Kasabach-Merritt Syndrome In A Patient With Klippel-Trenaunay Syndrome Undergoing Massive Transfusion.

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Citation

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Abstract

We present the case of a patient with extensive Klippel-Trenaunay Syndrome and underlying Kasabach Merritt Syndrome who encountered extensive intraoperative bleeding requiring a massive transfusion of greater than thirty liters of blood and blood products. This case highlights the coagulation challenges posed not only by massive transfusion but also by Klippel-Trenaunay Syndrome with concomitant Kasabach-Merritt Syndrome. This case also notes the value of massive transfusion protocols, while keeping in mind that these have been created from retrospective data.

CASE DESCRIPTION

A seventeen-year-old male with Klippel-Trenaunay Syndrome with extensive involvement of his right lower extremity was admitted to a tertiary care facility for management of a painful nonunion resulting from a right femoral fracture. He was scheduled for a transfemoral amputation, a procedure indicated for his increasing chronic right leg pain and syncope with standing secondary to extensive venous pooling (Figures 1 and 2). He required chronic opioids for his right leg pain. This patient also suffered from Kasabach-Merritt Syndrome, a chronic consumptive coagulopathy that can be associated with Klippel-Trenaunay Syndrome. Upon admission, his coagulation studies were: INR (International Normalized Ratio) of 1.3 (normal = 0.9-1.2), Activated Partial Thromboplastin Time (aPTT) of 32 seconds (normal = 21-33 sec), Fibrinogen 125 mg/dL (normal = 175-430 mg/dL) and Platelets 108 (x10^9/L; normal = 150-450 x10^9/L).

Under general anesthesia, a transfemoral amputation was performed, though complicated by an estimated blood loss of 5700 mL. Difficulty with hemostasis was attributed to non-compressible bleeding sites, underlying Kasabach-Merritt Syndrome and difficulty oversewing the venous malformations. In the thirteen postoperative days following the initial amputation, he had persistent and progressive sanguinous oozing from the surgical wound requiring increasingly frequent blood and blood product transfusions for blood-loss anemia and coagulopathy. The Anesthesia Inpatient Pain Service was consulted for rapidly increasing right stump pain and a subsequent dramatically accelerated opioid consumption. He described the pain as being ten on a ten-point pain scale, and was administered a total of 39 mg of intravenous (IV) hydromorphone over 2.5 hours without significant improvement.

The patient returned to the operating suite for wound examination and hematoma evacuation. Hemostasis was attained and he was transferred to the surgical intensive care unit. However, he continued to have persistent sanguinous oozing requiring further blood and blood product transfusions for both anemia and persistent coagulopathy. Over the next 12 hours he received seven units of packed red blood cells and one unit of filtered and washed red blood cells from blood salvage system. As the patient was not responding appropriately to blood transfusions he returned early the following morning to the operating suite for another wound examination and attempt at hematoma evacuation, irrigation and debridement. Preoperatively, his labs showed: Hgb 7.9 g/dL, Platelets 88 (x 10^9)/L, INR 1.3 and Fibrinogen 140 mg/dL. Extensive blood loss was anticipated, and the Anesthesia team prepared by instructing the blood bank to activate the hospital's massive transfusion protocol, by inserting multiple large bore peripheral and central venous catheters, and by priming a Belmont® rapid infusor machine.

Blood loss during this procedure was tremendous—an estimated blood loss of over thirty liters. In response, he received fifty-eight units packed red blood cells, forty-nine units fresh frozen plasma, twelve units cryoprecipitate and

six apheresis units platelets. During the resuscitation he experienced hyperglycemia and hyperkalemia with associated changes on his electrocardiogram. No inotropic or vasoconstrictive drugs were required to maintain blood pressure. Throughout the case he received three doses of recombinant Factor VIIa (15,000 units), 8.5 g calcium chloride, 2 g magnesium sulfate, 50 mEq sodium bicarbonate and 100 units insulin. Additionally, during the first twelve postoperative hours, he required three apheresis units of platelets and one unit of cryoprecipitate. A backup rapid infusion device was kept primed in the operating room in the case the primary system failed.

