Intraoperative embolism or type I hypersensitivity reaction to gelofusine®

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ABSTRACT

Despite rare reports of Type I Hypersensitivity reactions (anaphylaxis) to colloid plasma expanders, they find wide application during resuscitation and major surgeries. We present the case of a possible Type I hypersensitivity reaction to Gelofusine® in a 42-year-old female patient during oncological surgery. The delayed manifestation caused some diagnostic confusion with an embolic event. The patient was symptomatically treated and the rest of the surgery was completed uneventfully. A high index of suspicion is vital for prompt identification and treatment of anaphylaxis.

Keywords: *Gelofusine, Hypersensitivity reaction, Skin prick test.*

Allogenic blood transfusion has been implicated in cancer recurrence [1]. Synthetic colloids are a viable option for perioperative volume resuscitation when blood loss is within the acceptable range. Among the products available Gelofusine® is extremely popular [2]. Though Gelofusine® has the potential to cause anaphylaxis, the incidence is rare (6.2 in 100,000) [3]. We, as perioperative physicians quickly resort to its use to swiftly correct intraoperative hypovolemia. The rationale of this case report is to remind anaesthesiologists that hypersensitivity to Gelofusine® is a reality. It can have an atypical presentation and cause diagnostic confusion with embolism.

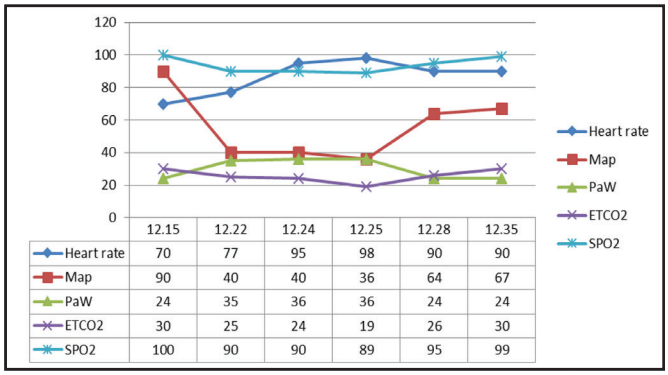
CASE REPORT

A 42-year-old female patient diagnosed with adenocarcinoma of the ovary, post 6 cycles of chemotherapy was scheduled for delayed cytoreductive surgery. Preoperative workup was within an acceptable range. There was a previous history of an uneventful surgery under general anesthesia (GA) following a road traffic accident.

On the day of surgery, standard monitors were applied and an epidural catheter inserted in the T9-10 interspace. GA was induced with intravenous (IV) fentanyl 90mcg, propofol 100mg and vecuronium 5mg at 9.30 am. After a negative intradermal test dose, IV Cefuroxime 1.5 gm was administered before the skin incision and 0.125% bupivacaine epidural infusion was initiated. The patient remained hemodynamically stable for 2.5 hours with a blood loss of 500ml. After administration of 2L crystalloids, Gelofusine® (B. Braun, manufacture date- 11.2017, expiry-10.2020, LOT no- 17462362) was started at 11.55 am. After 27 minutes, when >150ml of Gelofusine® had already been infused, the patient's blood pressure and saturation began to drop with the rise in peak airway pressure (Fig. 1). The sudden decrease in the end-tidal CO2 (ETCO2) along with the other signs misled us into assuming the event to be embolic.

Since we did not suspect a reaction to Gelofusine®, the remaining colloid was infused and the patient was started on a noradrenaline infusion. Meanwhile, her upper extremity was exposed in order to insert an arterial line. Mottling of the skin in both upper limbs was noticed at this point. The hemodynamics also responded to a bolus of IV adrenaline 20 µg. Hence, we started an adrenaline infusion of 0.2 µg/kg/hr and gradually her blood pressure stabilized.

A central venous catheter was inserted under ultrasound (USG) guidance for the administration of the vasoactive infusions. Surgery was completed and the patient shifted to the intensive care unit (ICU) for elective ventilation. Bedside echocardiogram (ECHO) and 12 lead electrocardiogram (ECG) were found normal, excluding the possibility of an embolic episode. Due to non-availability, serum tryptase levels were not



	12.15	12.22	12.24	12.25	12.28	12.35
Heart rate	70	77	95	98	90	90
Map	90	40	40	36	64	67
PaW	24	35	36	36	24	24
ETCO2	30	25	24	19	26	30
SPO2	100	90	90	89	95	99

Figure 1: intraoperative events (MAP=mean arterial pressure, PAW=peak airway pressure, ETCO2=end-tidal CO2, SpO2=oxygen saturation).

determined. The patient was weaned off from the vasopressors in 3 hours, extubated in 6 hours and shifted out of ICU in 2 days. A week later, just before her discharge, an intradermal test was performed after informed consent. A skin bleb with a diameter of 0.7mm was raised by injecting 0.05 ml of Gelofusine®. The wheal increased to 1.5mm after 15 minutes (<3mm increase in size is considered positive). This modest response was probably due to mast cell depletion which is likely to occur when the allergen test is performed in less than 4 weeks of anaphylaxis [4]. Type I hypersensitivity reaction to Gelofusine® was the most likely cause of the hemodynamic instability in our patient. The patient was uneventfully discharged on the 10th postoperative day and was informed of her allergy to Gelofusine®. The same details were also entered in her medical records.

