BMJ Case Reports

Rare disease

Severe haemolytic anaemia after valvuloplasty and annuloplasty

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Summary

Haemolytic anaemia is a well-recognised but rare complication of heart-valve prostheses. The authors report a case of an 80-year-old woman with severe haemolytic anaemia previously treated with valvuloplasty and annuloplasty without rings. To our knowledge, no cases of haemolysis have been described with this type of surgery.

BACKGROUND

Haemolytic anaemia is due to haemolysis, or the abnormal breakdown of red blood cells (RBCs). It has numerous possible causes, ranging from relatively harmless to life-threatening conditions.

To the best of our knowledge, there are no published cases about haemolytic anaemia associated with annuloplasty without rings. In presenting this case, we want to focus clinician attention on the importance of not excluding differential diagnosis in this type of intervention, though in the literature the procedure has not been associated with severe haemolysis.

CASE PRESENTATION

In March 2008, an 80-year-old woman was admitted to our hospital for fatigue and jaundice. In June 2007, the patient underwent mitral valvuloplasty with quadrangular resection of medial P2 and lateral P3. Annuloplasty was performed with a semicircular suture, and the annulus was kept at the appropriate size by tying the stitch. No prosthetic annuloplasty rings were used. Coronary angiography, performed before the procedure, showed no stenosis. The patient spent 3 postoperative days in the intensive care unit that were characterised by episodes of respiratory failure with hypoxia and hypercapnia, and unstable psychotic status (the patient became disoriented). In the following days, the patient developed atrial fibrillation. The administration of amiodarone led to severe anaphylactic shock, without resolution of the arrhythmia, and thus the patient was initiated on warfarin and a β-blocker (carvedilol). Echocardiography before discharge showed normal function of the valve with minimum residual regurgitation. At that time, haemoglobin (Hb) was 11 g/dl.

During the following months, the woman became progressively asthenic, and her psychotic status worsened. The progressive mental decline was attributed to the extracorporeal circulation during surgery and to the episodes of cerebral hypoxia that occurred in the intensive care unit.

In February 2008, the patient was subjected to electrical cardioversion, which was successful. At that time, there are no apparent modifications of the echocardiogram; Hb was 8.5 g/dl, and haematocrit was 24% with mean cell volume (MCV) 102 fl. Laboratory values for vitamin B12 were 160 pg/ml (nv. 193–982 pg/ml), and folate was 6 ng/ml (nv. 3–15 ng/ml); intramuscular B12 was initiated accordingly. During following days, she became very fatigued and developed jaundice, and her urine was red-brown. She came to our attention 9 months after valvuloplasty.

On admission to our unit, blood pressure was 150/90 mm Hg, pulse was 90 bpm and temperature was 36.4°C. Physical examination revealed pale skin and jaundice, red-brown urine, but no signs of cardiopulmonary failure.

Laboratory values on admission were Hb 5.4 g/dl, haematocrit 16%, MCV 108 fl, white cell count 7.010/cc, platelet count 308 000/cc, creatinine 1.25 mg/dl. Vitamin B12 and folate were normal after 1 month of supplementation, and reticulocytes were increased.

Haemolysis was obvious from an undetectable haptoglobin concentration, elevated reticulocyte count and high lactate dehydrogenase levels (5880 U/l; normal 240–480 U/l). Total bilirubin was 3.27 mg/dl, and direct bilirubin was 0.10 mg/dl. Haemoglobinuria was present in urine. A peripheral blood smear showed the presence of schistocytes.

Mitral-valve function was characterised using transoesophageal echocardiography (TEE) which revealed the presence of a hypomobile posterior leaflet and severe valve regurgitation. TEE also demonstrated the presence of two distinct regurgitant jets: the first laterally directed at the annulus level, and the second eccentric, due to the disrupted suture of the leaflets (figure 1).

We excluded other possible causes of haemolytic anaemia, such as infections, autoimmune haemolysis (Coombs test and the autoimmune pattern were both negative), hereditary haemolytic anaemia, and abnormalities of RBC membrane and interior. Haemolysis may be also associated with folate and vitamin B12 deficiency.[1] However, in this patient adequate B12 and folate supplementation did not improve haemolysis or normalise Hb levels as reported by Hartong *et al*.[1] Likewise, vitamin B12 supplementation did not lead to any improvement in mental status.

