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Severe Acute Respiratory Distress Syndrome in a Patient with Sickle-Cell Anemia Requiring Veno-Venous Extracorporeal Membrane Oxygenation Therapy: Case Report and Review of the Literature

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Abstract

Background: Sickle cell anemia is caused by a mutation in the beta globin gene, resulting in the production of sickle hemoglobin, which is less soluble than normal hemoglobin. The main disease features are related to hemolytic anemia and blood vessels occlusion, causing ischemia and infracts. Acute chest syndrome is one of its most dangerous manifestations, and may cause severe hypoxemia and acute respiratory failure. Conservative management is often successful, but in rare cases the syndrome may be refractory. Extracorporeal membrane oxygenation (ECMO) support may be life-saving in these extreme situations. **Case Report:** A 31-year-old male admitted to the intensive care unit (ICU) in our hospital due to acute chest syndrome and massive aspiration. Due to extreme hypoxemia and severe acute respiratory distress syndrome, veno-venous ECMO support was initiated with rapid improvement in both oxygenation and hemodynamic status. The patient was weaned of ECMO after 7 days. He was discharged 4 weeks later. Although initiation of ECMO in sickle cell patients is uncommon, in selected refractory cases it may be life-saving. **Conclusion:** Although initiation of ECMO therapy in sickle cell anemia patients is uncommon, and may be even controversial, in selected refractory cases it may be life-saving.

Keywords

Sickle Cell Anemia, VV ECMO, Acute Chest Syndrome, Mendelson Syndrome, Sickle Cell Crisis

1. Introduction

Sickle cell disease (SCD) is caused by a point mutation in the beta globin gene, which encodes hemoglobin beta chains. Valine is substituted for the normal glutamic acid at the seventh amino acid (HBBp.glu7val), creating sickled hemoglobin (HbS) [1].

While normal hemoglobin is soluble in the cytoplasm of red blood cells, HbS forms insoluble polymers when deoxygenated. Polymerized HbS damages the red blood cell membrane, interfering with membrane function, cell deformability and cell lifespan [2]. Following deoxygenation, the red blood cells gradually become irreversibly distorted, with the classic sickle shape in light microscopy or electron microscopy [3]. In addition, cell membrane damage causes release of membrane and intra-cellular particles, which increases endothelial adhesion and hypercoagulability [4]. Sickle cells are dense and fragile and are unable to traverse the microcirculation, causing vaso-occlusive disease [5], aggravated by hemolysis of the fragile cells. Sickle cells undergo intravascular and extravascular hemolysis, causing anemia with reticulocytosis [6]. Adherence of damaged blood cells to the endothelium causes vasoconstriction and inflammatory changes, and ischemia ensues [7].

Clinical manifestations of SCD include acute and chronic pain and tissue ischemia. Stroke, acute chest syndrome, renal and bone infraction and venous thromboembolism are common phenomena. Acute chest syndrome is a syndrome of fever, chest pain, hypoxemia, wheezing, cough and respiratory distress with new pulmonary infiltrates in chest X-ray [8]. 50% of SCD patients will endure at least one episode of acute chest syndrome through life [8], with considerable morbidity and mortality rates. Acute chest syndrome may be caused by several mechanisms, including vaso-occlusion, infection, hypoventilation, hypoxemia from other causes (pneumonia), smoking and thromboembolic events (including fat embolism) [9] [10].

Vaso-occlusion within pulmonary capillaries is the main pathological basis, and an inciting event triggers deoxygenation of HbS, sickling, endothelial injury and ischemia [11]. Hypoxia, hypercarbia, acidosis and inflammation further exacerbate the process, creating a vicious cycle.

Treatment includes analgesics, hydroxyurea, blood transfusion and supportive care (hydration, antibiotics if an infection is suspected, oxygen support). In severe acute respiratory failure, intubation and mechanical ventilation may be necessary [12]. If mechanical ventilation is insufficient, and refractory hypoxemia and/or hypercarbia ensue, extra corporeal membrane oxygenation (ECMO) may

be used. Use of ECMO in SCD patients has been described in several case reports [13]-[21] and two case series [22] [23].

Here we present a case of a young patient with SCD who was admitted to the intensive care unit (ICU) in our medical institution due to acute chest syndrome, severe hypoxemia and aspiration pneumonitis. Due to severe acute respiratory distress syndrome with refractory hypoxemia, veno-venous (VV) ECMO therapy was imitated with rapid improvement and survival to hospital discharge.

