

# Subclinical Sickle Cell Crisis during Cardiopulmonary Bypass

## Timely detection and early management

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### أزمة الخلية المنجلية دون السريرية أثناء المجازة القلبية الرئوية اكتشافها في الوقت المناسب وعلاجها مبكراً

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**المخلص:** يمكن أن تحدث أزمة الخلية المنجلية أثناء المجازة القلبية الرئوية لعمليات القلب الجراحية للمرضى الذين يعانون من هيموجلوبين الخلية المنجلية مما قد يؤدي إلى خلل خلايا الدم الحمراء. هناك القليل من هذه التقارير في العالم العربي. نقدم هنا حالتين من عُمان يعانيان من أزمة الخلية المنجلية دون السريرية أثناء المجازة القلبية الرئوية. اكتشفنا الحالة في الوقت المناسب وإجراء اللازم بشكل مبكر يؤديان إلى نتائج جيدة. تمت أيضاً مناقشة الممارسة السريرية الجيدة لعلاج مثل هؤلاء المرضى.

**مفتاح الكلمات:** سمة الخلية المنجلية، المجازة القلبية الرئوية، خلل خلايا الدم الحمراء، تقرير حالة، عُمان

**ABSTRACT** A sickle cell crisis can occur during cardiopulmonary bypass for cardiac surgical procedures in patients with sickle cell hemoglobin, which could lead to hemolysis. There is a dearth of such reports from the Arab world. We hereby present two cases from Oman with subclinical sickle cell crisis during cardiopulmonary bypass. The timely detection and early management resulted in good outcome. The good clinical practice for management of such patients is also discussed.

**Key words:** Sickle cell trait; Cardiopulmonary bypass; Hemolysis; Case report; Oman.

**A** SICKLE CELL CRISIS CAN OCCUR IN PATIENTS with sickle cell trait (SCT) under extremely stressfully conditions albeit the incidence is much less than in patients with sickle cell disease (SCD).<sup>1,2</sup> We report two consecutive cases of SCT who developed subclinical sickle cell crisis during cardiopulmonary bypass (CPB) resulting in haemolysis without overt haematuria. Observation of an alteration in the color of the ultrafiltrate and a simultaneous fall in haematocrit, as noticed in the intraoperative arterial blood gas analysis report, led to the detection and eventual mitigation of the problem.

## CASE REPORTS

### CASE 1

A 50-year lady underwent a coronary artery bypass graft (CABG) on CPB under a narcotic based general anesthesia and appropriate life support monitoring. The preoperative haematological results revealed sickle cell trait due to presence of heterozygous haemoglobin S (HbS) of 29.7%. The intraoperative arterial blood gas (ABG), inclusive of those on CPB, showed: pH ranging from 7.37 to 7.4, PaO<sub>2</sub>: 108 to 154, PaCO<sub>2</sub>: 34 to 38 and mixed venous saturations were more than 70%; all were suggestive of adequate perfusion. In addition, the temperature of the perfusate was maintained above 34°C and nitroglycerine infusion was administered to pre-

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**Table 1: Hematological values and markers of hemolysis**

Parameters	CASE 1				CASE 2			
	Pre-operative	During the hemolytic event	Post transfusion	Post operative (immediately on reaching the ICU)	Pre-operative	During the hemolytic event	Post transfusion	Post operative (immediately on reaching the ICU)
Hemoglobin [Hb] (g/dl)	11	5.4	8.4	9	11.2	5.8	7.8	9.2
Hematocrit (%)	33	16	24	24	34	18	22	28
Urinalysis	Clear	Free Hb	Trace of RBC	Clear	Clear	Free Hb	Clear	Clear
Total bilirubin [ $\mu\text{mol/L}$ ]	9.5	12.5	12.1	13.5	10.4	13.5	13.9	13.2
Serum haptoglobin (mg/L)	Not done	690	900	380	Not done	520	513	360
Serum LDH (IU/L)	Not done	298	108	100	Not done	304	104	102
Absolute reticulocyte count $10^9/\text{L}$	Not done	5	5	5	Not done	3.9	5.9	4.0

WNL: within normal limits

Normal Ranges: Hb: 10.9 – 16.1 g/dl, Hematocrit: 33-46%, Total bilirubin: 3-17  $\mu\text{mol/L}$ , Serum haptoglobin: 360-1950 mg/L, Serum LDH: 95-190 IU/L, Absolute reticulocyte count: 5-200 x  $10^9/\text{L}$

vent vasoconstriction. A centrifugal pump was used to minimize blood trauma. Myocardial protection was achieved using cold antegrade blood cardioplegia. However, as soon as the cardioplegia was given, the ultrafiltrate from the hemofilter became bloodstained without obvious haematuria. An ABG analysis was immediately repeated and showed a haematocrit of 16%. Blood samples for surrogate markers of haemolysis were sent [Table 1]. Even though the urine appeared clear, urinalysis showed presence of haemoglobin. Immediately, 2 units of cross-matched blood were added to the pump to increase the haematocrit to 24%. Shortly afterwards, the ultrafiltrate became clear. Following this, the surgery was completed uneventfully. The patient did well postoperatively. The preoperative hematology status, values of markers for haemolysis during haemolysis and after transfusion have been tabulated [Table 1].

