Staphylococcus Aureus Endocarditis on Transcatheter Aortic Valves

Endocarditis por Staphylococcus aureus sobre válvula aórtica percutánea

To the Editor,

Transcatheter aortic valves are becoming an alternative for patients with symptomatic severe aortic stenosis when comorbidity makes conventional valve replacement surgery an unaffordable risk. We describe one of the first cases of infective endocarditis on the CoreValve® model (Medtronic, Minneapolis, Minnesota) prosthetic aortic valve.

An 81-year-old male with dyspnea secondary to severe degenerative aortic stenosis. Comorbidity consisted of diabetes mellitus, chronic kidney failure, and a severely depressed left ventricular ejection fraction with pulmonary hypertension >60 mmHg. The coronary arteries showed no significant lesions. The surgical risk according to EuroSCORE was 29%, so it was decided to implant a CoreValve® transcatheter prosthesis, which took place after prophylaxis with ampicillin, with no major complications. According to the aortography, there was moderate, grade II/IV residual aortic regurgitation and the patient was discharged after a week.

During the following months, an improvement of 50% was seen in the left ventricular systolic function, with a decrease of pulmonary pressure to 45 mmHg. The patient remained asymptomatic, except for an admission 4 months after the implant for self-limiting gastrointestinal bleeding leading to anemia. A colonoscopy was performed without prior antibiotic prophylaxis and diverticulosis was diagnosed.
Two months after the colonoscopy, the patient was admitted with 2-week symptoms of discomfort, disorientation, fatigue, fever, cough, and dyspnea. The physical examination revealed basal crackles and normal prostatic sounds on auscultation. There was no hepatomegaly, splenomegaly, or skin lesions. The laboratory data showed systemic infection. The electrocardiogram showed left bundle branch block with a prolonged PR interval, similar to immediately after implantation of the prosthesis. The chest X-ray showed a diffuse interstitial pattern without clear condensation.

With the diagnosis of sepsis of probable pulmonary origin, blood cultures were taken and treatment started with cefazidime and ciprofloxacin. The patient’s clinical condition worsened with persistent fever and a decreased level of consciousness. A growth of methicillin-sensitive *Staphylococcus aureus* was observed in all 3 blood cultures. Transthoracic (Fig. 1) and transesophageal (Fig. 2 and Video) echocardiograms were performed that, despite the interference with the metal prosthetic mesh, showed a vegetation of 0.8 cm maximum diameter and area of 0.3 cm² attached to the aortic prosthesis, with no significant failure or signs of periannular complications. A 6-week treatment of cloxacinil and rifampicin was started, including gentamicin in the initial 2 weeks, following the current guidelines for treatment of staphylococcal prosthetic endocarditis. A computed tomography scan ruled out stroke. Later evolution was satisfactory, with disappearance of fever and an improved level of consciousness. At discharge the patient was asymptomatic, with no systemic infection evidenced in laboratory tests, negative blood cultures, and an echocardiogram showing no vegetation, with slight transprosthetic aortic insufficiency.

This was one of the first published cases of transcatheter aortic valve endocarditis. Patients eligible for transcatheter aortic valve replacement are at a higher risk of infection from these devices, given their comorbidity. The femoral and transapical access may be a gateway for the microorganism. However, in our case it was more probably related to the later admission, given that almost 6 months had passed from the prosthesis implant to onset of symptoms, and to the expected aggressiveness of any prosthetic staphylococcal infection. However, it must be stressed that most microorganisms associated with endocarditis after colonoscopy are enterococci or *Streptococcus bovis*. Given the symptoms, surgery was considered as a treatment and further endorsed by the improvement in left ventricular function and the disappearance of severe pulmonary hypertension, which reduced the operating risk. There are several cases of successful surgery within 30 days of a transcatheter valve implant, but only one within 6 months. Endothelialization of the prosthesis may have led to replacement of both the valve and aortic root, which would have increased the complexity of the surgery and surgical risk. This consideration, coupled with the favorable evolution of the medical treatment, led us to opt for conservative management.

Given the increasing use of transcatheter implantation, new cases of endocarditis on these devices will be seen. Maximizing asepsis and antibiotic prophylaxis during the implantation and in subsequent invasive procedures will be essential to minimizing the number of cases. The fragility of the recipients poses new diagnostic and treatment challenges. Records will need to be kept to monitor the peculiarities of this new phenomenon.

