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Case Report

Bronchospasm Precipitated by Ethanol Injection in Arteriovenous Malformation

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Summary: We present an interesting case of profound bronchospasm that we postulate was caused by injection of ethanol during embolization of a left transverse sinus dural fistula. There is excellent documentation in the literature of the development of transient pulmonary hypertension and decreased right-side cardiac output following embolization with this agent; however, there have been only anecdotal reports of a temporal relationship between ethanol embolization and bronchospasm. We present this case that occurred on the third ethanol embolization treatment series.

Embolization of brain vascular abnormalities has grown into a significant specialty since it was first introduced in the 1960s by Luessenhopf. The need for high-quality images with the absence of motion and the requirement for control of the vital signs have increased the use of general anesthesia for these delicate procedures. Thus, cerebral embolotherapy is fast becoming a viable preoperative adjunct and in certain cases a primary treatment technique for various types of vascular lesions and often necessitates the use of general anesthesia (1).

Case Report

Our patient was a 54-year-old woman undergoing her third arteriographic examination and embolic treatment. She had presented 2 years earlier with tinnitus, and a left transverse sinus dural arteriovenous fistula was diagnosed. She was anesthetized at that time and treated with endovascular transvenous occlusion of the fistula pouch with multiple platinum coils. She developed subsequent recanalization of the fistula from occipital, internal maxillary, and internal carotid arteries. This had been treated 1 year earlier with intraarterially delivered ethanol embolization under monitored anesthetic care. Both interventions had been uneventful.

Our patient had no medical problems. She had had previous neuroradiologic interventions that were uneventful and had had no adverse reaction to the anesthetic agents used (propofol, versed, fentanyl, and Demerol, for shivering on one occasion). Her only allergy was bioxin, which caused diarrhea. She had no history of reactive airways disease.

Preoperatively, her physical signs were unremarkable. Her weight was 82 kg and her blood pressure 123/66 mm Hg. Her pulse was 76 beats per minute, and her oxygen saturation findings were 99%.

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We began with diagnostic arteriography. The patient was given 1 mg of midazolam, and a propofol infusion was started at a rate of 50 μg/kg/min. Fentanyl (25 μg) was given for anesthesia before venipuncture. At 1 hour 15 minutes into the arteriographic examination, 1 inch of topical nitroglycerine paste was placed to prevent catheter-induced vasospasm. The angiographic results showed residual arteriovenous shunt surgery at the fistula site, so the decision was made to convert the patient to a general anesthetic before ethanol embolization. She was cardiovascularly stable at this stage, showing no reaction to sedation or contrast agents, which she had been received for approximately 1.5 hours.

Anesthesia was induced with 150 μg of fentanyl, 100 mg of propofol, and 50 mg of rocuronium. She underwent easy-mask ventilation, and it was decided to place a size 4 laryngeal mask airway (LMA). This was done on the first pass. She was ventilated via the LMA, easily achieving tidal volumes of approximately 650 mL and peak airway pressures of 16–20 cm H_2O. Her blood pressure reading was unchanged, going from a preinduction pressure of 116/67 mm Hg to 114/68 mm Hg by cuff reading. Anesthesia was maintained by O_2, N_2O, and 0.5% isoflurane.

The first 3 hours under anesthesia, her vital signs, airway pressures, and saturations remained stable. Immediately following the first intraarterial injection of ethanol, she suddenly developed audible, severe bilateral bronchospasm. Her saturations decreased from 100% to a low of 82%. Her airway pressures increased to a high of 44 cm H_2O, and she had bilateral wheezes that were audible without the need for auscultation. She was treated with albuterol inhalation via the LMA, 100% oxygen, and increased isolflurane to 2%. The patient remained cardiovascularly stable throughout the episode. After approximately 4 minutes, the brochospasm had resolved, and her peak inspiartory pressure returned to 20 cm H_2O. Saturation was again 100% on Fi O_2 of 50%. The neuroradiologic procedure was resumed until a further ethanol embolization occurred. The patient again developed profound brochospasm approximately 30 seconds after injection into the left external carotid artery. The patient responded well to treatment with beta-2 agonist, and the bronchospasm resolved rapidly. She was cardiovascularly stable throughout. Her pupils were pinpoint and central and she had no signs of being "light" on 2% isoflurane. Further ethanol embolization was abandoned because of our suspicion of a bronchospastic reaction to the ethanol as it shunted quickly through the arteriovenous shunt in the transverse sinus into the pulmonary vasculature.

Muscle relaxation was reversed with intravenous nesostigmine and glycopyrrolate at the end of the procedure. Recovery from anesthesia was uneventful, and the patient remained at her neurologic baseline without sequelae. She was transferred to the recovery room, and a serum tryptase was taken at approximately 1 hour after the initial episode of bronchospasm.