**CASE 2**

A 70 years old gentleman underwent CABG on CPB. Preoperative haematological tests revealed SCT (HbS 30%). Like in Case 1, all precautions were taken to avoid a sickling episode. However, soon after cardioplegia administration, the haematocrit dropped to 18% and the ultrafiltrate changed its colour without any change in the urine color. After sending blood specimens for identifying markers for haemolysis, two units of cross-matched blood were infused immediately. Soon after, the haematocrit improved to 22% and the ultrafiltrate cleared. The blood investigations are shown in Table 1.

**DISCUSSION**

In Oman, the prevalence of SCT is 6% and SCD is 0.9%.<sup>3</sup> Patients with sickle cell abnormalities undergoing surgery are generally at a greater risk of perioperative complications such as precipitation of a sickle cell crisis, microvascular occlusion, red cell membrane

fragility and haemolysis.<sup>1,2</sup> In addition, CPB can cause a sickling crisis due to aortic cross clamping, hypothermia, cold crystalloid cardioplegia, haemodilution and low perfusion pressures.

As both patients mentioned above were diagnosed to have SCT by routine sickle cell screen and subsequent haematological investigations, all steps were taken to prevent a haemolytic episode during surgery. However, immediately after cross clamping and cardioplegia administration, the ultra filtrate appeared bloodstained in both patients, which indicated haemolysis. The urine remained clear. We suggest that this event was triggered by haemodilution following cardioplegia administration with a precipitous fall in haematocrit.

Intraoperatively, it becomes difficult to make an immediate diagnosis of a sub-clinical sickling crisis and one has to depend on surrogate markers of haemolysis i.e. total bilirubin, serum lactate dehydrogenase (LDH) serum haptoglobin and absolute reticulocyte counts. The LDH levels were elevated in both patients (normal range: 95-190 IU/L) concurrent with a low haematocrit. Haptoglobin, an acute phase protein, was mildly elevated from the lower range of normalcy and absolute reticulocyte counts remained unchanged probably indicating that the haemolytic process had just begun. As soon as the ultrafiltrate became bloodstained, we suspected subclinical haemolysis, despite the fact that there was no obvious haematuria and transfused cross-matched blood to elevate the haematocrit to above 20%. The colour of the ultrafiltrate cleared and serum haptoglobin that was slightly elevated and serum LDH levels normalized rapidly indicating a short duration of a sickling related haemolysis.

Following a haemolytic episode, surrogate markers (total bilirubin, serum haptoglobin, serum LDH and reticulocyte counts) are usually elevated. The elevation of these markers depends to a large extent on the duration and severity of the episode. Total bilirubin, serum LDH and serum haptoglobin are sensitive indicators and are elevated earlier than absolute reticulocyte counts. When the surrogate markers are considered individually in both the patients, the total bilirubin was slightly elevated from its preoperative values. Serum haptoglobin levels, though within the normal range, were elevated during the episode compared to postoperative values. Serum LDH was elevated, but once again normalized postoperatively. It is true that the institution of a cardiopulmonary bypass

could derange several biochemical values. At the same time, macroscopic haemolysis and a drop in haematocrit per se are not markers for haemolysis. However, based on an overt change in ultrafiltrate colour that rapidly corrected after elevation of the haematocrit, presence of free haemoglobin in urine and mild elevation in some of the haemolytic markers, a working diagnosis of a short-lived subclinical haemolysis was made.

The shortcoming in this case report is that we did not measure the surrogate markers for haemolysis prior to surgery. This would have provided base line values for confirming the diagnosis and would have aided in identifying any pre-existing problems. Other than total bilirubin, as all the other markers were measured for the first time only intraoperatively, an elevation from their respective normal ranges was taken as diagnostic criteria.

In patients with sickle cell haemoglobin, preoperative partial exchange transfusion to achieve a haematocrit of 30% with HbS < 30% has been recommended for major surgery.<sup>1</sup> This is done to reduce the overall burden of HbS mass to less than 30% thereby avoiding a sickling episode. As both our patients had base line haemoglobin (Hb) levels above 10gms, no blood transfusions were administered preoperatively.

In conclusion, in the absence of other triggering factors, a drop in haematocrit during cardiopulmonary bypass in patients with sickle cell alone could lead to a subclinical sickle cell crisis and haemolysis. This might not necessarily be associated with haematuria. In the event of such a crisis being precipitated on CPB and if the cause is deemed to be haemodilution, rapid restoration of the haematocrit to above 20% would avoid further progress of the crisis. Lastly, a preoperative estimation of all the surrogate markers of haemolysis would aid in identifying any pre-existing problems as well as serve as base line values for identifying perioperative sickle cell related issues.

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