Informed consent could not be obtained due to the patient's neurological status during discharge. The case report is without any identifying personal details, in order to keep the patient's privacy.

2. Case Presentation

H.B, a 31 year old man, was admitted to our ICU on June 2022. Past medical history included SCD along with beta-thalassemia, G6PD deficiency, chronic leukocytosis and thrombocytosis, heavy smoking and poor compliance for therapy. He suffered from chronic neuropathic pain and had multiple hospitalizations due to acute occlusive pain. He was admitted to the emergency department due to acute chest syndrome, fever, severe pain, hypoxemia and diffuse bilateral infiltrates on chest X-ray (**Figure 1**). He received intravenous hydration, analgesics and one dose of intravenous ceftriaxone, but respiratory collapse soon ensued and the patient was sedated and intubated. The intubation was technically difficult and aspiration was noted during intubation attempts. The patient was admitted to the ICU after computed tomography of the chest excluded pulmonary embolism (**Figure 2**). He was treated with antibiotics and fluids. Initial HbS fraction was 75%. He received packed red blood cell and phlebotomy was also performed, in order to maintain HbS fraction around 30% - 40%. At first, arterial blood saturation was maintained above 90%, and the patient was hemodynamically stable. However, 7 days later, significant deterioration in his condition was noted, probably due to aspiration pneumonitis. He developed

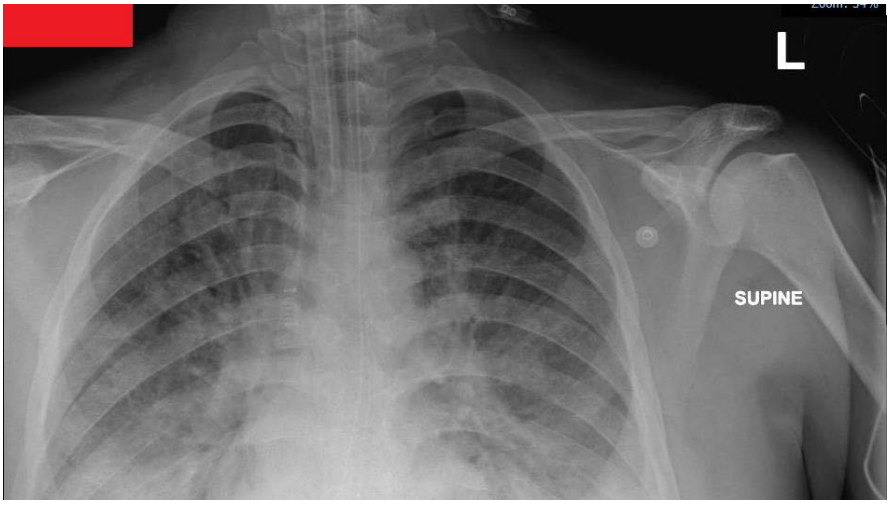

Figure 1. Chest C-ray during ICU admission.

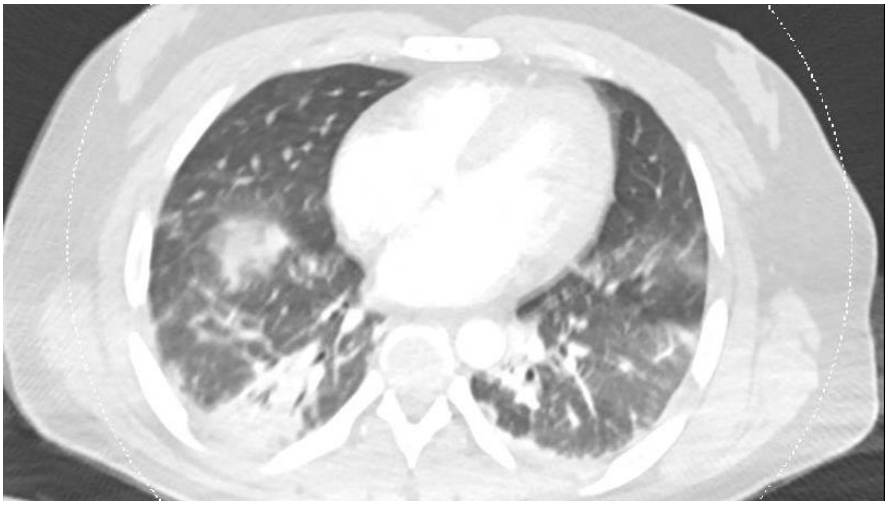

Figure 2. Chest computed tomography during ICU admission.

severe hypoxemia with P/F ration below 80, "white lungs" in chest X-ray and severe acute respiratory distress syndrome. Shock soon ensued due to increased pulmonary pressure and right ventricular failure. Prone position was attempted without significant improvement, and therefore VV ECMO therapy was initiated. The right internal jugular vein and right femoral vein were cannulated. Rapid improvement in oxygenation and hemodynamics was observed. Seven days later, after improvement in oxygenation, hemodynamics and chest x-ray, the patients was successfully weaned of ECMO.

