The first post-cardiac injury syndrome reported following transcatheter aortic valve implantation: a case report

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Background
Post-cardiac injury syndrome is a form of secondary pericarditis with or without pericardial effusion, which typically occurs weeks to months following an injury to the heart or pericardium. Disease activity can be followed with serial testing of inflammatory markers e.g. C-reactive protein (CRP) and/or sedimentation rate, electrocardiogram, and echocardiography.

Case summary
A 79-year-old woman was admitted with chest pain, dyspnoea at rest, cough, and low degree fever. The patient had undergone transcatheter aortic valve implantation (TAVI) 6 months before admission. Inflammatory markers were increased and a chest X-ray and computed tomography (CT) showed a minimal left pleural effusion. An empirical antibiotic treatment and ibuprofen to control chest pain were started on the presumption of an acute bronchitis. Despite 15 days of different antibiotic protocols the markers of inflammation remained increased. A positron emission tomography with computed tomography and cardiac magnetic resonance imaging showed signs of an aseptic pericarditis. After having excluded any infectious, metabolic, drug-induced or neoplastic genesis we considered the diagnosis of late onset autoimmune-mediated pericarditis. Subsequently, treatment was promptly initiated with colchicine and prednisone. The patient reported clinical improvement in the following days and the CRP value continuously decreased.

Discussion
To the best of our knowledge, this is the first reported case of post-cardiac injury syndrome after TAVI. It should be considered in those patients who have persistent chest pain, fever, fatigue, and elevated inflammatory markers after a TAVI procedure, even though it may occur weeks or months after the intervention. A triple therapy with colchicine, ibuprofen, and low-dosage steroids may be used for persistent symptoms.

Keywords
Case report • Transcatheter aortic valve implantation • Pericarditis • Cardiac magnetic resonance imaging • Fluorodeoxyglucose positron emission tomography with computed tomography

Learning points
• To the best of our knowledge, this is the first reported case of post-cardiac injury syndrome after transcatheter aortic valve implantation (TAVI).
• Such diagnosis should be considered in those patients who have persistent chest pain, fever, fatigue, and elevated inflammatory markers after a TAVI procedure, although it may occur weeks or months after the intervention.
**Introduction**

The term post-cardiac injury syndromes indicate a group of inflammatory pericardial syndromes including post-myocardial infarction pericarditis, post-pericardiotomy syndrome, and post-traumatic pericarditis. The immune-mediated pathogenesis is characterized by a latent period generally of a few weeks until the appearance of the first manifestations and the response to anti-inflammatory drugs (non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and colchicine). We hereby describe a case with post-cardiac injury syndrome after transcatheter aortic valve implantation (TAVI), which is the first case reported so far.

**Timeline**

| Time            | Events                                                                                                                                 |
|-----------------|----------------------------------------------------------------------------------------------------------------------------------------|
| 6 months earlier| Hospitalization due to severe symptomatic aortic stenosis (November 2016): uncomplicated transcatheter aortic valve implantation (TAVI). Cardiac biomarkers remained after TAVI within the normal limits (CK 96 U/L, CK-MB 17 U/L) |
| Day 1           | Patient presents to our department with fatigue, pleuritic chest pain, dyspnoea at rest, non-productive cough, and low degree fever (May 2017)  |
|                 | Chest X-ray and computed tomography showed a minimal left pleural effusion. Values of leucocytes and C-reactive protein (CRP) were increased. An antibiotic treatment with clarithromycin and piperacillin/tazobactam on the presumption of an acute bronchitis and ibuprofen to control chest pain were started |
| Day 2           | A transoesophageal echocardiography was performed to exclude any presence of endocarditis. It showed a TAVI bioprosthesis with normal opening movement with the presence of a low paravalvular leak (Grade 1) |
| Day 7           | Values of leucocytes and CRP were increased. The antibiotic therapy was changed to meropenem and vancomycin |
| Day 8           | The patient’s blood cultures and other examinations in medical microbiology and virology such as bacterial, viral, fungal, and parasitic infections were normal |
| Day 11          | The patient developed high fever (38.5°C), increased pleuritic chest pain and malaise. The leucocytes and CRP arrived at their peak.  |
|                 | We changed the antibiotic therapy to daptomycin, fosfomycin, and ceftazidime |
| Day 12          | A repeated echocardiographic examination showed a new small pericardial effusion (3 mm measured at end-diastole) extending to the right ventricular apex without signs of tamponade |
| Day 15          | Cardiac magnetic resonance imaging and fluorodeoxyglucose-positron emission tomography with computed tomography were performed. Diagnosis: post-cardiac injury syndrome |
|                 | Treatment with colchicine 0.5 mg, prednisone 20 mg, and ibuprofen 800 mg daily |
| Day 23          | The patient reported clinical improvement in the following days and CRP value continuously decreased. The patient was discharged |
| 3 months later   | At 3 months after discharge the patient had no symptoms. CRP had remained <5 mg/L |