**FUNDING**

This case was partially funded by the Red de Centros Cardiovasculares, which is in turn funded by the Instituto de Salud Carlos III, Madrid, Spain.
Management of a Hypersensitivity Reaction to Thienopyridines: Prasugrel-Induced Fever and Hepatitis Resolved After Switching to Clopidogrel

Abordaje de una reacción de hipersensibilidad a tienopiridinas: fiebre y hepatitis inducidas por prasugrel resueltas tras su sustitución por clopidogrel

To the Editor,

Approximately 1% of patients in treatment with clopidogrel experience type I or IV hypersensitivity reactions consisting, in general, of rash or hematologic disorders (thrombocytopenia or neutropenia).1 More exceptionally, there have been reports of liver toxicity and systemic inflammatory response syndrome.2 3 Recently, it has been proposed to replace this drug with prasugrel, a new third-generation thienopyridine,4 in situations in which antiplatelet therapy cannot be discontinued and it is therefore impossible to apply desensitization protocols.1 5 To our knowledge, there are no reports in the literature of the reverse procedure in which a serious hypersensitivity reaction to prasugrel resolves after discontinuation of the drug and initiation of treatment with clopidogrel.

A 40-year-old women with a history of smoking was attended in a center other than our own for oppressive precordial chest pain. After a positive result in the ischemia detection test, a coronary angiogram was performed. This showed severe lesions in the left anterior descending artery and the diagonal coronary artery; revascularization was achieved by direct stenting, with a good initial angiographic outcome. At the time, antiplatelet therapy with acetylsalicylic acid was initiated (100 mg/day) along with clopidogrel (300 mg loading dose). A few hours after the procedure, the patient developed acute pulmonary edema with 5T segment elevation in the anteroseptal leads. A repetition of the coronary angiogram showed complete acute thrombosis of the stent in the left anterior descending artery, and so the angioplasty procedure was repeated and clopidogrel was replaced by prasugrel (loading dose of 60 mg followed by 10 mg/day). Abiciximab was added. Cardiogenic shock required orotracheal intubation and mechanical ventilation, as well as hemodynamic support with vasoactive drugs and intra-aortic balloon contrapulsation. The patient was then transferred to our hospital. On admission, the patient had a body temperature of 38.1 °C, a blood pressure of 120/60 mmHg, and a heart rate of 65 bpm. In the laboratory tests, of note were leukocytes 7.23×10^9/L (eosinophils 2.4%); aspartate transaminase 208 UI/L; alanine transaminase 93 UI/L; gamma glutamyl transpeptidase 240 UI/L; and alkaline phosphatase 170 UI/L. In addition to the vasoactive drugs and antplatelet agents, treatment included ranitidine, sodium hepamin, furosemide, and epelenerone. After initiating infusion of levosimendan, the hemodynamic status of the patient progressively stabilized, and she was extubated and the vasoactive drugs and intra-aortic balloon contrapulsation were withdrawn. At the same time, there was a transient improvement in her liver function tests. However, despite starting empirical antibiotic therapy with meropenem and linezolid, fever persisted in the days that followed, with small daily oscillations in temperature (<1 °C) and transient remission after administration of antipyrretics. Microbiological study were sterile or negative; these included serial blood cultures, urine cultures, and cultures of endotracheal aspirate; serology for hepatotropic viruses and the human immunodeficiency virus cytomegalovirus antigenemia; and the Mantoux skin-prick test. Similarly, full autoimmune testing was negative. The fever did not remit after changing venous and arterial catheters or suspending various drugs (ranitidine, heparin, and epelenerone). After 12 days, the number of stools began to increase (6-8 per day), with no pathological contents and also with negative etiologic study (coproculture and detection of Clostridium difficile toxin). Both the leukocyte count and acute-phase reactants (C-reactive protein and procalcitonin) remained within normal limits at all times, although there was a progressive change in the liver function tests (day 23 after admission: aspartate transaminase 115 UI/L, alanine transaminase 155 UI/L, and gamma glutamyl transpeptidase 723 UI/L), and relative eosinophilia appeared (day 19, eosinophils 9.7%). Abdominal ultrasound did not reveal any liver or bile duct abnormalities. Finally, faced with suspected drug-mediated hypersensitivity reaction, it was decided to suspend prasugrel and start clopidogrel without making any other changes to therapy. In the first 24 h after the change, the fever and diarrhea remitted, and there was a progressive return to normal liver function tests and leukocyte differentials (Figure). After 7 days, the patient had a second episode of low cardiac output that required administration of vasoactive drugs. This time, there were no accompanying abnormal laboratory results or fever. As she had a left ventricular ejection fraction of 5% to 10%, with no possibility of revascularization, she was included on the waiting list for heart transplantation. This procedure was performed on day 32 after admission, without the reappearance of symptoms in the

REFERENCES
7. 2012 H. García-Pardo.
8. Address: hgarciapardo@hotmail.com (H. García-Pardo).
9. Available online 9 February 2012

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at doi:10.1016/j.rec.2011.11.004.

Héctor García-Pardo, Ana Revilla, Teresa Sevilla, Javier López, Carlos Ortiz, and José A. San Román

Instituto de Ciencias del Corazón, Hospital Clínico Universitario, Valladolid, Spain

* Corresponding author: E-mail address: hgarciapardo@hotmail.com (H. García-Pardo).

Available online 9 February 2012