Discussion

For embolization to be successful, three factors need to be considered: embolic agent selection, clinical application, and technical skill (2). A vast array of embolic agents is now routinely embolized through

microcatheters that can access the most distal circulation.

The choice of embolic agent is determined by various factors. The agents include platinum coils, absorbable gelatin pledgets, polyvinyl alcohol foam, cyanoacrylate glue, and ethanol. Distinct patterns of reaction have been noted to all these agents (3). Some authors have suggested that ethanol may provide permanent vascular occlusion (4), although this has not been substantiated among many practitioners.

Ethanol was chosen as the endovascular agent in this case because the vascular architecture of the treated lesion did not lend itself to optimal liquid adhesive therapy, because it was thought that particulate or coil treatment would not be efficacious, and because several similar lesions in our experience have responded to ethanol treatment with complete cure and no recanalization. Our experience has shown that if the ethanol can be delivered in a high enough concentration with sufficient contact time with the fistulas site, complete cure can be achieved. In our first embolization, a plethora of feeding vessels to the fisutae prevented the ethanol from reaching the target in sufficiently high concentrations.

Ethanol is the one of the most dangerous substances that can be injected (1). Nontarget embolization with ethanol will lead to tissue necrosis as capillary beds are entirely destroyed. Being a fluid agent, ethanol penetrates to the capillary level, devitalizing normal tissue. The suggested dose is variable, but 1 mL/kg is commonly suggested (4). Yakes reports idiosyncratic reactions to as little as 1 mL of ethanol (W. Yakes, personal communication). Thus, diligence should be exercised in all cases.

Vascular spasm, edematous tissues, and venous thrombosis have been reported. Skin ulceration, nerve injury, and damage of adjacent organs have all been documented, with rates of complication varying from 10% to 30%, depending on experience (5?). Pain is a consideration for which sedation or general anesthetic has proved more effective than selective injection of an anesthetic into the vascular territory to be embolized (lidocaine).

Cardiopulmonary collapse can occur as a very rare sequala. Yakes et al (1) have extrapolated that the sequence of events starts with a bolus of ethanol arriving at the pulmonary artery capillary bed and inducing precapillary spasm. This is corroborated by Jakupi et al (6), who have shown in dog studies that ethanol induces a dose-dependant contraction of pulmonary artery smooth muscle. These studies conclude that ethanol acting directly on pulmonary smooth muscle causes a transient precapillary spasm, increasing pulmonary artery pressure, which decreases right ventricular contractility and ultimately, in rare cases, causes profound cardiopulmonary collapse.

Because nontarget embolization with ethanol can cause smooth muscle spasms, we elucidate that the anatomic course led to a nontarget bolus of ethanol arriving in the bronchiole vasculature and causing severe bronchospasm via the above-described mechanism. It was conceivable that the bronchospasm could have been due to an anaphylactic reaction to an antigen; in this case, ethanol. Anaphylaxis is an immunologic description of a type 1 hypersensitivity reaction mediated by IgE or IgG. Anaphylactoid is used to describe reactions that are not mediated by IgE; however they have a clinically identical presentation. The term is used to describe a variable group of symptoms that is produced by several mechanisms: cardiopulmonary collapse, bronchospasm, urticaria, angio-edema (7).

It is unlikely that the bronchospastic response was a result of a reaction to the contrast used in this procedure. Contrast had been given hours before with no change to any vital parameters.

Histamine and tryptase are important early mediators in this process and are released by mast cell degranulation. Histamine levels decrease after 10 minutes (6). Tryptase, unlike histamine, is stable in blood for up to 6 hours (8). Thus, mast cell tryptase (MCT) is associated with immunologic reactions that are measurable up to 6 hours after the initial anaphylactic reaction. This result, coupled with a strong history, is a good predictor for severe allergy.

We measured tryptase after we had instituted resuscitation in our patient, to exclude the possibility that the bronchospasm had been due to previous sensitization to ethanol exposure causing an anaphylactic reaction. The result came back as 6.9 ng/mL (reference range, 1–10 ng/mL). The cut-off values for tryptase found 10 ng/mL to be optimal, with a sensitivity of 86% and a specificity of 88% (9). Thus, the bronchospasm was likely due to a direct toxic effect.

Conclusion

Although ethanol embolization offers a very minimally invasive treatment for arteriovenous malformations, it is associated with potential fatal complications that are still only becoming apparent. Radiologists and anesthesiologists need to work closely together to optimally treat these patients, and at our center we are instituting a dedicated anesthesia neurointerventional service to promote continuity of care.

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