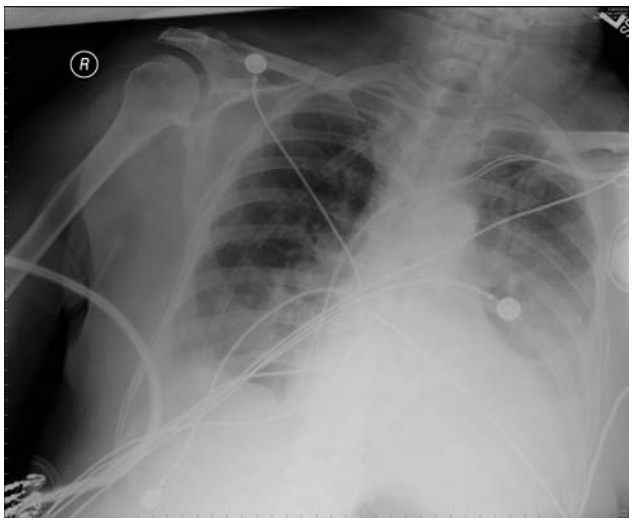
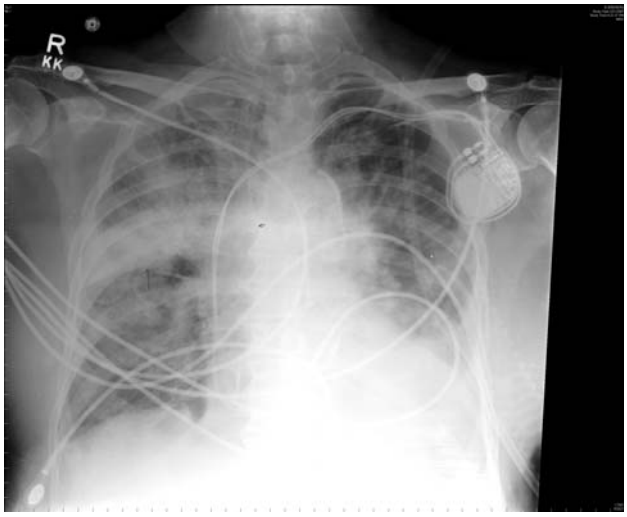
A TRANSFUSION–RELATED RESPIRATORY EVENT
A case history by Jim Perkins, M.D. (© 2009)

An 81 year old man was admitted to the hospital with increasing dyspnea due to congestive heart failure (CHF). A stroke the previous month left the patient with right sided weakness and aphasia, and he had an indwelling catheter. Other medical problems included hypertension, adult onset diabetes, and asthma, and the patient had a cardiac pacemaker. He was on home oxygen. The patient had pulmonary edema as revealed by physical examination (rales at both lung bases) and chest x-ray. The brain natriuretic peptide (BNP) was 1011 (upper limit of normal 130 pg/mL) on admission.

The patient was treated with diuretics and an angiotensin converting enzyme inhibitor (ACE inhibitor). On admission his hemoglobin level was 8.2 gm/dL, and one unit of Red Blood Cells (RBCs) was given at midnight which he tolerated without problem. An echocardiogram performed the next day revealed severe left ventricular hypertrophy with a low normal ejection fraction (50%) and impaired relaxation (stage 1 diastolic dysfunction), aortic stenosis and regurgitation, and moderate to severe mitral valve regurgitation. A second unit of RBCs was started at 14:25 at a rate of 133 mL/hour. After 15 minutes the patient appeared to be doing well and vital signs were unchanged. One half hour later (45 minutes into the transfusion, 100 mL of RBCs received) the patient's visitor notified the nurse that he was having trouble breathing. He was diaphoretic with an oxygen saturation (SO2) of 44% on 2 L of oxygen by nasal cannula. The blood pressure had increased from 131/60 to 164/74, and the patient was tachycardic (from 68 to 92). The transfusion was stopped at 15:00 and the patient was transferred to the intensive care unit for non-invasive ventilation (the family had refused intubation) which raised the SO2 to 94%. Diuretics were given. A chest x-ray showed increased parenchymal infiltrates consistent with aspiration or pulmonary edema. Troponin I and myoglobin levels were slightly elevated but had not increased significantly since the morning; the patient was known to have chronically elevated levels of these markers of cardiac ischemia. A complete blood count demonstrated a sharp drop in the total number of leukocytes from 7,500 before transfusion to 2,800/μL after, and the absolute neutrophil count fell from 5,600 to 1,400/μL. Fever was not evident at any time, before, during, or after this episode.



Admission chest x-ray



Chest x-ray taken soon after the reaction

Transfusion reaction evaluation was initiated at 16:00. A clerical check revealed no discrepancy, and there was no hemolysis evident on visual inspection of the patient's plasma. Serologic incompatibility was ruled out by repeat typing and direct antiglobulin testing of the pre- and post-transfusion patient specimens.

Questions:

1. What is the differential diagnosis of this reaction?

2. Based on your differential, is there any other history you would like to obtain, or are there any other tests you would like to do?

Additional history:

The patient developed progressive hypotension despite dopamine and was pronounced dead at 17:25, 2½ hours after transfusion. The cause of death was listed as cardiopulmonary arrest. The family did not allow an autopsy.

The BNP level on the pre- and post-transfusion specimens was 1118 and 1076, respectively (no change). The patient gained slightly over 2 kilograms over the course of the short hospitalization.

Culture of the unit was negative 5 day after the reaction. The table below shows the course of some of the patient's key laboratory findings.

Test	Normal range	Admission (afternoon)	Next morning	After reaction
Hemoglobin	13.0 – 17.0 mg/dL	8.2	9.5	12.5
Hematocrit	39.0 – 51.0 %	25.3	29.1	38.6
WBC	4,000 – 10,000 /μL	7,800	7,500	2,800
PMNs	1,500 – 8,000 /μL	5,700	5,600	1,400
BNP	< 130 pg/mL	1,011	1,091	1,076
Troponin I	0 – 0.06 ng/mL	0.09	0.09	0.11
Myoglobin	21 – 98 ng/mL	262	303	320

The blood center from which the unit came was contacted to obtain the demographic history of the donor; the donor was a 55 year old woman. Therefore, on the day after the reaction all patient specimens in the laboratory were identified. Blood anticoagulated with EDTA and heparin was submitted along with plasma from the donor's pilot tube for testing for anti-leukocyte antibodies.

The donor had antibodies against both class I and class II HLA antigens as well as against granulocytes. In flow cytometric assays with mixtures of latex beads, each with a single class I or II antigen (separate class I and II assays) the "PRA" was 95% and 91% respectively. The donor's plasma also reacted positively in granulocyte agglutination and immunofluorescence assays, but these assays are unable to distinguish between granulocyte and HLA class I antibodies. A Monoclonal Antibody Immobilization of Neutrophil Antigen (MAINA) assay was positive for antibodies against HNA-1a and -1b (NA1 & NA2). An IF crossmatch between the donor's plasma and the recipient's granulocytes was judged invalid because the negative and autologous controls were reactive, which is typical for target granulocytes more than 24 hours old. A similar limitation affected recipient neutrophil antigen typing, although the anti-HNA1b reacted much more strongly than the negative control. There were no recipient anti-HLA or granulocyte antibodies.

3. What is your diagnosis?

4. Given the information you have, do you think the second transfusion was indicated?