**Case presentation**

A 79-year-old woman with a history of hypertension and paroxysmal atrial fibrillation presented to our department complaining of fatigue, pleuritic chest pain (worsened with deep inspiration), dyspnoea at rest, non-productive cough, and low degree fever during the last few days. The patient had undergone an uncomplicated TAVI procedure (26 mm CoreValve Evolut Bioprosthesis) due to severe symptomatic aortic stenosis 6 months before. On physical examination we documented normal heart and lung sounds on auscultation, normal jugular venous pulse, oxygen saturation of 98% on room air, a breathing rate of 22/min, temperature of 38.0°C, heart rate of 112 beats/min, and blood pressure of 140/80 mmHg. An increase in white blood cell count of $14.4 \times 10^9$/L (3.6–10.5 $\times 10^9$/L), sedentary rate of 86 mm/h (<30 mm/h), procalcitonin of 0.05 ng/mL (<0.5 ng/mL), and an elevated C-reactive protein (CRP) of 177 mg/L (0.0–3.0 mg/L) were observed. Electrocardiogram before TAVI showed a regular rhythm with normal QRS at the heart rate of 75 b.p.m. At the visit to our hospital, left bundle branch block and PR segment elevation in increased voltage right arm (avr) were recorded (Figure 1). Cardiac enzymes were within the normal limits [CK 45 U/L (0–170 U/L), creatine kinase-muscle/brain (CK-MB) 13 U/L (0–24 U/L), Troponin-T 15 pg/mL (<14 pg/mL)]. A transoesophageal echocardiogram (Figure 2) showed a Medtronic TAVI bioprosthesis in regular position and normal opening movement with the presence of a mild paravalvular regurgitation (Grade 1). There were no signs of endocarditis. The left ventricular systolic function was normal (ejection fraction (EF) 65%). The patient was subjected to diagnostic imaging including abdominal ultrasound, X-ray, and computed tomography of the chest. Besides a minimal left pleural effusion these imaging studies did not reveal significant pathologic findings.

The case was presented at our weekly multidisciplinary meeting with cardiology doctors, respiratory doctors, and radiologists. Following team discussions, an empirical antibiotic treatment with clarithromycin and piperacillin/tazobactam together with an anti-inflammatory therapy with ibuprofen 400 mg twice daily to control chest pain were started on the presumption of an acute bronchitis. Despite 7 days of antibiotic therapy, the patient still reported no improvement of her initial symptoms. Furthermore, values of leucocytes (14.8 $\times 10^9$/L) and CRP (249.5 mg/L) were increased,
value of procalcitonin (0.05 ng/mL) remained normal. As a result, we changed the antibiotic therapy to meropenem and vancomycin. The patient’s blood cultures and other examinations in medical microbiology and virology such as bacterial, viral, fungal, and parasitic infections were normal.

After 11 days of antibiotic treatment, the patient developed high fever (38.5°C), increased pleuritic chest pain and malaise. The leucocytes count and CRP peaked at 19.9 x 10^9/L and 274.6 mg/L, respectively. We reconsidered antibiotic therapy and changed it to daptomycin, fosfomycin, and ceftazidime. A transthoracic echocardiographic examination showed a new small pericardial effusion (3 mm measured at end-diastole) extending to the right ventricular apex without signs of tamponade (Figure 2). A fluorodeoxyglucose positron emission tomography with computed tomography (FDG-PET/CT) showed diffused increased FDG-uptake of the pleura and the pericardium consistent with inflammatory changes (Figure 3).

In addition, a cardiac magnetic resonance imaging (MRI) study (Figures 4 and 5) was performed demonstrating an oedematous

Figure 1  Electrocardiography showing (A) regular rhythm with normal QRS—pre-transcatheter aortic valve implantation electrocardiogram, (B) left bundle branch block and PR segment elevation in AVR—Day 1 of hospitalization, and (C) normalization of PR segment changes—Day 18.

Figure 2  Transoesophageal echocardiography. (A) Apical four chambers view showing normal right atrial (RA) and left atrial (LA) dimensions and normal right ventricular (RV):left ventricular (LV) ratio with a 65% left ventricular systolic function (EF). (B) and (C) Medtronic transcatheter aortic valve implantation bioprosthesis in regular position with normal opening movement (arrows). (C) Mild pericardial effusion expanding to the right ventricular apex without signs of tamponade (arrowhead).
thickening of the pleura and pericardium with increased contrast enhancement corresponding to an aseptic pericarditis without a circumferential effusion. It showed a normal left ventricular function (EF 59%) with end-systolic volume of 41 mL and end-diastolic volume of 100 mL.

