy to a titanium-coated pacemaker. This is the first time eosinophil cationic protein and tryptase are detected at the inflammation site while diagnosing allergy to a titanium-coated pacemaker. This study concludes that the level of eosinophilic cationic protein and tryptase in the inflammation site is a promising marker in metal allergy diagnosis and requires further research.

Timely diagnosis of titanium allergy and the reimplantation of a gold-coated pacemaker prevent the recurrence of inflammatory changes in the area of pacemaker insertion and infectious complications, thereby significantly improving patient prognosis.

Keywords: pacemaker; titanium; allergy; tryptase; eosinophilic cationic protein.

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BACKGROUND

Hypersensitivity to the components of implantable cardioverter-defibrillator (ICD) is extremely rare. In 1970, S. Raque et al. [1] first described a case of ICD-induced dermatitis whereupon isolated reports of local and systemic allergic reactions to ICD began to appear in the literature [2–7]. Any component of the ICD system can act as an allergen in this situation, including titanium, nickel, mercury, epoxy resin, polyurethane, cadmium, chromates, cobalt, silicone, polytetrafluoroethylene, and others. A wide range of various materials in ICD systems, combined with low diagnostic efficacy of allergological examination in this group of patients, creates great difficulties in characterizing such allergic reactions.

In this report, we present our own observation of the development of an allergic reaction to titanium coating of an ICD device implanted in a 14-year-old patient.

CASE REPORT

Clinical presentation

From medical history. Since 2009, the Department of Pediatric Cardiology and Arrhythmology of the Veltischev Research and Clinical Institute for Pediatrics and Pediatric Surgery of the Pirogov Russian National Research Medical University Research Clinical Institute of Pediatrics of the Russian Ministry of Health has been monitoring a 14-year-old boy. The boy has been diagnosed with "hereditary long QT syndrome, syncopal form, transient I–III degree atrioventricular block (AV block)." Given the family history (sudden cardiac death of a sibling), the life-threatening nature of arrhythmia, the past syncope episodes, and the impossibility of prescribing an adequate dose of β-adrenergic blockers due to I–III degree AV block, in June 2009, the child underwent an implantation of automatic ICD (Virtuoso DR, Medtronic, USA) followed by the prescription of optimal therapy with β-blockers.

In September 2012, the child was readmitted with complaints of pain and erythema in the ICD bed area. During the examination, signs of an incipient decubitus of the ICD bed were identified. Accordingly, the boy underwent revision, debridement, and formation of a new ICD bed, with the previous ICD being implanted and connected to the electrodes.

During examination. After 3 months (at the end of December 2012), the boy was admitted to our clinic with complaints of redness, swelling, and pain in the ICD bed area. The examination in the left deltopectoral area revealed pronounced edema, fluctuation, and trophic changes in the skin over the ICD bed, and therefore, in January 2013, the patient underwent removal of the ICD system. Upon examining the ICD bed, signs of aseptic inflammation with necrotic changes and lysis of surrounding tissues were detected.

Diagnostic results

The patient underwent a full range of bacteriological, virological, and immunological examinations, as well as pathological ICD bed tissue biopsy examination, during which the infectious nature of the inflammatory process was excluded.

The patient was referred for consultation to the Department of Allergology and Clinical Immunology to rule out a possible allergic nature of the inflammatory process. In the child's personal and family history, there were no indications of allergic diseases, such as reactions upon contact with metal items, drugs, and food.

Allergen ImmunoCAP tests (Sweden) did not detect class E immunoglobulins (IgE) in the mixture of allergens screening panel (Phadiatop: tree pollen, grass, pet hair allergens, house dust mites, and mold) in the patient's blood serum; the serum eosinophilic cationic protein level was 11.3 μg/l (normal range: 5.5–13.3), and the tryptase level was 4.87 μg/l (normal range: 3.8–11.4).

A high concentration of eosinophilic cationic protein and tryptase 200 and 120 μg/l, respectively, was found in the supernatant of centrifuged (5,000 g, 15 min) exudate from the inflammatory focus in the ICD bed area.

At the second stage of examination, a 3-day application skin test was performed using a set of samples of all the materials ICD is composed of (this set was requested directly from the ICD manufacturer). All skin tests were negative.

