

## Unusual causes of anaphylaxis during surgery: Gelofusin-induced Kounis syndrome

Sir,

In the very interesting report<sup>[1]</sup> published recently in IJCCM, a 48-year-old female patient, who was planned to have laparoscopic donor nephrectomy, developed atrial premature complexes, flushing of both hands, falling blood pressure, and rising pulse rate after gelofusin infusion. Intravenous hydrocortisone, chlorpheniramine, mephentermine, adrenaline, vasopressors, ipratropium with salbutamol nebulization and positive pressure ventilation improved her condition. The scheduled surgery was postponed, and the allergic skin tests for antibiotics, anesthetics and gelofusin showed positive skin reaction to gelofusin. This case raises some important points concerning the cause and the type of this reaction and its pathophysiology. Gelofusin is a macromolecule made from succinylated bovine gelatin. Gelatins are proteins derived from collagen and are obtained from cow and pig bones and hides and fish skin. A similar case diagnosed as Type II variant of Kounis hypersensitivity-associated syndrome with peri-operative cardiac arrest due to gelofusin anaphylaxis, confirmed with skin prick tests, has been published recently.<sup>[2]</sup> It concerned a 57-year-old patient who developed anaphylactic shock during anesthesia and despite initial management with bolus doses of metaraminol and epinephrine intravenously, hypotension worsened, and cardiac output was reduced. The patient recovered gradually with intravenous antihistamines, steroids and myocardial ischemia protocol, thus supporting our view that anaphylactic shock is a manifestation of Kounis syndrome. In another report, anaphylaxis with cardiovascular symptoms such as profound hypotension, tachycardia, and elevated airway pressures have been reported following intraosseous gelatin administration.<sup>[3]</sup> Drug capsules, suppositories, plasma expanders, and vaccine stabilizers including diphtheria-tetanus-pertussis, measles, mumps, rubella, varicella, yellow fever, rabies, and some influenza vaccines contain bovine and porcine gelatins as heat stabilizers. Since gelatin is contained in various vaccines given in children, then vaccination is regarded as a primary route of

sensitization. Indeed, specific gelatin antibodies have been detected in patients following vaccination<sup>[4]</sup> and Type I hypersensitivity reactions to gelatin have been even reported with specific IgE levels as low as 0.8 kUA/L. When, gelatins are used intravenously as modified fluid gelatins and as plasma substitutes and expanders they can induce severe allergic reactions such as in the described case.

The described patient had received, before gelofusin administration, a total 10 different drugs in an effort to induce anesthesia. Despite negative skin tests, substances such as lactated ringer, ranitidine, fentanyl, ondansetron, cefotaxime, thiopentone, suxamethonium, isoflurane, vecuronium, and mannitol, could have acted as antigens and have joined forces with gelofusin in order to induce anaphylaxis and Kounis syndrome. It is known that anaphylaxis resulting in Kounis syndrome occurs when 2000 nearby antibodies attached to mast cell surface are bridged by corresponding antigens and make the critical number of 1000 bridges. On the other hand, IgE antibodies with different specificities can have additive effects and small, even subthreshold numbers of them can join forces and trigger the cells to release their mediators.<sup>[5]</sup>

Therefore, anesthetic drugs used during surgery can join forces with substances acting as antigens and can induce anaphylaxis and Kounis anaphylaxis-associated syndrome. Anesthetists and surgeons should be aware of this consequence in order to timely receive protective, preventive, and therapeutic measures.

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**DOI:** 10.4103/0972-5229.133956