Reversible Cardiac Arrest After Polidocanol Sclerotherapy of Peripheral Venous Malformation

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BACKGROUND. **Polidocanol sclerotherapy is a well-established therapeutic modality for the treatment of venous malformations. Systemic complications are extremely rare.**
OBJECTIVE. **To report a case of cardiac complication after polidocanol injection of peripheral venous malformation.**
METHODS. **A case report and a review of the English language literature using a published MEDLINE search strategy.**
RESULTS. **A patient undergoing polidocanol sclerotherapy for a symptomatic venous malformation of the right inferior limb developed cardiac arrest shortly after injection of the sclerosing agent which was promptly reversed.**
CONCLUSION. **Systemic complications following sclerotherapy may occur even when the sclerosant is injected in peripheral veins or venous malformations. Clinicians should be alerted to the possibility of uncommon but life-threatening adverse effects.**

SCLEROTHERAPY IS a safe and worldwide used therapeutic modality for the treatment of many different conditions including esophageal varices, vascular malformations, recurrent pleural effusion, ganglions, hemorrhoids, and peripheral varicose veins. The common mechanism of action of all sclerosing agents is the destruction of endothelial surfaces with subsequent thrombosis, leading to intimal fibrosis and obliteration of the vessel lumen.[1]

Polidocanol is a safe and effective sclerosing agent with an extremely low risk of local and systemic complications.[2] We report the case of a pediatric patient who experienced reversible cardiac arrest following polidocanol injection for the treatment of a symptomatic peripheral venous malformation.

Case Report

A 5-year-old patient with Klippel–Trenaunay syndrome was admitted for recurrent disabling pain in the right lower limb. The patient's parents also reported the occurrence of tenderness, ecchymosis, and development of phleboliths within the malformation. Clinical history was negative for cardiac symptoms.

The affected limb presented with a cutaneous capillary malformation and a venous malformation of the lateral and posterior aspects of the right thigh and buttock. A slight enlargement of the affected limb was also present. Physical examination was otherwise unremarkable. Electrocardiogram and chest radiograph were normal. Blood cell count and chemistries were normal. The patient's body mass index was 16.52 (height 110 cm, weight 20 kg).

A Doppler ultrasound scanning confirmed the presence of a venous malformation of the right lower limb connected with the internal iliac system via the gluteal veins. No deep vein abnormalities were detected. The patient was then referred for sclerotherapy, which was performed with general anesthesia, deemed necessary to ensure adequate compliance of the pediatric patient.

The patient received oral premedication with 5 mg of midazolam and 0.5 mg of atropine. In the operating room, monitoring was begun with an electrocardiograph, pulse oximetry, and noninvasive blood pressure, and venous access was established for administration of fluids and drugs.

Anesthesia was induced with 80 mg of thiopental and tracheal intubation was facilitated with 2 mg of vecuronium bromide. Anesthesia was maintained with sevoflurane (2%) and an equal mixture of oxygen and nitrous oxide using a nonrebreathing system. The concentrations of inhaled and exhaled gases, including end-tidal CO_2 tension, were also monitored. Vital signs were normal and remained stable until after the sclerotherapeutic procedure was performed.

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Manual compression and a tourniquet were applied proximally to the venous malformation in order to contain the sclerosing agent within the lesion during the injection and shortly after. A 25-gauge needle connected to a syringe containing 1% polidocanol was inserted into the venous space and the intraluminal position of its tip was confirmed by the aspiration of blood. Four milliliters of the sclerosant were slowly injected into the lesion. Shortly after the injection the patient developed rapidly progressive sinus bradycardia with eventual asystolic cardiac arrest. Cardiopulmonary resuscitation was immediately performed by means of discontinuation of anesthetics, ventilation with 100% oxygen, external cardiac massage, and intravenous administration of 0.05 mg of orciprenaline. Spontaneous and effective cardiac activity was promptly restored.

Postoperatively the patient underwent a Doppler echocardiographic evaluation that showed the absence of anatomic and functional abnormalities. The postoperative course was uneventful and the patient was discharged on the third postoperative day.