Percutaneous tracheostomy was performed, and he was gradually weaned of sedation. Due to severe delirium head computed tomography was performed, demonstrating multiple small infracts in watershed zones (**Figure 3**). In addition, deep vein thrombosis was observed in ultrasonography at the former cannulation sites (**Figure 4**), and full anticoagulation with enoxaparin was initiated.

The patient gradually regained consciousness and was weaned of mechanical ventilation. Decannulation was performed. He was discharged from the ICU approximately one month following admission. After 45 days of rehabilitation he was discharged home in good clinical condition. He regained full consciousness and required only minimal help during daily activities.

3. Discussion

ECMO therapy is an important salvage tool for patients with refractory cardiorespiratory failure. Due to the increasing availability of ECMO equipment and staff, many medical conditions which have been considered in the past to be relative or even absolute contraindications for ECMO, are now being considered as acceptable indications. Acute chest syndrome is the most common cause of mortality in adults with SCD, and ECMO therapy may be beneficial for two main reasons: first, the severe hemodynamic compromise following acute chest syndrome may require circulatory support via VA ECMO, and second, resolving

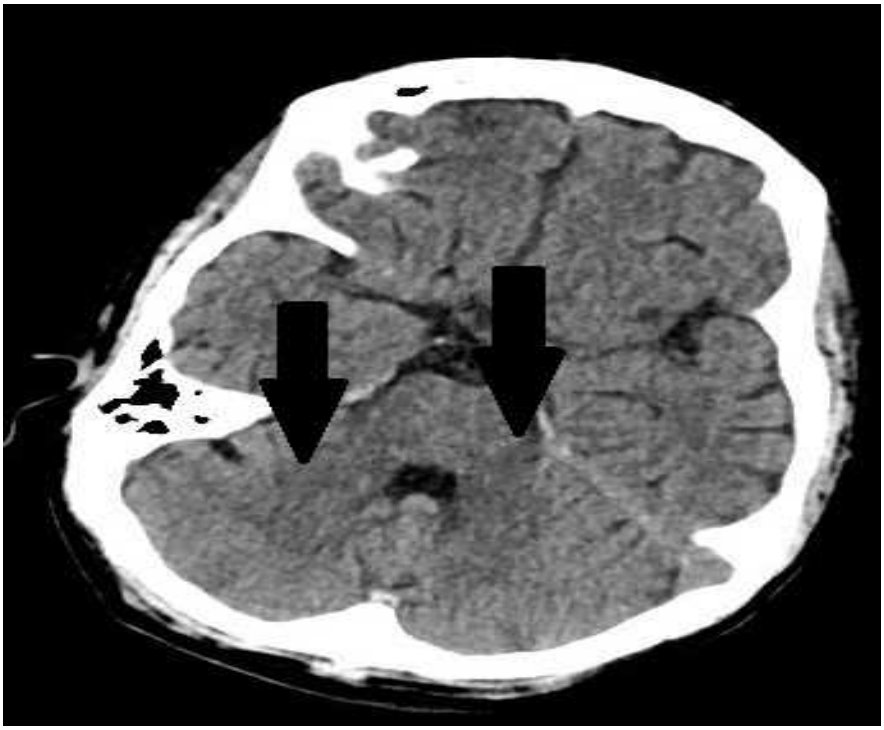

Figure 3. Computed tomography of the brain showing multiple brain infracts.

