Aortic homograft for aortic valve replacement in patient with Alpha-Gal allergy

Aortic homograft and alpha-Gal allergy

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Abstract:

Allergy to Galactose-Alpha-1,3-Galactose is an allergy to mammalian proteins, that are present on the surface of standard bioprosthestic valves, and could result in catastrophic allergic reaction or may cause early deterioration of the bioprostheses. Aortic homograft is an acceptable alternative to standard prosthetic valves (biological and mechanical) to avoid a potential allergic manifestation and the need of definitive oral anticoagulation. We report the implantation of an aortic homograft in a patient with an aortic stenosis who present a documented Alpha-Gal allergy.

Introduction:

Allergy to mammalian proteins, resulting in heterogenous anaphylactic manifestations and an increased specific IgE alpha-gal titer, has been poorly described in cardiac surgery. Only a few articles report hypersensitivity reaction (1) and bioprosthetic valve degeneration associated with allergy to Galactose-Alpha-1,3-Galactose (2). We report the implantation of an aortic homograft (AH) in a patient with an aortic stenosis who present a documented Alpha-Gal allergy.

Case report:

A 70 year-old male with medical history of hypercholesterolemia, diabetes and hypertension was referred to our center with dyspnea and chest pain. Allergy to mammalian meat was identified in 2012 after anaphylactic shock with a specific IgE alpha-gal titer > 100 kUA/L (reference range < 0.35 kUA/L), specific IgE bovine and porcine meet antibodies respectively of 32.6 kUA/L and 27.7 kUA/L (reference range < 0.10 kUA/L). Since the diagnosis, no allergic reaction occurred with a diet excluding mammalian meet. The echocardiography revealed a severe aortic stenosis with a mean gradient of 44 mmHg, maximal blood flow greater than 4 m/s and normal left ventricular ejection fraction (LVEF). Preoperative chest computed tomography showed normal size of the ascending aorta (left ventricular outflow tract (LVOT): 23 mm, Valsalva sinuses: 32 mm, sino-tubular junction: 26 mm, ascending aorta: 34 mm). Preoperative immunologic investigations revealed a positive IgE to Gelofusine® (B. Braun, Melsungen, Germany) and latex. No specific allergy concerning the non-

fractioned heparin used in our institution was observed after testing. After discussion with the patient and according to guidelines, an aortic homograft was chosen as a substitute of the aortic valve (patient's will: no oral anticoagulation, no mechanical prothesis). Surgery was performed throw full median sternotomy. Conventional normothermic cardiopulmonary bypass (CPB) was set between an aortic canula and a venous canula inserted in the right atrium. CPB was performed with a Physio® phosphorylcholine-coated closed circuit (Liva Nova, London, UK). Non-fractioned heparin was administrated during cardiopulmonary bypass with an objective of activated cloating time (ACT) more than 350 seconds (according to local institution's protocol of CPB). Intermittent cold cardioplegia with 4/1 mix of blood and Plegisol® (Pfizer, New York, USA) was injected with selective cannulation of the coronary arteries with myocardial temperature monitoring. After ultimate LVOT sizing (23 mm), a root replacement procedure was performed with a running suture of the proximal and the distal suture of the AH. Coronary arteries were implanted in the AH in anatomic position with a standard running suture. No perioperative complication occurred, especially concerning anaphylactic event or postoperative bleeding. Postoperative cares were uneventful, except a paroxysmal atrial fibrillation (< 48 hours) reduced with a loading dose of beta blockers. At patient's discharge from hospital (day 8), mean aortic gradient of the aortic homograft implanted was of 11 mmHg, without curative oral anticoagulation.

Institutional Review Board approval was waived because it was not required by Ethics Committee according to French regulation, concerning this case report.

