CASE REPORT

Pulmonary oedema in the emergency room: what is hidden beyond an apparently common presentation

Catarina Patrício, Filipa Pais da Silva, Vítor Brotas

Department of Internal Medicine-3, Hospital de Santo António dos Capuchos, Lisboa, Portugal

Correspondence to

Dr Catarina Patrício,
ana.catarina.lp@gmail.com

Accepted 8 April 2014

SUMMARY

Cardiogenic flash pulmonary oedema is a common and potentially fatal cause of acute respiratory distress. Although it often results from acute decompensated heart failure, abrupt-onset aortic regurgitation can sharply rise cardiac filling pressure and, consequently, pulmonary venous pressure, leading to rapid fluid accumulation in the interstitial and alveolar spaces. We report a case of a 64-year-old woman admitted to the emergency department with a flash pulmonary oedema; a careful clinical investigation subsequently revealed a rare aetiology for this 'common' presentation. After a detailed auscultation that unmasked a diastolic cardiac murmur, an acute severe aortic insufficiency was further confirmed by echocardiography, showing inflammation and thickening of the entire aorta wall. The patient was submitted to valve replacement surgery, and histological examination, to our surprise, showed features of aortitis, remarkable for the presence of giant cells. A diagnosis of idiopathic aortitis versus inaugural giant cell arteritis was proposed and treatment started with corticosteroids.

BACKGROUND

Pulmonary oedema is one of the most common emergencies that the clinician faces in the emergency department. Although cardiogenic oedema is the most frequent presentation, disorders in which factors other than elevated pulmonary capillary wedge pressure are responsible for fluid accumulation in the alveoli must be considered. The acute onset of severe aortic regurgitation is a medical emergency due to the inability of the left ventricle to quickly adapt to the rapid increase in end-diastolic volume caused by regurgitant blood. We found this case of extreme relevance for different reasons: first, to remind the clinician of the sometimes underestimated importance of a detailed clinical examination, with special attention to cardiac auscultation, since it can provide important diagnostic clues and unmask what is behind an ordinary disorder, such as pulmonary oedema. Second, to report an extremely rare cause of acute aortic insufficiency: the rare and under-recognised vasculitis named 'idiopathic aortitis', a disorder still difficult to differentiate from other giant-cell vasculitides that can present exclusively with aortic involvement.

oedema. On observation, the patient had intense dyspnoea, diaphoresis, cyanosis and peripheral vasoconstriction suggesting (cardiogenic) shock; the pulse pressure was normal, and the pulse rapid and thread. Although at first cardiac auscultation was apparently non-revealing because of the pulmonary findings supremacy, a later detailed examination after patient improvement and ward admittance revealed an early diastolic murmur, suspicious of aortic regurgitation.

INVESTIGATIONS

The thoracic roentgenogram showed signs of bilateral pulmonary congestion (figure 1), and the ECG evidenced only non-specific ST and T wave abnormalities.

An urgent echocardiography was performed in the context of an acute aortic regurgitation suspected by the cardiac auscultation. The transthoracic echocardiographic study confirmed an acute, severe aortic valve insufficiency, with pressure half-time 156/206 ms, holodiastolic flow reversal in the descending thoracic aorta and an estimated pulmonary artery pressure of 65 mm Hg; there were no signs of aortic dissection, vegetations or left ventricle dysfunction, with only minimal left ventricle enlargement. The transoesophageal imaging showed a thickened, apparently infiltrated and homogeneous echodense aortic wall, suggestive of non-specific aortitis; total absence of aortic valve cusp coaptation, right thickened coronary cusp and severe regurgitation; mitral valve with significant fluttering and mild mitral insufficiency. Coronary angiography showed no lesions. A

Figure 1 Roentgenogram of the thorax showing marked pulmonary congestion with bilateral alveolar infiltrates, according to acute heart failure/flash pulmonary oedema.