Toward the end of the operative case, the anesthesia team experienced difficulty ventilating and oxygenating the patient due to very high peak and plateau airway pressures. Vital signs were: pulse 124 (increasing from baseline of 60-80), arterial BP 131/77 (trending down from 170's/80's), S_pO_2 77%, end-tidal CO_2 51 mmHg (normal 35-45 mmHg), peak airway pressure 77 cmH_2O and mean airway pressure 57 cmH_2O (increased from baselines of ~24 and ~12 cmH_2O, respectively). Arterial blood gas analysis at that time revealed acute respiratory acidosis: pH 7.25, P_{O2} 82 mmHg, P_{CO2} 61 mmHg on 100% F_{IO2}. On physical exam he had bilateral breath sounds and a distended and tense abdomen. A bedside transesophageal echocardiogram showed compression of the right ventricle, likely attributed to an enlarged liver, and a hyperdynamic, under-filled left ventricle. No air or clot was seen in the heart chambers or pulmonary arteries, and the valves appeared grossly normal.

Though urine output seemed adequate, the tense abdomen, ventilation difficulty, and echocardiogram findings suggested a diagnosis of abdominal compartment syndrome. An emergent decompressive midline laparotomy was performed with immediate improvement of ventilation and oxygenation. A decision was made to pack the abdomen and delay wound closure until ventilation parameters remained stable. The patient was transferred to the surgical ICU intubated for further hemodynamic monitoring and management. In the following days he underwent several subsequent surgical procedures to facilitate abdominal wound and leg stump closure. Additionally, he underwent a splenectomy with the aim of improving his Kasabach-Merritt Syndrome coagulopathy. Ten weeks later he was discharged home in stable condition with near-complete resolution of his right lower extremity pain. In total during his admission, he received 155 units packed red blood cells, 103 units fresh frozen plasma and 20 apheresis units platelets.

The patient described has provided permission to present this case.

Figure 1

Figure 1: Scout film demonstrating marked edema of the right lower extremity and pelvis and contracture of the right lower extremity with a hypoplastic right femur.

