

# Severe *Yersinia enterocolitica* sepsis after blood transfusion

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## ABSTRACT

A 23-year-old male received multiple blood transfusions following complicated thoracic surgery. He developed progressive haemorrhagic shock and multiple organ dysfunction syndrome. Blood cultures grew *Yersinia enterocolitica*. The patient was proven negative for *Yersinia enterocolitica*; however, one of the donors was found to be positive. Although strict selection of blood transfusion donors is warranted in the Netherlands, contamination of blood components may still occur and therefore should be considered whenever adverse events occur during or after blood transfusion.

## KEYWORDS

Adverse events, blood transfusion, contamination, sepsis, *Yersinia enterocolitica*

## INTRODUCTION

In the treatment of patients with severe haemorrhagic shock, control of the bleeding focus, restoration of the intravascular volume and haemoglobin levels are essential initial treatment goals. Therefore, massive blood transfusions are often needed for resuscitation in uncontrolled bleeding. However, blood transfusions are not without side effects and complications.<sup>1</sup>

Although blood transfusions in the Netherlands are relatively safe, side effects may occur.<sup>1</sup> In the Netherlands a rigorous screening programme aims to reduce blood transfusion reactions and side effects and has reduced the incidence to 0.14%. This screening programme comprises questionnaires to obtain information on the current state of health of the donor at the time of donation, testing for infection markers and quality control of blood components.<sup>2</sup>

We present a surgical patient who developed progressive circulatory shock and progressive organ dysfunction after haemorrhagic shock, even after adequate bleeding control and resuscitation. A rare complication of blood transfusion was found to be the underlying cause.

## CASE REPORT

A 23-year-old male was admitted to the pulmonary ward with symptoms of a recurrent spontaneous right-sided pneumothorax. Video-assisted thoracoscopy (VATS) and pleurectomy were performed. A chest tube was inserted perioperatively. Postoperatively the patient developed hypotension and haemoglobin (Hb) levels dropped to 3.4 mmol/l (8.5-11.0 mmol/l). Although the chest tube was not productive, chest X-ray showed a massive right-sided pleural effusion suggestive of a haemothorax. Re-exploration revealed an intercostal arterial bleeding focus that was surgically repaired. The patient received six units of packed erythrocyte concentrates and two units of fresh frozen plasma and was admitted to the intensive care unit.

Postoperatively, the patient became febrile with a temperature of up to 39.3°C. Blood, sputum and urine cultures were taken and subsequently intravenous cefotaxime was started. At that stage no relation with the blood transfusions was considered. For progressive circulatory shock even after adequate volume resuscitation, noradrenaline and dopamine were commenced. Corticosteroids were administered. The platelet count dropped to  $12 \times 10^9/l$  ( $150-400 \times 10^9/l$ ) due to diffuse intravascular coagulation and consumption coagulopathy. Renal function deteriorated indicated by a rise in serum creatinine to 149  $\mu\text{mol/l}$  ( $60-110 \mu\text{mol/l}$ ) and mechanical ventilation had to be continued for acute lung injury

(P/F-ratio: 62). Severe sepsis with multiple organ dysfunction syndrome was diagnosed. Surprisingly, the blood cultures grew *Yersinia enterocolitica* type III. Cefotaxime was switched to ciprofloxacin.

Initially, bacterial translocation due to severe shock and mesenteric hypoperfusion was considered, but cultures from the patient's stools and early post-sepsis serological tests for *Yersinia* antibodies were negative. His partner's blood and stool cultures were also negative for *Yersinia*. All blood cultures grew gram-negative rods. *Yersinia* typing was performed by identification using API 20NE (bioMérieux, Boxtel, the Netherlands) technology. Anti-*Yersinia enterocolitica* test serum (SIFIN, Berlin, Germany) was used in our present case.

Therefore, the possible source of the *Yersinia* infection was suggested to be contaminated blood transfusions. The patient was weaned successfully and could be discharged from our hospital with no persistent sequelae after 21 days.

All donors were serologically screened using homemade Western Blot technology able to identify *Yersinia* IgG and in case of positive testing, an additional IgA antibody test for *Yersinia* outer protein (YOP) was performed (UMCN, Nijmegen, the Netherlands). In one donor only *Yersinia* IgG antibodies were found indicating a *Yersinia* infection before donation. A second donor presented with both IgG and IgA *Yersinia* antibodies, and stool cultures positive for *Yersinia enterocolitica*. At the time of donation this donor did not have any symptoms such as diarrhoea or abdominal pain. Thus, the most likely source of contamination was this specific *Yersinia*-positive donor. However, DNA testing revealed that these two *Yersinia* strains were not identical. Therefore, the other donor could also have been the source. Both donors were removed from the blood donor programme.

## DISCUSSION

We present a rare case of a *Yersinia enterocolitica* sepsis likely related to contaminated blood of a *Yersinia*-infected blood donor. Initially, clinical signs were related to haemorrhage and it was only later that the clinical symptoms indicating sepsis became more pronounced.

Fever and emerging multiple organ dysfunction led us to review other causes than an inflammatory response after severe haemorrhagic shock, such as sepsis. A transfusion-related cause was not initially considered.