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To cite: Patrício C, Silva FP da, Brotas V. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-204131

CASE PRESENTATION

The patient was a 64-year-old woman, with a history of monoclonal gammopathy of undetermined significance and hepatitis B, admitted in the emergency department with flash pulmonary

thoracoabdominopelvic CT scan revealed moderate pericardial effusion; concentric parietal thickening of the entire thoracic aorta and minimal in the abdominal aorta, with extension to the supra-aortic trunks, namely the brachiocephalic until the bifurcation and the proximal left carotid. No aneurysmal dilations or aortic ulcers were detected, and the rest of the imagiological evaluation was completely normal, including no signs of pulmonary embolism.

Blood analyses performed in the emergency department were unremarkable, except for slightly elevated troponin I (0.17 ng/mL), myoglobin (104.9 ng/mL) and D-dimer (974.0 µg/L) that subsequently lowered. Additional laboratory analyses showed: C reactive protein 17.5–30.9 mg/L; erythrocyte sedimentation rate (ESR) 22–50 mm/h; protein electrophoresis with already known monoclonal peak in the γ region; negative serology for syphilis (rapid plasma reagin (RPR) and T pallidum haemagglutination (TPHA)) and Lyme disease; negative cryoglobulins and negative blood (2) and urine cultures.

TREATMENT

After temporary medical stabilisation, the patient was submitted to aortic valve replacement surgery, with implantation of a biological prosthesis. Histological examination of the resected aortic wall showed lymphoplasmocitary inflammatory foci in the media and adventitia, one of them resembling an epithelioid granuloma with central necrosis; multinucleated giant Langhans cells (figures 2 and 3). Acid-alcohol-fast bacilli detection was negative.

The patient started treatment with prednisolone 1 mg/kg/day (60 mg/day), which was tapered to 40 mg/day after 1 month.

OUTCOME AND FOLLOW-UP

Three weeks after starting the treatment with corticosteroids, the inflammatory parameters became negative: C reactive protein 0.4 mg/L and ESR 5 mm/h. The patient reported no relevant symptoms and there were no subsequent medical interurrences. Prednisolone dose was gradually tapered to 40 mg/day in the following month.

DISCUSSION

Pulmonary oedema is one of the most common and potentially fatal forms of acute respiratory distress. The clinical presentation is characterised by the development of dyspnoea, associated with rapid accumulation of protein-poor fluid within the lung's interstitial and/or alveolar spaces, almost always the result of acutely elevated cardiac filling pressures.¹ However, the

Figure 2 Endomyocardial fibrosis, with marked hypertrophy of the myocytes, and subendocardial and interstitial fibrosis.

Figure 3 Foci of lymphoplasmocitary infiltrates in the adventitia and media layer of the aorta, one of which outlines an epithelioid granuloma with central necrosis; giant cells of Langhans are identified.

distinction between cardiogenic and non-cardiogenic causes is not always possible, since the clinical syndrome may represent a combination of several different disorders. The major causes of non-cardiogenic pulmonary oedema to be considered are acute respiratory distress syndrome and, less often, high altitude and neurogenic pulmonary oedema, pulmonary oedema due to narcotic overdose, pulmonary embolism, eclampsia and transfusion-related acute lung injury.² In the case of our patient, there were no risk factors detected in the history that could suggest a non-cardiogenic aetiology, leading us to assume at the admission that we were in the presence of a ‘flash pulmonary oedema’, a term used to describe a particularly dramatic form of cardiogenic alveolar pulmonary oedema, related to a sudden rise in left ventricle diastolic pressure. In this setting, myocardial ischaemia with or without myocardial infarction, acute severe mitral regurgitation, hypertensive crisis, acute aortic regurgitation and stress-induced (takotsubo) cardiomyopathy should be included in the differential diagnosis.³ At the admission, our patient reported no history of heart failure, heart valve disease or hypertension, and she presented with a sudden installation of dyspnoea, without chest pain, nausea, vomiting or other angina equivalents. Accordingly, there were no ST/T wave abnormalities or elevation of cardiac biomarkers suggestive of myocardial ischaemia, and no elevated arterial pressure values that could explain a hypertensive flash pulmonary oedema.

