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Too Late Allergic Reaction in Patient with Permanent Pacemaker: Searching the Causality and Pathophysiology

Kalıcı Kalp Pili Olan Hastada Çok Geç Alerjik Reaksiyon: Nedensellik ve Patofizyolojinin Araştırılması

LETTER TO THE EDITOR
EDİTÖRE MEKTUP

In the current cardiology practice, several medical devices for assisting cardiac function and closing patent cardiac defects have proven to be life-saving devices and include among others pacemakers, defibrillators, stents, artificial cardiac valves, and cardiac assist devices. All these devices have scaffold parts that contain metals.[1] Their use is associated, occasionally, with allergic, hypersensitivity, and rarely, daunting and devastating anaphylactic reactions including Kounis syndrome.[2] The cardiac pacemakers alone or with defibrillators function have generators that are covered with titanium with leads attached to titanium capsule through a header (usually poly-methyl-met hacrylate and silicone rubber). The conductor wires of the pacemaker consist of an alloy of nickel, cobalt, chromium, and molybdenum. The pacing electrodes are made of platinum alloyed with 10%-20% iridium.[3] All these metals can induce allergic reactions. In the very important report published in the Archives of the Turkish Society of cariology[4] a 94-year-old male patient, having permanent pacemaker implantation that had been replaced 3 years earlier, developed redness and itching in the left chest location for 1 week. The dermatologist diagnosed allergic contact dermatitis, and with topical 0.1% mometasone furoate, the symptoms subsided and the patient is now, 6 months after, still asymptomatic. An unspecified patch test was proven negative. This report raises issues on the cause and delayed appearance of the reaction. The variety of metals the pacemaker components bear such as titanium, nickel, cobalt, chromium, molybdenum, platinum, and iridium can act as antigens and can induce allergic reactions.[5] Moreover, the poly-methyl-methacrylate used for connection of the pacemaker lead with the titanium capsule can cause allergic reactions and even anaphylactic shock,[6] as well as the rubber and silicon do.[7] Mast cells and basophil cells bring in their surface-specific high-affinity FceRI and FCgRI and low-affinity FCeRII and FCgRII receptors where the IgE antibodies are attached. An allergic reaction can take place when a critical number of allergens, in the described case the pacemaker components, cross bridge corresponding receptor-bound IgE antibody molecules in the mast cell or basophil surface. This critical number of bridged IgE molecules is estimated to be in the order of 2000, in order to make a total of 1000 bridges that are necessary to trigger the cell to degranulate and release inflammatory mediators to induce an allergic reaction, out of a maximal number of some 500 000-1 000 000 IgE-circulating molecules.[8] When this number is not reached, an allergic reaction is not induced despite that allergens, namely metals in the described case, are present in the blood. That is why the described patient developed delayed allergic contact dermatitis possibly when the critical number of 1000 bridges between antigens (pacemaker components) and antibodies were achieved. Moreover, a delayed reaction that is mediated by T cells and monocytes/macrophages rather than by antibodies could be the cause of the described pacemaker reaction. The delayed reactions are also termed type IV hypersensitivity reactions. Undesirable consequences of delayed-type allergic reactions include contact dermatitis as in the described patient, granulomatous inflammation as in sarcoidosis and Crohn's disease, allograft rejection, graft versus host disease, and autoimmune hypersensitivity reactions.[9]

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We believe that history-taking regarding previous hypersensitivities, monitoring of inflammatory mediators during the using the device period, and lymphocyte transformation studies especially for the titanium because titanium-specific T-lymphocytes demonstrate strong and specific antigenicity of titanium ions released by biocorrosion.[10]

Declaration of Interests: The authors declare that they have no competing interest.

References

1. Kounis NG, Soufras GD, Davlouros P, Tsigkas G, Hahalis G. Thrombus formation patterns in HeartMate II continuous-flow left ventricular assist devices: a multifactorial phenomenon involving Kounis syndrome? *ASAIO J*. 2014;60(4):369-371. [CrossRef]
2. Kounis NG, Soufras GD, Tsigkas G, Hahalis G. Device thrombosis with continuous-flow left ventricular assist devices: is Kounis syndrome involved? *Artif Organs*. 2014;38(6):521-523. [CrossRef]
3. Honari G, Ellis SG, Wilkoff BL, Aronica MA, Svensson LG, Taylor JS. Hypersensitivity reactions associated with endovascular devices. *Contact Dermatitis*. 2008;59(1):7-22. [CrossRef]
4. Akkuş F, Taylan G. Too late allergic reaction in patient with permanent pacemaker. *Turk Kardiyol Dern Ars*. 2022;50(3):225-227. Available at https://archivestsc.com/en/too-late-allergic-reaction-in-a-patient-with-permanent-pacemaker-138229. [CrossRef]
5. Vrbova R, Podzimek S, Himmlova L, et al. Titanium and other metal hypersensitivity diagnosed by MELISA® test: follow-up study. *BioMed Res Int*. 2021;2021:5512091. [CrossRef]
6. Ten Hagen A, Doldersum P, van Raaij T. Anaphylactic shock during cement implantation of a total hip arthroplasty in a patient with underlying mastocytosis: case report of a rare intraoperative complication. *Patient Saf Surg*. 2016;10:25. [CrossRef]
7. Jevon P, Shamsi S. Management of anaphylaxis in the dental practice: an update. *Br Dent J*. 2020;229(11):721-728. [CrossRef]
8. Kounis NG, Koniari I, Plotas P, et al. Kounis syndrome caused by double allergens: the more allergens present, the easier, the quicker, and the more severe the anaphylaxis. *Chin Med J (Engl)*. 2020;133(15):1889-1890. [CrossRef]
9. Copaescu A, Gibson A, Li Y, Trubiano JA, Phillips EJ. An updated review of the diagnostic methods in delayed drug hypersensitivity. *Front Pharmacol*. 2020;11:573573. [CrossRef]
10. Suito H, Iwawaki Y, Goto T, Tomotake Y, Ichikawa T. Oral factors affecting titanium elution and corrosion: an in vitro study using simulated body fluid. *PLoS ONE*. 2013;8(6):e66052. [CrossRef]