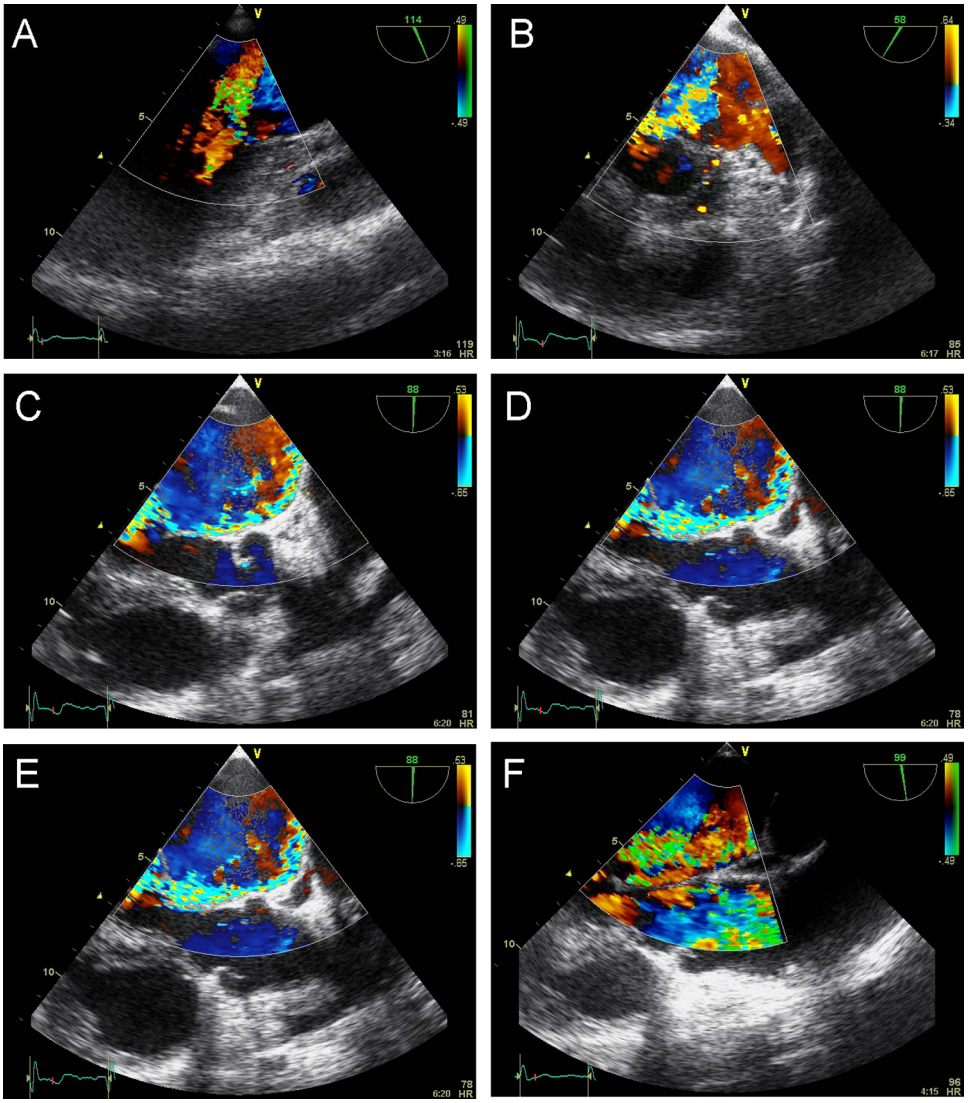

Figure 1 Transoesophageal echocardiography: colour Doppler imaging demonstrates the jet of mitral regurgitation during an episode of haemolysis.

During hospitalisation, the patient needed transfusions of packed RBCs twice a week (total of 8 units) to maintain Hb at 9 g/dl. The severity of haemolysis led to progressive worsening of renal function.

As far as the mechanisms of haemolysis are concerned, Garcia *et al*[2] studied the hydrodynamic properties of the regurgitant jets and employed a classification system which described the geometry of the jet into five patterns as fragmentation, collision, rapid acceleration, free jet or slow deceleration. Using fluid-dynamic-simulation models, these authors showed that fragmentation, rapid acceleration and collision jets were associated with high shear-stress forces (>3000 dynes/cm^2) and may thus produce haemolysis. In this case, we hypothesise that one or more of the three cited mechanisms may be implicated. It is also possible that the disrupted suture of the leaflets is the main candidate for RBC haemolysis in this patient.