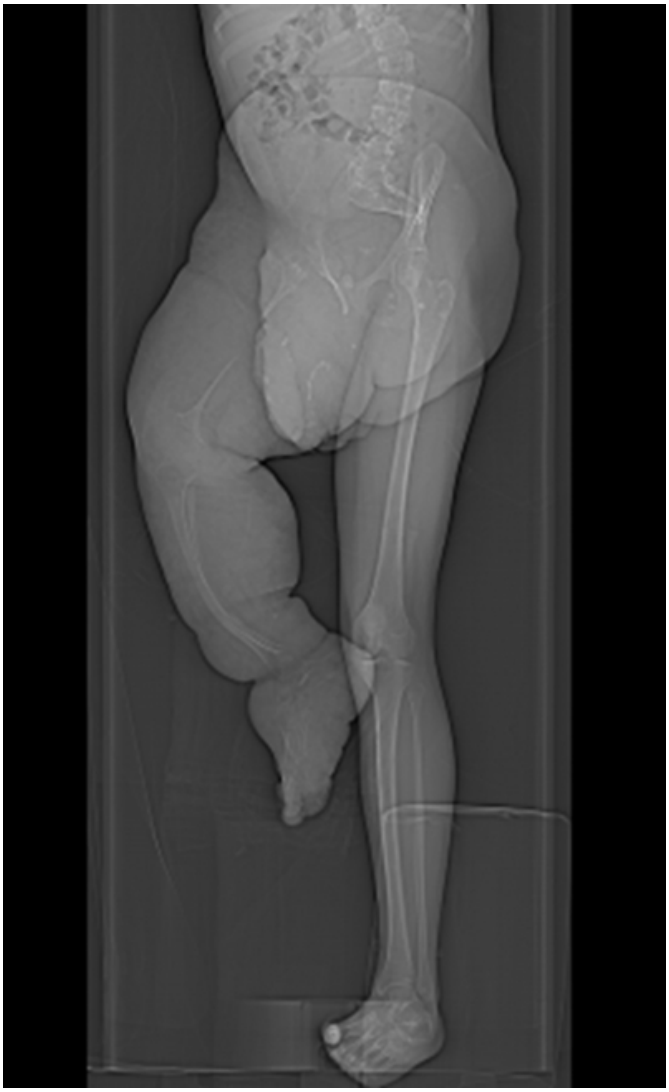
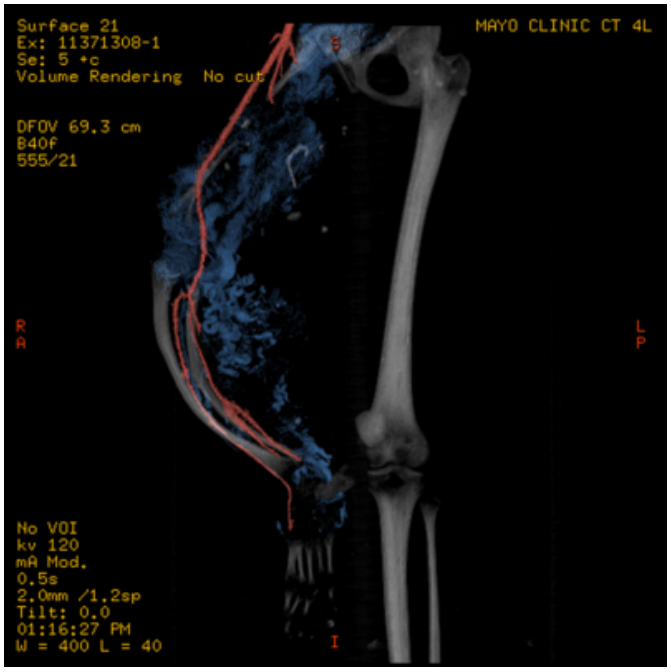


Figure 2

Figure 2: Three-dimensional reconstruction of CT angiogram of the right lower extremity with arterial and venous phases demonstrating extensive venous pools and evidence of arteriovenous malformations (Red = arterial structures, Blue = venous structu



DISCUSSION

Klippel-Trenaunay Syndrome (KTS) is a congenital disorder of angiogenesis manifested by venous and lymphatic malformations, hemangiomas, lymphangiomas and arteriovenous malformations, often with adjacent bone growth abnormalities. The malformations are typically unilateral and are most prevalent in the lower extremity.[1] Of interest to this case, KTS can be associated with Kasabach-Merritt Syndrome (KMS) and disseminated intravascular coagulation (DIC). Kasabach-Merritt Syndrome is usually caused by a hemangioendothelioma or other vascular tumor, often present at birth. Although these tumors are relatively common, it is rare for them to cause KMS. If these tumors are abnormally large, or if they grow rapidly, they can trap platelets, causing severe thrombocytopenia. Tumors can be found in the trunk, upper and lower extremities, retroperitoneum, and in the cervical and facial areas. In this case, KMS was suspected because of the consumptive coagulopathy due to high turnover of coagulation factors possibly initiated by vascular stasis and exposed collagen within the large vascular malformations of KTS patients. Thrombocytopenia and hypofibrinogenemia resulted. Prothrombin time and activated partial thromboplastin time in Kasabach-Merritt Syndrome are typically normal or only slightly elevated.[2] Worsening of Kasabach-Merritt Syndrome may result in frank DIC with elevations of INR and aPTT (activated partial thromboplastin time), depletion of fibrinogen and platelets and evidence of thrombosis and/or hemorrhage. Trauma (including surgery) and sepsis are factors which might exacerbate an underlying Kasabach-Merritt Syndrome and cause a full DIC presentation.[3]

Ideally, this patient's Kasabach-Merritt coagulopathy would have been corrected more pre-operatively, however the compartment syndrome which had developed in his leg required emergent surgical intervention. This patient's clinical status was guarded due to his chronic underlying coagulopathy which was exacerbated by surgical manipulation and the list of complications caused by massive transfusion.

