Case Report

Massive Transfusion in a case of Hepatocellular Carcinoma

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ABSTRACT

The mortality in massive transfusion is high due to many associated complications. We share our experience with massive blood transfusion in a young patient with 71 units of blood products transfused within 24 hours and 90 more blood components required in subsequent days. The case highlights the importance of massive transfusion protocol to improve clinical outcomes in the patient and judicious use of precious blood units. Blood transfusion services and the clinical team should have good communication and coordination to deal with such situations. Furthermore, in view of cost, constant increased demand, urgency, limited availability and risk of associated infections, more research in the area of blood substitutes is highly re-commanded. This case report also emphasizes on future research to make blood substitute with more similarities and minimum complications.

Key words: 71 units, Complications, Early communication, Massive transfusion protocol

Massive transfusion (MTx) is defined as transfusion of >1 blood volume, that is, ≥10 RBC units in 24 h, or replacement of >50% of total blood volume (TBV) by blood products within 3 h, or >4 RBC units in 1 h with anticipation of the continued need for blood product support in adults or an exchange transfusion in case of an infant [1]. The mortality associated with MTx is very high ranging from 34% to 40% as per the published literature of the UK [2]. It can lead to 54% deaths in the first 6 h due to the use of disproportionate blood products [3]. Dealing a case of MTx requires team efforts from clinical as well as blood transfusion services (BTSs). It is imperative to recognize major blood loss early and institute effective action promptly if shock and consequences are to be prevented.

The aim of this case report is to share our experience of massive transfusion in a young patient and prompt interventions carried out by clinical team and BTS. A timely taken decision of administering rFactor VII proved as boon for positive outcome in this case scenario and saved life of patient.

CASE REPORT

A 26-year-old male patient (blood group: "O" Rh positive, weight: 68 kg, height: 158 cm, approximate TBV 4.8 L) was posted for partial hepatectomy for fibrolamellar hepatocellular carcinoma (HCC). In view of major surgery of vascular liver in an anemic patient, BTS was requested for reservation of four units each of packed red blood cells (PRBC), and fresh frozen plasma (FFP). His pre-operative investigations were as shown in Table 1.

During surgery, profuse bleeding was observed while dissecting lymph nodes adherent to a major vessel. The intravenous crystalloid infusion was started immediately and BTS was alerted. At first, two units each of PRBC and thawed FFP were released from BTS. Details of intra-operative blood loss and blood components transfused are presented in Table 1 and 2. There was a blood loss of 15.1L (approximately 3 blood volumes of patient). Different blood components like PRBC, FFP, Cryoprecipitate , and platelets were transfused. Throughout the surgery we tried to maintain the PRBC: FFP ratio as 1:1 (with 33 PRBC, 28 FFP, 4 Cryoprecipitate, 1 SDP and 3 RDP units). We could manage to transfuse all blood components of patient's blood type only i.e. O Rh positive. At one point Blood bank had to issue 2 units of Whole blood unit, after discussing the situation to clinical team; in view of depletion of stock and shortage of time for component preparation.

During surgery, drugs were started as inj. Ca gluconate 200 mg IV, inj. $NaHCO_3$ 40 ml IV, and inj. Mg SO4 2 gm IV to minimize electrolyte imbalances. Vasopressor support was given with adrenaline to maintain blood pressure (BP) (achieved 90/60 mmHg). The bleeding was continuing in spite of the surgical repair of the vessel, so recombinant factor VIIa (NovoSeven) [4] was given 6 mg IV to achieve hemostasis and exicion site was packed. Patient was shifted to recovery unit and was maintained on mechanical ventilation. His hematological and biochemical parameters and arterial blood gas (ABG)reports were monitored

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Table 1: Patient's laboratory parameters

Parameters	Pre-operative parameters	Intraoperative 5:00 pm 4 L blood loss	Post-operative day 1	Reexploration	Post-operative 1 month
Hb (13–17 g/dL)	7.7 gm/dL	2.9	7.5	10	8
RBC (4.5–5.5 X 10^{12})	RBC: 2.76 × 10^{12}/L	1.2	2.25	3	3.6
Hct (40–50%)	Hct: 25%	10	22.5	36	23
PLT (1.5–4.5 lakh/L)	93,000/µL	78	64	69	98
PT (12–15.7 s)	27.2 s	27	25	22	19
aPTT (24–35 s)	51.2 s	51	30.8	29	38
INR	2.16	2.15	1.9	1.7	1.6
AST (<50 U/L)	-	1877	3890	2970	86
ALT (<50 U/L)	-	757	1670	880	38
Total bilirubin (0.3–1.2 mg/dL)	-	3	3.38	3.7	19
Electrolytes	Na^+:144 mmol/L, K^+ :4.15 mmol/L, Cl^- :106 mmol/L, Ca^{2+}:7.9 mg/dL, Mg^{2+}:2.49 mg/Dl	Normal range	Na+ raised, rest normal	Normal range	Normal range

Hb: Hemoglobin, Hct: Hematocrit, PLT: Platelet count test, PT: Prothrombin time, aPTT: activated partial thromboplastin time, INR: International normalized ratio, AST: Aspartate aminotransferase, ALT: Alanine transaminase

Table 2: Patient's intraoperative electrolyte status

Parameters	02:15 pm	05:00 pm 4 L blood loss	07:35 pm	10:38 pm	00:06 am
Na+mmol/L	131	135	132	139	136
K+mmol/L	4.24	4.35	4.07	4.01	4.12
Cl_mmol/L	98	101.8	100.2	99	99.3
Ca++ mg/dL	4.16	4.15	3.76	3.32	3.34
Lactate	2.4	4.0	14	15.6	15.8
pH	7.29	7.27	7.06	7.08	7.08

at timely intervals during and after surgery to observe and manage effects of massive transfusion [Table 1 and 2].