We excluded any infectious, metabolic, drug-induced, or neoplastic genesis and considered the diagnosis of late onset autoimmune-mediated pericarditis after TAVI (post-cardiac injury syndrome). Therefore, treatment was immediately initiated with colchicine 0.5 mg and prednisone 20 mg daily in addition to the nonsteroidal anti-inflammatory therapy that had already been started.\textsuperscript{1-3}

The patient reported clinical improvement in the following days even though the white blood cell count remained high (likely due to prednisolone effect). The CRP value continuously decreased down to 16.8 mg/L on the day the patient was discharged (Figure 6). Repeated electrocardiography controls demonstrated a normalization of PR segment changes. A chest ultrasound showed resolution of the pleural effusion. The dose of prednisolone was then reduced to 5 mg daily, and the anti-inflammatory therapy was stopped. A 3-
month combined therapy with prednisone and colchicine was recommended.

At 3 months after discharge, the patient had no dyspnoea, no fever, and no chest pain after having taken regularly steroids and colchicine. In a follow-up visit at the local cardiologist, the presence of a minimal, haemodynamically insignificant pericardial effusion was documented. The pleural effusions were completely resolved. Her CRP value had remained under 5 mg/L.

**Discussion**

Post-cardiac injury syndrome is a form of secondary pericarditis with or without pericardial effusion, which occurs as a result of injury to

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**Figure 5** T1-weighted inversion-recovery sequences showing increased contrast enhancement of the pericardium (arrows in A and B) and the pleura (arrowheads in A) without associated pericardial or pleural effusion.

**Figure 6** Chronological changes in baseline C-reactive protein concentrations under antibiotics and after therapy initiation with colchicine, prednisolone, and ibuprofen.
the heart or pericardium. It was first described in the post-myocardial infarction period occurring in the weeks to months following infarction consisting of fever, pericarditis, and elevated inflammatory markers. The differential diagnosis should include pulmonary embolism, pneumonia, myocardial infarction, congestive heart failure, and possible malignancy. Disease activity can be followed with serial testing of inflammatory markers e.g. CRP and/or sedimentation rate. Echocardiography, cardiac computed tomography, PET/CT, and cardiac MRI can characterize active inflammation, oedema, pericardial thickness, and pericardial effusion.

The majority of patients with acute pericarditis associated with pleural effusions have a benign course. Risk factors for developing recurrent pericarditis include non-use of colchicine, a persistently elevated CRP, and an incomplete response to NSAIDs. As per the current European Society of Cardiology guidelines, an anti-inflammatory therapy with aspirin or NSAIDs and colchicine is the first choice for treatment of inflammatory pericardial syndromes. Low-dose corticosteroids should be considered for persistent symptoms after an infectious cause has been excluded.

Our patient’s presentation, previous recent cardiac intervention (TAVI), lack of other identifiable cause, and prompt response to treatment suggested post-cardiac injury syndrome. According to the best of our knowledge, this is the first reported case of post-cardiac injury syndrome after TAVI.

Such diagnosis should be considered in those patients who have persistent chest pain, fever, fatigue, and elevated inflammatory markers after a TAVI procedure, after having excluded any infectious genesis prior to starting treatment, although it may occur weeks or months after the intervention.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

References

1. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, Brucato A, Gueret P, Klingel K, Lionis C, Masch B, Mayosi B, Pavie A, Ristic AD, Sabaté Tenas M, Seferovic P, Swedberg K, Tomkowski W; ESC Scientific Document Group. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: the Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2015;36:2921–2964.
2. Imazio M. New clinical trials in acute and recurrent pericarditis. Curr Cardiol Rep 2015;17:23.
3. Imazio M, Hoit BD. Post-cardiac injury syndromes. An emerging cause of pericardial diseases. Int J Cardiol 2013;168:648–652.
4. Alraies MC, Baibars M, Klein AL. When does pericarditis merit a workup for autoimmune or inflammatory disease? Cleve Clin J Med 2015;82:285–286.
5. Yingchoncharoen T, Alraies MC, Kwon DH, Rodriguez ER, Tan CD, Klein AL. Emerging role of multimodality imaging in management of inflammatory pericardial diseases. Expert Rev Cardiovasc Ther 2013;11:1211–1225.
6. Porcel JM. Pleural effusions in acute idiopathic pericarditis and postcardiac injury syndrome. Curr Opin Pulm Med 2017;23:346–350.