1. Abstract

Thalassemia is of the most frequent haemoglobinopathy that includes a heterogeneous group of inherited autosomal recessive pathologies caused by defective synthesis of globin subunit that comprise haemoglobin production. In β-thalassemia, insufficient quantities of β-globin chains are produced, causing ineffective erythropoiesis and microcytic hypochromic anaemia. The clinical severity of the disease, ranging from minor (or trait) to major forms (also known as Cooley anaemia), depending on the severity of the reduction in β-globin synthesis and the consequences of hyper haemolysis leading to iron overload and extramedullary erythropoiesis [1, 2]. The β-thalassemias are mainly widespread in populations originating from the Mediterranean rim, Middle East, Asia and Africa. In France, only 350 people present severe forms, the prevalence is estimated of 1/200000 [3-5]. Thalassemia intermedia presents commonly with asymptomatic mild anaemia but some particular clinical conditions, such as cardiopulmonary bypass (CPB) for cardiac surgery, may raise a particular risk of perioperative haemolysis and its related complications [6].

2. Case Report

We report here the case of a 72-year-old patient originated from Caucasus region with a personal history of smoking and type 2 diabetes treated by Metformin. He presented with stable angina pectoris clinically controlled with medical treatment (Acetyl salicylic acid 75mg/day, Amlodipine 5mg/d, bisoprolol 2.5mg x 2/d). Preoperative coronary angiography showed significant stenosis (70 to 90%) of the first diagonal, the bisecting artery, more than 90% stenosis of the middle circumflex artery and the first segment of the right coronary artery. Ischemic heart disease requiring multi-vessel coronary revascularisation by elective surgical coronary bypass graft with cardio-pulmonary bypass (CPB) was scheduled. The preoperative echocardiographic evaluation revealed normal ventricular dimensions and function (left ventricular ejection fraction LVEF = 55%) without any significant valvulopathy or signs of pulmonary hypertension (Systolic Pulmonary Arterial Pressure PAPS = 21mmHg), that was confirmed by per-operative right heart catheterisation. The identification on systematic preoperative biological exams of a mild microcytic anaemia with Haemoglobin (Hb) 115...
Supra-normal results obtained at the first preoperative evaluation of 2.56 L (respectively 77% and 79% of normal), compared with vital capacity (FVC) of 2.67L and forced expired volume (FEV1) pulmonary functional tests were still altered with diminished forced and mean SpO2 of 94% on room air). On the other hand, pulmonary artery pressure monitoring, continuous cardiac output and mixed venous oxygen saturation (SvO2) monitoring (HemoSphere monitor Edwards Lifescience Guyancourt, France). Anesthesia was conducted using propofol and Sufentanil in a Total intravenous anesthesia (TIVA) protocol using target controlled infusion (Orchestra® base Primea device - Fresenius Vial SAS Brézins France). A single IV bolus of myorelaxant (atracurium 35mg) was used for tracheal intubation. Perioperative antibiotic prophylaxis used 1.5g Cefuroxim IV bolus and 0.75g/2h followed by 0.75g every 6h for 48 h. The patient blood management strategy included preoperative administration of tranexamic acid (total dose of 35mg/kg, 0.9g in 30min and 0.4 g/h for 5 hours), cell salvage with Livanova Xtra auto-transfusion device and transfusion trigger was set for Hb 75g/L or Ht 25%. Anticoagulation for CPB was obtained with unfractionated Heparin IV bolus of 300U/kg and monitored with ACT 2 point of care device (Medtronic Minnesota USA) with a target activated clotting time over 400s. Surgery consisted in a 5 fold coronary artery bypass (anterior, bisecting and diagonal interventricular arteries were bypassed with bilateral internal thoracic arteries, marginal and posterior interventricular artery with saphenous vein graft) using a roller pump driven cardopulmonary bypass and aortic cross clamp. Myocardial protection was carried out using antegrade sequential normothermic blood cardioplegia. The CPB priming solution used 500ml fluid gelatin 40 mg/ml (Gelofusine B Braun Médical) and 1000ml Lactates ringers 5000U of unfractionated heparin, 0.5g tranexamic acid and 750mg of cefuroxim. Blood pressure was maintained with IV nor-epinephrine continuous infusion up to 0.2µg/min begun 20 min before CPB started to maintain MAP over 65mmHg. During CPB, rapid lowering of SvO2 (<55%) and low venous reservoir volume causing low flow alarm associated with blood lactate rise (up to 2.8mmol/L) led to give volume therapy (RL 500ml) causing Haemoglobin fall (nadir of 74g/L, Ht 23%). As CPB transfusion trigger was set at Ht 25%, one homologous packed red blood cell was transfused, raising Haemoglobin up to 83g/L and SvO2 from 52 to 75% (Figure 1). Afterward, SvO2 measures remained stable over 70% during and after CPB weaning (with pulmonary catheter). The bypass and aortic cross-clamping duration were respectively 105 and 92 minutes. Anticoagulation reversal was achieved with protamine administration of 100% of the initial heparin dose.
After CPB weaning, the remaining CPB circuit blood volume was treated with a cell salvage device (Sorin Xtra® Autotransfusion System – LivaNova SAS) for volume reduction and 480ml (Ht 48%) were returned to the patient, Hb concentration rose up to 89 g/dL. Total fluid balance was 1000ml. On the first postoperative workup (4h after CPB termination) haemoglobin concentration was 94 g/L, haematocrit was 30.7%, Serum lactate concentration returned to normal (2.0 mmol/L). There wasn’t any biological signs of haemolysis or disseminated intravascular coagulopathy (haemolysis index of 4 mg/dL, disseminated intravascular coagulation index of 0.16 mg/dL), and normal bilirubin of 8µmol/l [8]. Troponin rose up to 297 ng/L on day 1 and declined steadily thereafter and was considered as an acceptable value in this post CBAG context. Clinical Hemodynamic stability and absence of identified complication authorised the awakening and mechanical ventilation weaning 4h after the end of surgery. A 3l/min nasal oxygenotherapy was maintained and definitively stopped on the second postoperative day. Chest radiogram presented mild diffuse interstitial syndrome. Chest drain volume was 290ml on day 1 and they were removed on the 4th postoperative day. Thromboembolic prevention used subcutaneous enoxaparin 4000U/d. As clinical course and monitoring were uneventful, patient was discharged from intensive care unit on day 1 and transferred to surgery ward. Hospital discharge was possible on 9th postoperative day, without residual dyspnoea at room air. Last haemoglobin measure was 10.4 g/dL. Echocardiographic evaluation before discharge did not reveal any change in ventricular function and any sign of pericardial effusion. Pulmonary functional test performed 2 month after showed complete spirometric recovery with normal FVC and FEV1 (respectively 3L or 90% of normal values and 2.5L or 99% of normal values) but persistent DLCO impairment (4.23mmol/min i.e. 56% of normal).