Potential complications of massive transfusion include: hypocalcemia, hyperkalemia, metabolic acidosis, coagulopathy, hypothermia, transfusion related acute lung injury (TRALI), transfusion associated circulatory overload (TACO), and abdominal compartment syndrome. Coagulopathy from massive transfusion may have several causes including hypothermia, dilutional thrombocytopenia, dilutional coagulation deficiency, dilutional fibrinogen deficiency and DIC.[4,5] In addition to the dilutional coagulopathy of massive transfusion, the patient presented in this report had a concomitant consumptive coagulopathy secondary to Kasabach-Merritt syndrome.

There is no clear consensus for the ratio of blood products to be administered during massive transfusion. The goal of administering a proper ratio of blood products is to prevent dilutional coagulopathy and to compensate for blood component consumption. A patient can lose up to 70% of their coagulation factors before developing a clinical bleeding diathesis, so the goal is the ensure the levels of coagulation factors remain above 30% of normal. A coagulation factor level of 30% correlates to a PT (prothrombin time) and aPTT of 1.5 times normal. Similarly, clinically significant coagulopathy occurs when fibrinogen levels fall below 100 mg/dL or platelets fall below 80 x 10^9/L.[4]

The transfusion ratios used during the primary procedure described in this case were RBC:FFP:Platelets of 1:0.84:0.62 (or FFP:RBC of 1:1.2, and Platelets:RBC of 1:1.6). Numerous retrospective studies have demonstrated improved

outcomes with increased platelet-to-RBC ratio and increased FFP-to-RBC ratio. Perhaps the most compelling data is from a multicenter retrospective study by Holcomb et al. which showed a significant association between increased FFP-to-RBC ratios (>1:2) and increased platelet-to-RBC ratios (>1:2) with increased survival at 24 hours and 30 days from admission.[6] Massive transfusion protocols are associated with decreased pneumonia, respiratory failure, sepsis, multi-organ failure and abdominal compartment syndrome.[7] Likewise, a review by Ketchum et al. found a reduction in coagulopathy from massive transfusion if FFP and platelets were administered early in resuscitation.[8] These retrospective studies are hindered by survival bias. Currently, prospective studies on the effect of massive transfusion ratios are lacking and are necessary to guide future massive transfusion recommendations.

Regardless of the precise ratio used during massive transfusion, the clinician must be aware of potential coagulopathy and monitor for this consequence of massive transfusion. Several groups recommend following basic coagulation studies including PT, aPTT, Fibrinogen and platelet levels throughout massive transfusion. In order to follow a patient's more global coagulation function, one could follow serial Thromboelastograms™ (TEG).[4,9] PT, aPTT, Fibrinogen, platelets and TEG™ can be used to guide necessary blood product replacement.[4,5,6]

Blood component ratios are useful during massive transfusion because during a massive resuscitation by the time the laboratory values are available for assessment the patient has often lost and received a large amount of blood and blood products. In this scenario, the laboratory values may not reflect the patient's current coagulation status.

A final point is effective multi-specialty communication and coordination of care was essential for success in this case. Four primary services were involved in the operating suite including Anesthesiology, Orthopedic Surgery, Vascular Surgery and General Surgery. At times, when the patient was hypovolemic, the surgical services would pause and hold pressure on the bleeding surfaces and underlying vascular structures in order to allow time for resuscitation. At the conclusion of the case, there was a concerted diagnosis and very rapid treatment of the patient's abdominal compartment syndrome. Without open communication and collaboration both before and during this case, the outcome may not have been so positive.

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