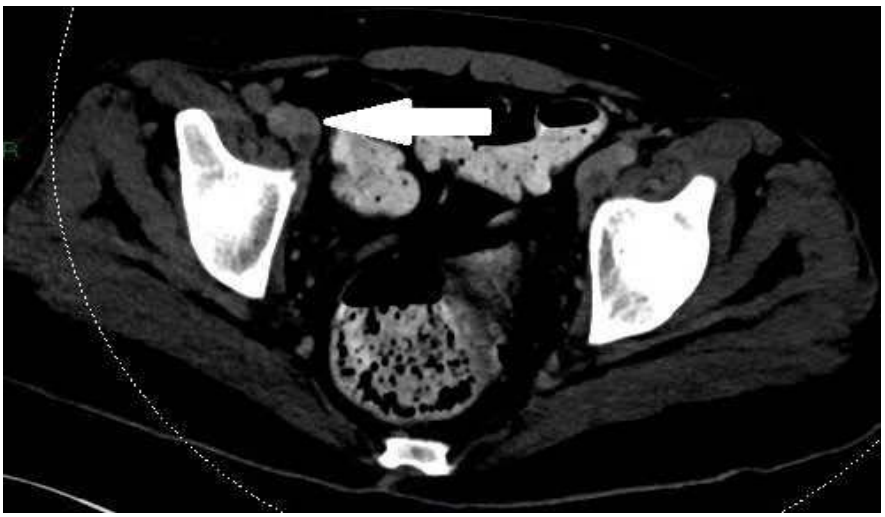

Figure 4. Ultrasound of the femoral vein showing deep venous thrombosis.

hypoxemia is crucial to relieve the hypoxic pulmonary vasoconstriction, further relieving sickling and vaso-occlusion. This purpose may be achieved with VV ECMO [22]. Most reports regarding ECMO in SCD patients in the literature are pediatric, and only few reports are available in the literature regarding adult SCD patients requiring VV ECMO therapy [24]. The first report of adult SCD patient with acute chest syndrome requiring VV ECMO was published by Sewaralthahab *et al.* [16]. Boissier *et al.* [22] investigated 22 adult SCD patients, 10 of them were treated with VV ECMO and 12 with VA ECMO. In hospital survival was 27%. KUO *et al.* [23] studied 65 pediatric SCD patients from the ELSO-registry

in years 1990-2012. 80% of patients were treated with VA ECMO, even though the most common indication for ECMO was acute respiratory failure. 69% of them had acute chest syndrome or acute respiratory failure from other causes, 9% had sepsis, 4% had cardiac arrest and 7% had other reasons for ECMO therapy. Overall in-hospital survival was 52%, with better survival in the VV ECMO group (85% vs. 43% in the VA ECMO group). The most common complications were acute kidney injury, in 45% of patients, significant hemorrhage necessitating administration of blood products (25%), need for inotropic support (40%) and oxygenator membrane clotting (15%).

Regarding ECMO therapy, SCD patients may present unique challenges. Since SCD is often manifested by hemolysis, vaso-occlusion and increased thrombogenicity, ECMO therapy was considered to be a relative contraindication in those patients in the past. Increased risk for thrombosis or bleeding in the cannulation sites, cerebrovascular infracts, pulmonary emboli, oxygenator clotting and hemolysis, all pose a significant risk in those patients. H.B indeed developed both intracerebral infracts and deep vein thrombosis in the cannulation sites. However, considering the refractoriness of his hypoxemia and cardiorespiratory failure, VV ECMO was the only possible option for salvage therapy. His condition was critical during ICU admission, with SAPS-II score of 68, indicating in-hospital mortality rate of 81% despite his young age. Not only he had acute chest syndrome during admission, a condition severe enough in SCD patients to cause high mortality, he also had massive aspiration during intubation attempts in the emergency department, aspiration pneumonitis and severe acute respiratory distress syndrome, further aggravating the vicious cycle of hypoxemia, vaso-occlusion and sickling. During consultation with other large ECMO centers before initiating ECMO therapy in H.B, there was controversy whether he is a good candidate for this therapy; since the mortality rate in these patients on ECMO is high [22] and the patients had very high SAPS-II score with very high in hospital mortality risk. However, due to his young age and critical refractory hypoxemia we decided to initiate ECMO anyway. Fortunately, the patient responded well to this therapy and eventually was discharged in good condition.

"Awake ECMO" is a possible option in selected patients. In SCD patients it might have the benefit of recognizing neurologic deficits due to intracerebral infracts earlier. In a study by Avgeridou *et al.* [24], they described a similar case of a young man with SCD and acute chest syndrome, with refractory cardiorespiratory failure requiring VV ECMO. They were able to maintain the patient awake while on ECMO. In the case of H.B, due to poor lung compliance and severe delirium this option was not viable.

4. Conclusion

Although initiation of ECMO therapy in SCD patients is uncommon, and may be even controversial, in selected refractory cases it may be life-saving, and should be considered a potential option for those patients. Further and larger studies are

required to determine outcome of SCD patients after ECMO therapy.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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