

Case Report

Anaphylactic Shock After Intravenous Fluorescein Administration for Intraoperative Cystoscopy

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BACKGROUND: Rates of administration of intravenous sodium fluorescein during cystoscopy have increased since indigotindisulfonate sodium was removed from the market in 2014. Although sodium fluorescein has been extensively evaluated and found to be safe, side effects including anaphylaxis have been observed, with an incidence between 0.05% and 1.0%.

CASE: We present a case of anaphylactic shock after administration of intravenous sodium fluorescein for the assessment of ureteral efflux in a patient with a history of frequent severe allergic reactions undergoing urethral lysis and cystoscopy for urinary retention. Cardiopulmonary structure and function were evaluated and found to be normal. An elevated serum tryptase level was identified, indicating an anaphylactoid reaction. Timely recognition of symptoms associated with a severe allergic reaction in the setting of hemodynamic instability with prompt supportive and pharmacologic therapy was vital in the patient's recovery.

CONCLUSION: Health care providers must be aware of this potential complication, especially in patients with a history of severe allergic reactions.

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Teaching Points

1. Severe, systemic allergic reactions to intravenous sodium fluorescein occur.
2. Serum tryptase level may aid in identifying an allergic reaction.

Sodium fluorescein is a water-soluble fluorescent dye developed by Adolf Baeyer in 1871. He described fluorescein, a green fluorescence, as “visible even at very strong dilution,” making it a good dye for silk and wool.¹ The first medical application of sodium fluorescein was at the Mayo Clinic. In the 1950s, it was used to evaluate cardiac output and septal defects.² More recently, intravenous (IV) sodium fluorescein has been used to study blood flow through the retina and iris and in brain surgery to aid in delineation of malignant tumors.³

The most common side effects reported for sodium fluorescein are nausea (2.9%) and vomiting (1.2%).⁴ The incidence of severe and anaphylactic reactions has been reported at 0.05–1.0%.⁵ In the past, indigotindisulfonate sodium (indigo carmine) has been used during cystoscopy to stain the urine to facilitate visualization of urine spill from ureteral orifices. Although considered pharmacologically inert, case reports of anaphylactic reactions after indigotindisulfonate sodium administration exist. The rate is unknown.⁶

Currently, there is a nationwide shortage of indigotindisulfonate sodium. Of the two manufacturers, one has discontinued production and the other continues to make it in limited supply based on the availability of the raw materials.⁷ As a result of this shortage, alternative agents such as methylene blue, phenazopyridine, 10% dextrose solution, and sodium fluorescein are used to evaluate ureteral efflux during cystoscopy. All of these agents have potential side effects. For instance, methylene blue, a monoamine oxidase inhibitor, may increase the risk of serotonin syndrome in patients taking certain antidepressive agents.⁸ Dextrose solution has been associated with increased postoperative urinary tract infection rates.⁹

Sodium fluorescein has been the most promising alternative agent, administered intravenously minutes before cystoscopy at a dose of 25 mg (0.25 mL of 10% solution).¹⁰ Initial reports have shown it to be



efficient, reliable, and inexpensive¹⁰ and compare it positively with other agents.^{11–13} Few complications have been reported thus far. We present a case of anaphylactic shock after administration of sodium fluorescein during intraoperative cystoscopy.

CASE

A 59-year-old woman presented for evaluation of recent-onset voiding dysfunction and incomplete bladder emptying. She had undergone placement of a polypropylene midurethral sling 20 years previously. The patient was performing intermittent self-catheterization for postvoid residual volumes between 200 and 900 mL. She had undergone a sling revision 5 months previously. Fluorescein was not used at that time. The sling revision did not improve her voiding function, and she was scheduled to undergo urethral lysis.

The patient's medical history included type I anaphylactic hypersensitivity reactions to nonsteroidal antiinflammatory drugs, penicillin, sulfonamides, amlodipine, and nitrofurantoin, with the latter requiring admission to the intensive care unit. A type I hypersensitivity reaction is an allergic or immunoglobulin E (IgE)-mediated hypersensitivity. Immunoglobulin E binds to the allergen. The allergen and IgE cross-linked complex in turn binds to mast cells, causing the release of vasoactive particles resulting in vasodilation. Reactions range from a localized rash to systemic anaphylactic shock. The remaining type II, III, and IV hypersensitivity reactions are associated with autoimmune disorders.¹⁴