A detailed cardiac auscultation, after clearance of the breath sounds by the successful therapeutic measures, detected a low-pitched early diastolic murmur beginning after S2 together with a soft/nearly absent S1, in contrast to the high pitched holodiastolic decrescendo murmur of chronic aortic regurgitation. The diagnosis of acute aortic regurgitation was confirmed by the typical echocardiography findings, including a pressure half-time >200 ms, due to rapid equalisation of diastolic pressures in the aorta and left ventricle, and the presence of holodiastolic flow reversal in the descending thoracic aorta, with normal ventricular size and function.^{4–6} The transoesophageal imaging and the thoracic CT scan excluded the main causes of native-aortic-valve acute insufficiency (dissection or endocarditis), and provided an important clue to an uncommon aetiology: a diffuse and inflammatory non-specific process, aortitis.

Since the treatment for acute severe aortic regurgitation is emergency aortic valve replacement, the patient was submitted to biological valve substitution surgery after a brief period of medical stabilisation. Histological examination of the resected aorta confirmed an inflammatory process with a mixture

lymphoplasmocitary infiltrate, and surprised us for the presence of granuloma with multinucleated giant Langhans cells. Given this pathological finding, our diagnostic approach encompassed the main aetiologies of aortitis, focusing on those presenting with infiltration of the aorta by giant cells, a relatively non-specific feature.

The most common causes of aortitis are the large-vessel vasculitides giant-cell arteritis (GCA) and Takayasu arteritis (TA); although they present with distinct epidemiological and clinical features, there is significant overlap in histopathological findings.⁷ GCA and TA are associated with an inflammatory cellular infiltrate of the media, adventitia and vasa vasorum that contains a predominance of lymphocytes, macrophages and multinucleated giant cells, with occasional granuloma formation.⁷ GCA is the leading cause of inflammatory aortitis, occurring in 3–18%^{8–9} of patients with this disorder, clinically silent or presenting with aortic arch syndrome. Temporal involvement usually precedes aortic involvement, but aortitis may be the presenting feature of this large-vessel vasculitis, although the presence of giant cells in the vessel histopathological study is not usually the isolated manifestation of GCA.¹⁰ Our patient did not have any other features suggestive of temporal arteritis, namely new-onset headache, jaw claudication, polymyalgia rheumatica, ESR >50 mm/h or temporal artery tenderness, induration or decreased pulse at palpation.¹¹ She also did not show any characteristic signs of TA: age of disease onset <40 year, claudication of the extremities, decreased brachial arterial pulse, blood pressure difference >10 mm Hg or audible bruit over the subclavian arteries or the aorta.¹² There is an increasingly described and under-recognised vasculitis—idiopathic aortitis—virtually histologically indistinguishable from GCA and TA, which may be more common than previously thought.¹³ In a 12-year nationwide Danish population-based study, Schmidt *et al*¹⁴ report a prevalence of 6.1% aortitis among 1,210 resected aorta surgical samples, with nearly three-quarters of cases being idiopathic; only 14% were linked to GCA or TA. Idiopathic aortitis usually manifests as an aneurysm of the ascending aorta (95%)¹⁰ or is subclinical in nature, often diagnosed incidentally during the histopathological study of the aortic wall following a thoracic procedure. This disorder may be underdiagnosed for several reasons: the course of the disease may remain asymptomatic for a long time; patients are diagnosed when complications occur, mainly in the form of aortic aneurysms requiring surgery; nearly half of surgical samples are not submitted for pathological examination and some cases of idiopathic aortitis may not be recognised.¹⁴ It is therefore a condition deserving further epidemiological and pathophysiological studies, with emphasis in older female patients (mean age 73) and patients with diabetes, lying at the one end of a disease spectrum encompassing both GCA and TA.^{10–13} Three features are helpful to distinguish isolated idiopathic aortitis from other forms of ascending aortitis: absence of symptoms or signs of extra-aortic arteritis, absence of systemic disease such as autoimmune connective tissue disorders, and usually favourable outcome even in the absence of anti-inflammatory therapy.^{15–16} The optimal management of these patients is uncertain, and the decision to treat with a course of glucocorticoid therapy should be considered on a case-by-case basis, depending on the clinical presentation and location and extent of inflammation, along with appropriate investigations of inflammatory markers (ESR, C reactive protein).⁷ Elevated acute phase reactants, as markers of systemic inflammation, can be present in some patients.¹⁰ These patients require careful follow-up because small-case series have identified a propensity towards aneurysm formation