Diagnosis

Considering the history of repeated occurrence of delayed inflammation of the ICD bed after its implantation, extremely high levels of eosinophilic cationic protein and tryptase in the inflammation focus exudate, and the absence of objective data in favor of the infectious nature of inflammation, the patient's condition was a delayed-type allergic reaction to the titanium coating of the ICD.

Treatment and outcomes

Reimplantation of ICD with gold-plated generator is recommended.

After 2 months of ICD removal, the child underwent reimplantation of gold-plated ICD (Consulta CRT-D, Medtronic, USA). The postoperative period proceeded without any complications.

During the next 8 years of patient observation, there were no recurrences of inflammatory changes in the ICD system area.

DISCUSSION

Currently, titanium is widely used in implants, including ICDs, because it is well tolerated by patients and rarely causes allergic reactions. Skin application tests with titanium have low sensitivity and, as a result, low diagnostic efficacy of allergy to this metal. In this regard, in our clinical case, negative results of skin application tests with titanium did not justify the exclusion of allergy diagnosis. Such observations may be associated with the use of titanium tetrachloride in

allergy testing, which, because of its strong dilution, can yield a false negative result, according to a number of authors [4, 8].

A work of R. Yamauchi et al. [9] was able to document a positive reaction during skin scarification tests with patients' blood serum that had previously been incubated with titanium particles for 1 month, while skin patch tests with titanium were also negative. In addition, there is evidence that hypersensitivity to titanium, particularly in dental implants, is not associated with the adaptive immune system activation, but is a consequence of a nonspecific pro-inflammatory reaction induced by the hyper-reactivity of macrophages to metal nanoparticles [10]. In this regard, when titanium allergy is suspected, the expediency of performing and interpreting standard allergological tests is controversial, while clinical signs of inflammation (edema, hyperemia, exudation, etc.) in the implant area remain the leading diagnostic criterion.

Tryptase is a neutral serine protease contained in mast cells' secretory granules; therefore, tryptase blood plasma level is a specific marker reflecting their activation during the development of allergic response. In turn, serum concentration of eosinophilic cationic protein, one of the main mediators of eosinophils released from their granules, can also be an informative nonspecific marker of eosinophil activation, specifically in various allergic diseases. In our clinical case, along with negative results of allergy screening, the concentration of eosinophilic cationic protein and tryptase in patient's blood serum was within the normal range, while in the inflammatory focus exudate, it was extremely high. In our opinion, high levels of mast cell degranulation and eosinophil activation markers determine the local inflammatory response in ICD bed and may hold some diagnostic value in verifying hypersensitivity to titanium. Such observations are first described in our work and have not previously been found in the literature. In this regard, the detection of eosinophilic cationic protein and tryptase levels in inflammation focus in the diagnosis of metal allergy appears promising and requires further research.

Use of glucocorticosteroids in the treatment of allergic reactions to ICD components will help relieve acute symptoms in the skin and mucous membranes (erythema, edema, and hyperemia) [11]. However, the effect is certainly temporary and does not eliminate the recurrence of inflammation. The main treatment of patients in this situation is the removal and replacement of the ICD system with a device consisting of the most hypoallergenic materials, and gold-plated ICD devices can act as an alternative in this case [4, 5, 7]. Gold has high biocompatibility, anti-inflammatory, and bactericidal properties; thus, it is one of the main materials to consider upon choosing implants for patients with high risk of developing allergies, including allergy to titanium. In the presented case, in a patient with hypersensitivity to titanium-plated ICD, gold-plated ICD was used as an alternative. It is extremely important to note that after the replacement of the pacemaker, long-term monitoring of the patient's condition is necessary, since an allergic reaction to the metal is usually delayed. In this study, during the 8-year follow-up period after reimplantation of the ICD device with gold coating, there were no recurrences of inflammatory changes in the ICD system area, which indicates the correct diagnostic search algorithm, timely diagnosis verification, and optimal selection of patient management tactics.

CONCLUSION

Thus, despite the considerably good tolerance of titanium medical devices, allergic reactions to this metal are possible in routine clinical practice, which is confirmed by the presented clinical case.

The diagnosis of hypersensitivity to titanium is extremely difficult, and in this regard, assessment of history and clinical evidence is the leading criterion, the use of standard allergological tests is not always justified and conclusive, which demonstrates the relevance of the search for new promising diagnostic methods and markers.

A timely and correct diagnosis is of decisive importance in the choice of management tactics for this group of patients and significantly improves the patient's prognosis.

ADDITIONAL INFORMATION

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