Comment:

Alpha-Gal allergy is rare and poorly described disease in cardiothoracic surgery, especially because of the difficulty of predicting the occurrence of allergic symptoms during the cardiac surgery, in a significantly underdiagnosed population. Indeed, Burk *et al* found in a group of patients who underwent upper endoscopic study that almost 25% of them were sensitized to alpha-Gal (3). To date, there is no strong data concerning the relationship between early deterioration of bioprosthetic valves and alpha-Gal allergy. Nevertheless, some studies have shown the presence of alpha-Gal epitope on

the leaflets of the bioprosthetic valves (4). On the other hand, Mangold *et al* (5) showed that alpha-Gal specific IgG was significantly increased 3 months after implantation of bioprostheses compared to preoperative values and was significantly higher than alpha-Gal specific IgG level in patients who received mechanical valves. Based on these observations, the immunologic reaction associated with the presence of alpha-Gal epitope on the bioprotheses would be responsible for their early deterioration (2). To avoid early structural degradation of the porcine or bovine pericardial valve, implantation of a mechanical prosthesis is a suitable alternative, with however the need for a curative oral anticoagulation and some potential heparin substitute during further surgeries. Total decellularization of the bioprotheses using different protocols instead of the standard glutaraldehyde treatment would provide also less immunologic deterioration of the prostheses (6). In this particular case, the patient categorically refused to take prolonged anticoagulation. As a result, an AH was implanted in place of the native aortic root, with a modified Bentall procedure during a well prepared elective surgical intervention, avoiding every potential adverse event related to the presence of alpha-Gal allergen in the operating room (except intravenous heparin, needed for CPB). AH used as valvular substitute are in loss of interest for several reasons: difficulty for implantation, reoperation and similar long term results, compared to standard aortic prosthetic valves, and insufficient supply. However, AH allows such patients to avoid mechanical valve implantation and their adverse events related to oral anticoagulation. In addition, no switch of heparin and oral anticoagulation is required (for other surgeries), knowing that most of the injectable heparins are derived from porcine intestinal tissues, and that way decrease the risk of anaphylactic shock in case of other surgeries to be performed after cardiac surgery or hospitalizations.

Conclusion: Aortic homograft implantation is an acceptable alternative to biological and mechanical prosthetic valves in case of documented alpha-Gal allergy. Further investigation should be performed to evaluate its long term performance. Alpha-Gal allergy should be considered in case of early bioprosthetic valve deterioration when no patient-related mismatch is documented.

References:

1 SM Mozzicato, A Tripathi, JB Posthumus, TAE Platts-Mills, SP Commins. Porcine or bovine valve replacement in three patients with IgE antibodies to the mammalian oligosaccharide galactose-alpha-1,3-galactose. J Allergy Clin Immunol Pract. 2014;2(5):637-638

2 RB Hawkins, HL Frischtak, IL Kron, RK Ghanta. Premature bioprosthetic aortic valve degeneration associated with allergy to Galactose-Alpha-1,3-Galactose. J Card Surg. 2016 July;31(7):446-448

3 Burk CM, Beitia R, Lund PK, Dellon ES. High Rate of galactose-alpha- 1,3-galactose sensitization in both eosinophilic esophagitis and patients undergoing upper endoscopy. Dis Esophagus. 2016;29(6):558-62.

4 KZ Konacki, B Bohle, R Blumer, W Hoetzenecher, G Roth, B Moser *et al*. Alpha-Gal on bioprotheses: xenograft immune response in cardiac surgery. Eur J Clin Invest 2005;35(1):17-23

5 A Mangold, T Szerafin, K Hoetzenecker, S Hacker, M Lichtenauer, T Niederpold *et al*. Alpha-Gal Speficic IgG Immune Response afer Implantation of Bioprotheses. Thorac Cardiov Surg. 2009:57;191-195

6 O Bloch, P Golde, PM Dohmen, S Posner, W Konertz, W Erdbrügger. Immune Response in Patients Receiving a Bioprosthetic Heart Valve: Lack of Response with Decellularized Valves. Tissue Eng Part A 2011 oct:17(19-20);2399-405