3. Discussion

beta-thalassemia has variable clinical presentations and consequences ranging from simple asymptomatic microcytic anaemia for minor forms to chronic haemolysis in thalassemia intermedia and major that may be complicated by iron overload, hepato and splenomegaly, pulmonary arterial hypertension and cardiac vulnerability linked to volume overload and hypersiderosis [9, 10]. Few data exist on case of cardiac surgery using CPB for patients presenting minor or intermedia thalassemia. Some published cases reports (e.g. valve replacement) describe exacerbation of haemolysis during bypass [11-13]. On the other hand, uneventful coronary artery bypass surgery in a patient with Beta-thalassemia have been reported, suggesting that β-thalassemia erythrocytes do not seem to present higher mechanical fragility under CPB [14]. Criterions for specific CPB hemolysis risk evaluation are lacking.

As this pathology is rare in France, our experience was minimal so we considered and managed the case as a high risk patient. The case we present here seems to be more a minor thalassemia than thalassemia intermedia. The pathology was detected early with standard biological screening performed at the first surgeon consultation. This strategy, recommended in PBM guidelines, gave time for further evaluation by referring the patient to the anaemia clinic team who completed clinical and biological screening that led to the diagnosis. The team also elaborated a patient centred blood management plan that comprised tranexamic acid administration, cell salvage use, hemodynamic monitoring and tissue oxygen delivery surrogate parameters of anaemia tolerance to diag-
nose promptly adverse events. The need PRBC transfusion could be discussed as observed SvO2 rose (+20%) mainly after volume administration, the rise after PRBC transfusion was only +3 to 5%, that can be considered as futile, but the decision was guided by the need for tissue oxygenation improvement, witnessed by lactate rise, and the pre-established transfusion trigger at 75g/L. The context of coronavirus pneumopathy led to postpone for 10 weeks the surgical management of coronary artery disease regarding the benefit and risk balance. Our choice could be criticised in view of the severity of coronary artery disease but, as little was known at the time on COVID pneumopathy, the most cautious approach was chosen through close clinical follow-up. A limitation in our case may be the absence of any adverse event. However, thalassemia is a rare disease in our country and the association with coronavirus infection led us to take the maximum possible measures to manage such an unusual clinical situation. In conclusion, uneventful surgical coronary revascularization using cardio-pulmonary bypass has been performed in a patient with minor beta-thalassemia convalescent of COVID19 pneumopathy. The perioperative patient blood management strategy associating careful preoperative evaluation, tailored patient centred perioperative care may have been essential in the case management.

References