Re-exploration after 48 hours reveled collected blood in retro-peritoneal space and diffuse ooze was observed. Hence rFactor VII was repeated as 3mg IV dose. Bleeding was stopped and surgical site was closed. The patient was shifted to a recovery room and kept on mechanical ventilation. The patient had deep icterus on inspection. Subsequently, the patient was improving hemodynamically and investigations were satisfactory, so he was extubated. He got discharged from ICU on Post-opeartive day 7. Overall, he was transfused with 161 blood components during the hospital stay [Table 3]. The patient had followed up to the primary consultant for the underlying malignancy regularly and doing well. He was tested for TTI (HBsAg, HIV-1 and 2, and HCV by available third-generation ELISA on regular intervals of 1, 3, and 6 months which were non-reactive).

Table 3: Overall transfusion of blood products

Components	Day of surgery	POD 1	Reexploration	Total
Whole blood	02	-	-	02
Packed red cells	33	13	08	54
FFP	28	28	14	70
Cryoprecipitate	04	06	06	16
Single donor platelets (SDP)	01	02	00	03
Random donor platelets (RDP)	03	11	03	17
Total	71	60	31	162

DISCUSSION

Massive transfusion in patients with severe blood loss serves as life saver. It can be life threatening too; if complications related with it are not addressed. Massive transfusion initiated for massive bleeding leads to a classical triad of complication, that is, tissue hypoxia causing metabolic acidosis, blood transfusion, and crystalloid infusion causing hypothermia and dilution of coagulation factors, platelets, leading to dilutional coagulopathy [5]. The complications of MTx are depicted in Fig. 1. Massive transfusion protocol (MTP) is defined as an empirical treatment that optimizes the management of resuscitation and correction of coagulopathy arising from severe hemorrhage [6]. It includes local adaptation, activation, and cessation of transfusion with coordination of clinical, hematological, and laboratory team.

MTx cases pose a great challenge for both treating clinicians and transfusion services in not only providing safe and adequate blood products in appropriate ratio but in correlating it with the clinical condition and laboratory investigations also. The main aim is to optimize cardiac output, tissue perfusion, oxygenation, and metabolic state, and monitor complete blood count, coagulation screen, ionized calcium, and ABGs every 30–60 min. The goals

are to maintain temperature more than 35°C, pH >7.2, base excess <4 mmol/L, and ionized calcium >2.1 mmol/L. Platelets should be >50 × 10^9/L, PT/aPTT < 1.5 times normal, and fibrinogen levels >0.8 gm/L [6]. Checking of blood products in operation theater is must and in case of any disparity or typographic error found, the blood should be sent back to blood bank within 30 min of the release of blood products from the blood bank [6,7].

In our case, the following measures were instituted to minimize detrimental effects of MTx: Use of inline warmer for transfusion and IV fluids infusion to prevent hypothermia, use of PRBCs and FFP in the ratio of approximately1:1 to prevent dilutional coagulopathy, limiting the use of colloids as they affect coagulation profile, inj. $NaHCO_3$ for hyperkalemia and metabolic acidosis, inj. Ca. gluconate for hypocalcemia, and inj. $MgSO_4$ for hypomagnesemia. Subsequently, inj. KCl was administered to combat hypokalemia, judicious use blood components, and timely decision to use factor VIIa concentrate to achieve hemostasis [6] (mechanism of action is explained in Fig. 2), use of a point-of-care system such as TEG, ABG analysis, BTS, and OTs is nearby (in reach of less than 10 min), dedicated coordination at both ends (BTS and operating team) and with laboratory services.

Such cases can at times have to be dealt as unplanned surgeries in case of trauma situations. To tackle such cases, each BTS should have an existing MTP and also SOPs to handle them medicolegally. Ensuring enough blood availability by good communication and contacts with fellow blood banks, blood sample adequacy, and accuracy for testing and technical issues such as assigning red cell processor, process in batches should be

(Classical Triad: Dilutional coagulopathy, Hypothermia, Acidosis)