Discussion

Polidocanol consists of 95% hydroxypolyethoxydodecane and 5% ethyl alcohol.[3] The former, a urethane local anesthetic that differs from the more classic ester and amide anesthetic agents by lacking an aromatic ring, is the active component of the product. Its detergent action induces a rapid overhydration of endothelial cells, leading to vascular injury. The latter is added as a preservative.[3]

Polidocanol is an effective, though relatively weak sclerosant successfully employed for the treatment of venous malformations.[1,4] It is virtually painless upon injection and has shown an extremely low incidence of skin necrosis and hyperpigmentation.[3]

In order to identify clinical studies that might report adverse effects after sclerotherapy with polidocanol, we reviewed the English language literature by means of a standardized and previously published search strategy of electronic databases (MEDLINE, NHS Center for Review and Dissemination, Cochrane Library, and the Controlled Trials Registry) from January 1966 to April 2001.[5]

We found that allergic and anaphylactic reactions are infrequent, with a reported incidence that varies between 0 and 0.3% of cases.[2] However, allergy to polidocanol may be more common than usually estimated.[2,6]

Cardiac complications following polidocanol injections are extremely rare, and when they occur are due to its local anesthetic properties.[7,8] Following systemic absorption, all local anesthetics cause a decrease in the rate of depolarization in the fast conducting tissues of Purkinje fibers and ventricular muscle due to a decrease in the availability of fast sodium (Na^+) channels in cardiac membranes.[9] The action potential duration and the effective refractory period are also decreased.[9] As a result, local anesthetics, proportionally to their blood levels, reduce the electrical excitability and conduction rate through of the heart and depress spontaneous pacemaker activity in the sinus node, resulting in progressive sinus bradycardia and eventual sinus arrest. They also depress cardiac contractility by means of several mechanisms, including blockade of inward calcium (Ca^{2+}) and Na^+ currents.[9]

We hypothesize that the occurrence of the complication reported herein was due to the effect of polidocanol passing into the systemic circulation from the site of injection. To the best of our knowledge, only two cases of cardiac complications after polidocanol injection, including reversible cardiac arrest[7] and heart failure,[8] have been reported thus far. In both cases the patient had undergone sclerotherapy for esophageal varices, a procedure during which it is virtually impossible to prevent the systemic spread of the sclerosant. In contrast, when polidocanol is injected in peripheral veins, proximal compression is usually applied to contain the agent and maximize its effect by increasing the duration of contact with the venous walls. Hence the quantity of polidocanol that reaches the systemic circulation is theoretically negligible, provided that the sclerosant is injected at the recommended daily dose of 2 mg/kg.[2] However, as demonstrated by the case reported herein, even under those circumstances there is an actual risk of systemic diffusion of the sclerosing agent and, consequently, of the occurrence of systemic complications due to its toxic effects.

This observation is also supported by the reported occurrence of a reversible ischemic neurologic deficit after sclerotherapy of varicose veins of the leg.[10] According to the authors, this complication may be regarded as a warning sign that hemostasis can be activated by polidocanol.[10] However, the effect of sclerotherapy on the blood coagulation system is still controversial and has yet to be established.[1]

Following polidocanol sclerotherapy, hemoglobinuria can occur, secondary to intralesional hemolysis,[1] and if massive it may lead to acute renal failure.[4] This is due to both intratubular obstruction, caused by the local precipitation of hemoglobin, and direct tubular toxicity of hematin, a component of the pigment released at a urine pH of 5.6 or less.[4] Accordingly, there is an actual risk of hemoglobinuria-related acute renal failure during extracellular fluid depletion with low urinary flow and acid urine. Hence we recommend hydrating patients during and right after the procedure in order to enhance urinary flow. When there is evi-

dence of gross hemoglobinuria, urine should be alkalinized to limit the generation of free hematin. Volume output should also be monitored, because when oliguric acute renal failure occurs, fluid infusion should be reduced.

In conclusion, the observation reported herein draws attention to the risk of the systemic effects of drugs employed for sclerotherapy of peripheral venous malformations and varicose veins.

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