Sepsis is defined as the presence of at least two criteria of the systemic inflammatory response syndrome (SIRS) related to an infection.<sup>3</sup> SIRS criteria are: 1. Body temperature <36°C or >38°C; 2. Heart rate >90 beats/min; 3. Hyperventilation, evidenced by respiratory rate >20/min or PaCO<sub>2</sub> <32 mmHg; 4. White blood cell count >12.0 x 10<sup>9</sup>/l or 4.0 x 10<sup>9</sup>/l. SIRS criteria can also be found

in allergic and anaphylactic reactions, after ischaemia/reperfusion and after multiple blood transfusions.<sup>4</sup>

Donation of blood in the Netherlands is only allowed if rigorous restrictions are respected to prevent contamination of the donated blood. Furthermore, there are no financial or other incentives for blood donation in the Netherlands, and extensive questionnaires are used and physical examination is performed. The health status, lifestyle and background of the donors are extensively addressed. In addition, donated blood is tested for HIV, hepatitis B and C, syphilis and human T cell lymphotropic virus in every case.<sup>5</sup> Bacterial transmission through blood transfusion is extremely rare. The overall incidence rate is estimated at 0.2% of all blood products. Mild infections may go unnoticed.<sup>6</sup>

Bacterial contamination of blood may occur during donation or processing and usually involves commensal bacteria. In addition, contamination may also be caused by bacteraemia in the donor during donation.<sup>6</sup> This latter mechanism may have played a role in our patient.

Of all blood products, platelets are most at risk for bacterial contamination because these are stored at 20 to 24°C. To prevent bacterial contamination all platelet transfusions are cultured. Fresh frozen plasma is frozen for six months. If all serological and other tests are negative at the next donation, the plasma is released.<sup>5</sup>

In contrast to these rigorous measures for platelets and plasma, packed red-blood cells are only cultured in quality control samples and indirectly in case of thrombocyte transfusion processing from the same donor. With thrombocyte donation (20-30% of cases), cultures are always performed. If these thrombocyte transfusions are bacterially contaminated, all blood components including red packed cells from this specific donor are removed.

Thus, bacterial contamination of packed red blood cells may go unseen in the majority of cases. However, bacterial contamination of red blood cells is extremely rare and estimated at only 1 in 500,000. This low rate may be partly due to the low storage temperatures of 4°C preventing bacterial outgrowth.

Severe transfusion-related infections are mainly caused by gram-negative bacteria and in particular by *Yersinia enterocolitica* as these bacteria are able to grow at low temperatures. Furthermore, they show enhanced growth in environments rich in iron. Thus, packed red cells can be considered to be an ideal culture medium for *Yersinia enterocolitica*.<sup>7-10</sup>

It is not compulsory to notify health authorities of *Yersinia* infections. Therefore it is hard to predict the prevalence precisely. However, it is estimated at a few 100 cases of gastroenteritis per year in the Netherlands. *Yersinia* sepsis is extremely rare and is most frequently related to blood transfusions. Often the clinical course is severe. Mortality of *Yersinia* sepsis is around 50%.<sup>11</sup> Quinolones are first-line antibiotics for treatment.

Our case has some limitations: the molecular typing of the *Yersinia enterocolitica* from our patient could not be genetically related to the *Yersinia enterocolitica* from the culture-positive donor. Another possible explanation could be that the culture-positive donor was infected with multiple *Yersinia* species and a different strain contaminated the blood than we isolated from the stools. However, multiple species infections have not been reported in the literature. Still, it seems very unlikely that our patient could have had a source of *Yersinia* sepsis other than blood transfusions. Therefore, the *Yersinia* probably originated from the other donor who presented only serological positivity for *Yersinia*. Due to the fact that we were unable to culture *Yersinia* in this donor we were unable to prove genetic identity.

It is well known that *Yersinia*-infected patients may have antibodies against this bacterium while stool cultures remain negative. The fact that our patient tested negative, and that only a limited number of people per year in the Netherlands have proven *Yersinia enterocolitica* infections, serological positivity for *Yersinia* still could suggest a causal relation.<sup>12</sup>

The question to be answered remains whether we should put more efforts into preventive measures by applying more specific tests for bacterial contamination. Specific PCR assays for *Yersinia enterocolitica* are available, but other bacteria would not test positive so the clinical relevance in using this strategy may be very limited.<sup>13</sup>

To markedly increase the sensitivity, all samples could be cultured, but this will result in more cultures and incur higher costs. However, in general, patients who receive blood transfusions are not in good health and thus at risk of developing severe consequences from bacterial contamination. Therefore, selective sampling of packed erythrocyte concentrates for quality control and indirectly through thrombocyte component culturing could be reconsidered. Other techniques are under evaluation such as the Mirasol pathogen reduction process based on riboflavin photochemistry. Recently, costs and benefits of bacterial culturing and pathogen reduction (PRT) for platelet transfusions were evaluated and the authors concluded that blood cultures are without doubt more cost-effective than PRT in the Netherlands.<sup>14</sup> This debate will not solve the actual problem of many red blood cell transfusions that are not cultured.

In conclusion, we present a case of *Yersinia enterocolitica* bacteraemia very likely due to contaminated blood

transfusion of red packed cells, leading to severe sepsis and multiple organ dysfunction syndrome.

We strongly advocate to further reduce risks and complications of our treatments, and suggest more effort is put into the reduction of bacterial contamination of blood transfusions, even if this incurs higher costs. The time has come not to selectively culture, but to culture all blood transfusions to further reduce this risk.

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