On the day of surgery, the patient underwent urethral lysis under general anesthesia with a laryngeal mask airway. A latex-free silicone catheter was placed at the beginning of the procedure. At the conclusion of the case, 0.25 mL of 10% sodium fluorescein was administered intravenously as part of a routine assessment of ureteral patency. Cystoscopy was performed, and efflux of urine was observed from both ureteral orifices. Bladder spasms were visualized. The cystoscope was removed, and a Foley catheter was placed. Within 3 minutes of IV fluorescein administration, the patient became acutely hypotensive, bradycardic, and hypoxic. Her mean arterial pressure and oxygen saturation dropped to 40 mm Hg and 70%, respectively. The laryngeal mask airway was removed, and the airway was secured with an endotracheal tube. Arterial and central venous lines were placed. Her blood pressure recovered with IV norepinephrine and vasopressin. Cardiac monitoring revealed ST segment elevations; however, a 12-lead electrocardiogram did not show evidence of myocardial infarction. A migratory erythematous rash was noticed by a member of the surgical team. These events took place in a time span of approximately 20 minutes.

After stabilization, the patient was transported to the intensive care unit. The differential diagnosis at this time included acute myocardial infarction, pulmonary embolism, and an anaphylactic reaction. The patient received IV epinephrine, diphenhydramine, famotidine, and prednisone. She was started on a heparin drip for the potential

of a pulmonary embolus. A bedside transthoracic echocardiogram was negative for evidence of right-sided heart strain or cardiogenic etiology. Computed tomography angiography was performed and was negative for pulmonary embolism. Heparin was discontinued. Cardiac troponins collected serially remained negative. Serum tryptase level was found to be elevated at 55 micrograms/L (normal range 0–10 micrograms/L), consistent with an allergic response secondary to mast cell activation.¹⁵ A baseline tryptase level 6 months prior was 4.2.

The patient improved within 90 minutes of her arrival in the intensive care unit, and she was weaned off IV vasopressors and extubated within 4 hours. She was discharged on postoperative day 1 and followed up with allergy and immunology services as an outpatient. The allergist agreed with the diagnosis of anaphylaxis based on the clinical events and tryptase level. No further testing was necessary, because there is no clear consensus on how to confirm hypersensitivity to sodium fluorescein.¹⁶ The patient was advised to avoid fluorescein in the future and was prescribed an epinephrine pen.

COMMENT

Anaphylactic reactions can occur suddenly and have the potential to be life-threatening. Symptoms may include hives, respiratory distress, angioedema, tonic-clonic seizure, and cardiovascular collapse.¹⁷ When an anaphylactic reaction is suspected, treatment should begin immediately. Anaphylactic-type hypersensitivity reactions can be caused by both IgE-mediated (type I) and non-IgE-mediated pathways.¹⁸ Assessing serum tryptase levels at the time of the allergic event can confirm a type I, IgE-mediated reaction, because higher levels are observed.¹⁶ Our patient had a tryptase level greater than five times the normal limit, confirming the diagnosis of type I anaphylaxis.

Although serious adverse reactions are rare, appropriate patient selection for use of sodium fluorescein during cystoscopy is important. Serious reactions have also been observed during first exposure to sodium fluorescein.¹⁹ Kwiterovich et al⁴ found that patients undergoing their first sodium fluorescein angiography were more likely to experience an allergic reaction compared with those with the previous uncomplicated angiography. Like with most pharmaceuticals, sodium fluorescein administration should be used with caution in patients with a history of severe allergic reactions to any agent.²⁰

The use of fluorescein for this indication has been recent and the collective experience with rare side effects has therefore been scant. An online search was performed using the terms “fluorescein,” “cystoscopy,” “anaphylaxis,” and “allergic reaction” in



PubMed, Ovid, and Google Scholar from 1970 to 2017. The ophthalmologic literature reports the incidence of severe reactions as 0.5–1.0% and the risk of death as 1 in 220,000 patient administrations.⁵ The typical dose administered in an ophthalmologic setting is 5 mL of 10% (500 mg) sodium fluorescein,⁴ which is 20 times higher than the dose used for cystoscopy, showcasing a severe allergic response to a low IV dosage. Cases of severe allergic reactions have also been observed with topical and oral fluorescein administration.^{21,22}

Intravenous sodium fluorescein appears to be a relatively safe, efficient, and cost-effective method for assessing ureteral patency during routine intraoperative cystoscopy. However, like with any drug, severe allergic reactions can occur. Users must be aware of this potential complication to recognize it early and initiate appropriate interventions. Sodium fluorescein should not be administered to patients with any prior allergic reaction to it. Furthermore, it should be administered with caution to patients with a history of anaphylactic reactions.

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