Haemolytic anaemia is a well-recognised but rare complication of heart-valve prostheses,[3–6 8 11 12] though no cases of haemolysis with valvuloplasty and annuloplasty without rings have been described.

Reintervention with re-repair or mitral-valve replacement[9–11] is safe and effectively relieves haemolysis.

Nevertheless, reintervention of the damaged valve was not recommended by the consulting cardiac surgeon, due to the high intraoperative risk and the patient's refusal to undergo the procedure. At present, the patient requires monthly transfusions[6–10] of packed RBCs and is also treated with recombinant human erythropoietin to reduce the need for blood transfusions, as demonstrated by Hirawat *et al*.[13]

DIFFERENTIAL DIAGNOSIS

We excluded other possible causes of haemolytic anaemia, such as infections, autoimmune haemolysis (Coombs test and the autoimmune pattern were both negative), hereditary haemolytic anaemia, and abnormalities of RBC membrane and interior. Haemolysis may be also associated with folate and vitamin B12 deficiency,[1] but in this patient

BMJ Case Reports 2010; doi:10.1136/bcr.09.2008.1022

adequate supplementation did not lead to improvement of haemolysis and normalisation of Hb levels as reported by Hartong *et al*.[1]

TREATMENT

During hospitalisation, the patient needed transfusions of packed RBCs twice a week (total of 8 units) to maintain Hb at 9 g/dl. The severity of haemolysis led to progressive worsening of renal function.

OUTCOME AND FOLLOW-UP

A second procedure on the damaged valve was not recommended by the consulting cardiac surgeon, due to the high intraoperative risk and the patient's refusal to undergo the intervention. At present, the patient requires monthly transfusions of packed RBCs and is also treated with recombinant human erythropoietin to reduce the need for blood transfusions, as demonstrated by Hirawat *et al*.[13]

DISCUSSION

To our knowledge, there is[5–7] no ideal technique for annuloplasty. According to Fundarò *et al*,[5] suture annuloplasty is currently the preferred surgical technique in only a few centres and for selected cases. This is partly because rupture of annuloplasty sutures is a rare but well-known complication of isolated annuloplasty (1.5% by Nagy and 4% by Komoda).[14 15] Czer *et al*[16] have also demonstrated that the suture technique provides a less effective reduction of mitral regurgitation than does ring annuloplasty (1.5% vs 0.5%). However, no cases of haemolysis with valvuloplasty and annuloplasty without rings have been described until now. Thanks to its reliability, reproducibility and good long-term, prosthetic ring annuloplasty is generally the technique of choice for mitral-valve repair. Haemolysis is a both disadvantage and a rare complication of prosthetic-ring annuloplasty surgery.

Demirsoy *et al*[12] described 3.8%, while Cerfolio *et al*[17] reported 1% of haemolytic anaemia cases with this technique. Various mechanisms are been proposed as the cause for the haemolysis[17]: high shear stress produced by the regurgitant jet that could occur even when the site of initial repair remains intact, dehisced annuloplasty ring producing para-ring regurgitant jets, protruding paravalvular suture material, nonendothelialisation of sutures or rings and mitral-valve regurgitation. An important finding[17] is that the occurrence of haemolysis is independent of the severity of mitral regurgitation after mitral repair.

We hypothesise that in this patient the severe haemolytic anaemia, which is a complication attributed only to the intervention of valvuloplasty with ring, may also be a complication of the suture valve repair due to mechanical fragmentation of red cells through the disrupted suture of the leaflets.

Reintervention with re-repair or mitral-valve replacement[9–11] is safe and effectively relieves the haemolysis, but in this case it was considered to be a high-risk option and was also refused by the patient.

Learning points

- Valvuloplasty and annuloplasty without rings can cause severe haemolysis.
- There is probably mechanical fragmentation of red cells through the disrupted suture of the leaflets.
- Reintervention with re-repair or mitral-valve replacement is safe and effectively relieves the haemolysis.

Competing interests None.

Patient consent Obtained.

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