DISCUSSION

Gelofusine® is succinylated gelatin, supplied in 500ml biocompatible containers and acts as a plasma expander for 1-2 hours. Its use in the perioperative period is increasing especially in oncological surgery where allogeneic blood transfusion is associated with an increased incidence of cancer recurrence [1]. In a recent multinational trial, succinylated gelatins were the second most common colloid used after albumin [2]. According to the allergen survey 6th National Audit Project conducted by Royal College of Anesthetists, the annual exposure rate to gelatin-based solutions during surgery in the UK is 1.7% i.e. 48203 patients while the calculated incidence of severe anaphylaxis is 6.2 per 100000, a rate similar to that of rocuronium [3].

Zhu et al in their article expressed that succinylated gelatin allergy, which is IgE antibody-mediated has no relation to either age or sex but there's an association with pre-existing penicillin and animal protein allergy. The allergic reaction usually occurs intraoperatively with 169.7 ± 104.1ml infusion over an interval of 11.78 ± 11.47 min [5].

Perioperative anaphylaxis detection is always a challenge and Rose et al propose a comprehensive classification that will help guide the clinician to identify severe anaphylaxis and treat the patient with the correct adrenaline dose [6] (Table 1). Perioperative anaphylaxis can have a wide spectrum of symptoms and signs. Our patient had a sudden elevation of the peak airway pressure followed by hypotension and precipitous fall in ETCO2. Given the situation of a pelvic malignancy treated with chemotherapy, these signs initially raised the suspicion of pulmonary embolism [7].

Hypotension, tachycardia, fall in saturation and ETCO2 are the commonest signs of pulmonary embolism during a general anesthetic [8]. The incidence of perioperative pulmonary embolism in gynecological malignancies is reported to be 0.3%-4.1% [9]. Thus, the remaining Gelofusine® was given for volume resuscitation. To add to the confusion was that the upper part of the body was covered by surgical drapes and there was a latency period for the reaction. The initial inotrope started was noradrenaline but the poor response prompted us to administer an adrenaline bolus which produced hemodynamic

Table 1: Perioperative Anaphylaxis Grading System (6)

Grade A	Grade B	Grade C
Moderate perioperative anaphylaxis	**Life-threatening perioperative anaphylaxis**	**Cardiac arrest with or without respiratory arrest associated with perioperative anaphylaxis**
Measurable derangements in one or more major organ systems The derangements are unexpected for the stage of the patient's perioperative course Non-life-threatening	Life-threatening cardiovascular or respiratory derangement, or both	Cardiac or respiratory arrest, or both
Cardiovascular system (i) Hypotension (ii) Tachycardia or bradycardia (iii) Arrhythmia	Cardiovascular system (i) Systolic blood pressure of <60 mm Hg (ii) Life-threatening tachy- or bradyarrhythmia	Cardiovascular system (i) Cardiac arrest
Respiratory system (i) Cough (ii) Wheeze (iii) Difficult ventilation (3) Oxygen desaturation (3) Difficulty swallowing Rhinorrhoea	Respiratory system (i) Oxygen saturation <90% (ii) Inspiratory pressures of >40 cm H2O (iii) Severe difficulty inflating the lungs (3) Airway angioedema	Respiratory system (i) Respiratory arrest or complete failure of ventilation
Other systems (i) Unexpected change in consciousness (ii) Agitation (iii) Gastrointestinal upset		
Cutaneous signs (e.g. flushing, urticaria, angioedema) may or may not be present. At least one other system is involved for the diagnosis		

stability. This raised the clinical suspicion of an allergic reaction to Gelofusine® as no new drug had been administered in the last 30 min.

Most case reports of anaphylaxis to Gelofusine® mention serum tryptase levels and/or skin prick test/intradermal test to establish the diagnosis [4, 10-12]. An increase in serum tryptase at the time of reaction above 1.2 × baseline +2 µg/L is considered clinically relevant [13]. The basophil activation test is an in-vitro assay to predict or confirm sensitivity to Gelofusine® [14]. Performance and interpretation of the tests are well elucidated in a recent article by Farooque et al, which we used as a guide [12].

Skin prick testing is performed with undiluted or 1:10 diluted allergen. A wheel diameter of ≥ 3 mm at 15 min is considered positive along with the relevant clinical history. If the skin prick test is negative or inconclusive, the intradermal test on the forearm is performed with increasing concentrations of the allergen from a dilution of 1 in 10,000 to undiluted allergen. A bleb of 4–6 mm is raised by injecting 0.03–0.05 ml and a wheel diameter of < 3 mm larger than the negative control at 20 min is considered positive. If the intradermal test is also negative then an intravenous test is performed in controlled conditions [12].

Though rare, Gelofusine® has the potential to cause a severe anaphylactic reaction with a variable latency period and presentation intraoperatively. It has the unusual distinction of causing the same hypotension it is used to treat. It may be well worth periodically examining the patient under the drapes once Gelofusine® infusion is initiated and watch out for unexplained respiratory and hemodynamic changes.

CONCLUSION

It is prudent to restrict the use of Gelofusine® to compelling circumstances and exercise caution while using it. Unexplained decompensation associated with Gelofusine® administration should be regarded with a high index of suspicion.

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