in other vascular beds over time.^{15–16} In a large-scale, 20-year retrospective study of 52 patients with idiopathic aortitis from a cohort of 1204 surgical cases, none of the 11 patients treated with corticosteroids (mean follow-up 35.5 months) developed new aneurysms, while 6 of 25 who did not receive therapy developed additional aneurysms.¹⁶

Our decision based on the severity of initial presentation, elevation of inflammatory markers and review of the literature was to start treatment with 1 mg/kg/day of prednisolone. After 3 weeks, the patient reported no intercurrents and the inflammatory markers (ESR and C reactive protein) became negative. The authors believe that the aortitis was the most probable cause of the aortic valve insufficiency, since the inflammatory process involved the whole vessel from its proximal origin, and there were no additional causes found on the clinical history, laboratory and histological investigations.

We are still intrigued about this recently described entity because we can never be sure if the incidentally diagnosed aortic inflammation represents an inaugural systemic disease (namely temporal arteritis), whose entire features will only be unmasked with long-term follow-up, or just an idiopathic and isolated vasculitis. Although there is evidence that isolated idiopathic aortitis with giant cells is distinct and unrelated to giant-cell (temporal) arteritis,^{15–17–18} the possibility of systemic complications, especially ocular involvement with visual loss, was also a determinant factor for initiating treatment.

Although large-vessel vasculitides are the most common cause of aortic inflammation, it can also be associated with several other rheumatological diseases, such as lupus erythematosus, rheumatoid arthritis, the human leucocyte antigen (HLA)-B27-associated spondylarthropathies, antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (granulomatosis with polyangiitis—Wegener's), Behçet disease, Cogan syndrome, sarcoidosis, Ormond's disease⁷ and IgG4-related

Learning points

- ▶ Flash pulmonary oedema is a life-threatening emergency usually resulting from acute decompensated heart failure, although non-cardiogenic aetiologies must be considered. Acute severe aortic regurgitation is a rare cause of cardiogenic pulmonary oedema that can pass under-recognised, if not suspected by a careful cardiac auscultation.
- ▶ Echocardiography establishes the diagnosis of acute aortic insufficiency, enables the identification of its cause, and should be followed by emergency surgical treatment with aortic valve replacement and aortic repair.
- ▶ Aortitis presentation varies across a clinical spectrum that includes a catastrophic acute aortic syndrome, such as aortic dissection and rupture.
- ▶ Isolated idiopathic aortitis is a poorly described vasculitis, histologically indistinguishable from the most common causes of aortitis, the large-vessel vasculitides giant-cell arteritis and Takayasu arteritis, with remarkable presence of Langhans giant cells. Given its subclinical nature, it is usually diagnosed incidentally from the resected surgical specimen.
- ▶ Treatment with corticosteroids may be beneficial, but it is still not well validated given the recent identification of this disorder, and should be planned on a case-by-case basis.

disease.¹⁹ Infectious aetiologies are rare but potentially life-threatening, generally occurring in patients with an atherosclerotic or other subjacent vessel frailty that allows bacterial seeding via the vasa vasorum; the most common isolated microorganisms are the *Salmonella* and staphylococcal species, along with *Streptococcus pneumoniae*.^{20 21} Although HIV, histoplasmosis, luetic and tuberculous aortitis are exceedingly rare and coexist with other systemic manifestations, one should keep these entities in mind, especially because they can present histologically with giant multinucleated cell infiltration.

Acknowledgements The authors acknowledge the colleagues from the Cardiology Department of Hospital de Santa Marta, who collaborated with them in the diagnosis and follow-up of the patient, and Dr Nuno Banazol, the chief cardiothoracic surgeon who intervened in this case.

Contributors CP wrote the manuscript and is the physician responsible for the follow-up of the patient. FPS and VB also contributed for and revised the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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