Early (<24 h)		Delayed (> 24 h)	
Metabolic complications	**Immunological transfusion reactions**	**Non immunological**	**Immunological**
a) Hypocalcaemia: Because of citrate overload from rapid transfusion of blood products **b) Hypomagnesaemia:** Because of large volume of magnesium-poor fluid and citrate overload **c) Hyperkalemia:** Because of hemolysis of RBC from storage, irradiation, or both **d) Hypokalemia:** Because of reentry into transfused RBCs, release of stress hormones, or metabolic alkalosis **e) Metabolic alkalosis:** Because of citrate overload **f) Acidosis:** Because of hypoperfusion, liver dysfunction, and citrate overload **g) Hypothermia:** Because of infusion of cold fluid and blood products, opening of body cavities, decrease heat production, and impaired thermal control **h) Hemostatic defects:** Platelet related/coagulation factor related	**a) Allergic:** Anaphylaxis, urticarial, etc. **b) Hemolysis:** HTR, mechanical c) Febrile non-hemolytic transfusion reactions (FNHTRs) d) Transfusion related acute lung injury (TRALI)	a) Transfusion transmitted infections (TTIs) b) Transfusion associated circulatory overload (TACO) c) Air embolism d) Hemostatic defects	a) Hemolysis (DSHTR) b) Transfusion Related Immuno-modulation (TRIM) c) Transfusion associated-Graft verses Host Disease (Ta-GvHD) d) Post-transfusion purpura (PTP)

Figure 1: Complications of Massive Transfusion

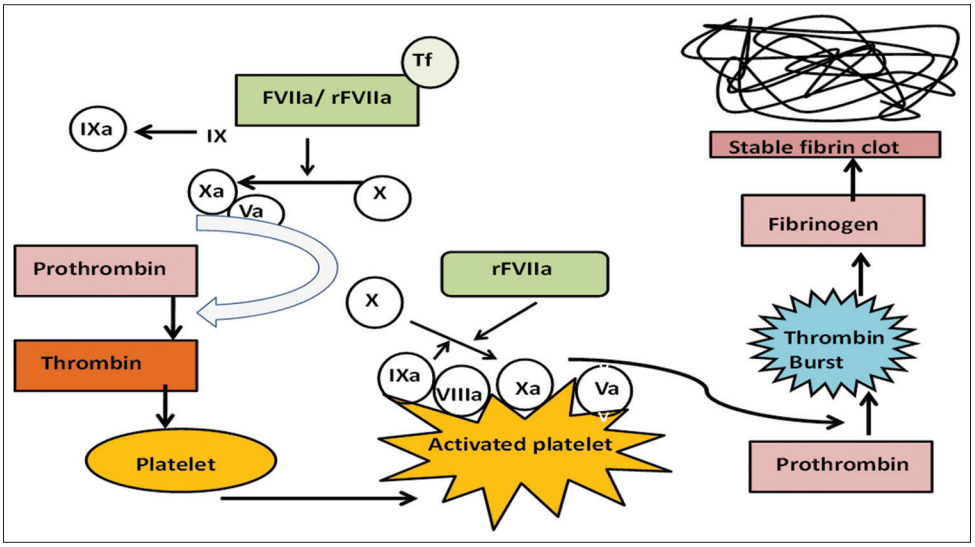

Figure 2: Mechanism of rFVIIa action: FVIIa binds to Tf (endothelial surface of vascular lesion). TF-FVIIa complex then activates factors IX and X, which leads to the formation of small initial amount of thrombin. Thrombin subsequently activates blood platelets and other coagulation factors (FV and FVIII) at the site of vascular lesion, which results into the "thrombin burst." This huge amount of thrombin then enables the conversion of fibrinogen into fibrin and the formation of fibrin clot [9,10]

considered. One can use abbreviated cross-match if less time is available provided institutional SOPs are established.

Use of compatible blood type, that is, allowable switch over the blood group when group-specific units are unavailable and use of Rh-positive components for Rh-negative recipient is desirable when Rh-negative components is not available. In such situations, SOP should be followed for the administration of Rh-Ig by calculated doses. Thawing of FFP in batches of 4-6 units as it takes 25-30 minutes, maintaining adequate platelet and blood inventory, and arrangement of blood donors are crucial steps to tackle such inevitable situations. To save on time in technical parts while issuing blood components MTP plays important role. PTS (Pneumatic Tube system) for transportation is highly re-commanded to save time, however it is desirable to assign dedicated porters in case there is accidental breakdown of PTS. Documentation of all the details of transfusion at BTS and clinical side is mandate [1,7,8].

After the activation of MTP, laboratory staff, hematologists, anesthetists, and general duty attendants have specific described roles. To prepare and issue blood components as requested, anticipate repeat testing and blood component requirement, minimize turnaround time of tests, and consider staff resources are detrimental. Hematologists should liaise regularly with the laboratory and clinical team to assist in the interpretation of results and advice on blood component support.

CONCLUSION

This case of massive transfusion requiring three blood volumes was managed successfully because of prompt action and close coordination between the surgical, anesthesia teams, as well as BTS. Transfusion of PRBC and plasma maintaining 1:1 ratio and other needed components as per laboratory reports proved beneficial. Timely decision of administering r Factor VIIa proved lifesaver to achieve hemostasis. This helped to salvage on precious blood units in blood bank for other patients. Establishing a MTP helps in the rational utilization of blood components. To achieve better outcomes in such cases, every BTS should have suitable institutional MTP. There is a need for clinical research in different blood substitutes and limit biological products as they are limited.

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