

Fluorescein-induced allergic reaction

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Background: Adverse reactions following intravenous sodium fluorescein are very unusual and their mechanism is still uncertain. We report the case of a patient who suffered an adverse reaction during a fluorescein ocular angiography. Positive allergy tests to fluorescein suggest an IgE-mediated mechanism.

Objective: Report the allergy evaluation performed in a patient who suffered an adverse reaction during an intravenous fluorescein administration.

Methods: We selected the case of a patient who suffered dizziness, diaphoresis, generalized pallor, nausea, sphincter relaxation, hypotension, and intense malaise during a fluorescein ocular angiography and compared the results to other nonreactive subjects. Allergy evaluation: Prick and intradermal skin tests and serial determinations of serum tryptase were performed on the patient and four control subjects who underwent and tolerated the same procedure as well as on a patient who developed an intense vagal reaction during blood extraction.

Results: Positive skin tests and dramatic increase of serum tryptase (67U/I) were observed in our patient. The rest of the patients had negative skin tests and did not have any variation in their serum tryptase.

Conclusions: An IgE-mediated mechanism is suggested as responsible for this adverse reaction. We recommend that a complete allergy evaluation should be performed in all patients who have adverse reactions to fluorescein in order to differentiate true allergic reactions from other types of reactions.

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INTRODUCTION

Fluorescein angiography is very useful in the diagnosis and treatment of a number of ocular conditions. The incidence of side effects following the intravenous administration of sodium fluorescein is about 5%. Mild adverse reactions (nausea and vomiting) are the most frequent adverse effects but severe reactions are extremely rare.^{1–6} The pathogenic mechanism of most reactions is unknown and allergy evaluation in these patients have not been reported in the literature. We present an adverse protracted, moderate degree reaction after intravenous administration of sodium fluorescein and immunologic investigation. Serial blood samples were obtained following the

onset of symptoms to explore mast cell involvement.⁷

CASE REPORT

A 67-year-old woman with hypertension and type II diabetes was being studied for vision loss. Immediately after intravenous administration of 3 mL of 20% fluorescein she suffered dizziness, diaphoresis, generalized pallor, nausea, sphincter relaxation, hypotension, and intense malaise that required treatment with antihistamines and corticosteroids. She had a slow response to treatment and was observed at the Emergency Department for 24 hours.

She had already undergone four previous fluorescein tests and had suffered milder reactions (nausea) in the last two.

ALLERGY INVESTIGATIONS

Prick tests to fluorescein (200 mg/mL) and intradermal tests to fluorescein (2 mg/mL) were positive (Figs 1 and 2). Four diabetic patients that had received

several fluorescein doses and 15 healthy individuals after informed consent served as controls. All controls were negative to both skin tests. Skin tests were also performed with structural molecules closely related to fluorescein such as eosin and mercurochrome. Prick and intradermal skin tests were negative on the patient. Serum tryptase levels (RIACT™-Pharmacia, Uppsala) obtained 35 minutes, 2, 4, 6, 24 hours and 7 days later, measured 66.21, 29.83, 14.78, 5.26, 1.08, and 0.92 U/L respectively (Fig 3). Four patients who had tolerated fluorescein angiography and a patient with an intense vasovagal reaction were used as negative controls. None of the latter had any increase in serum tryptase during 24 hours (Fig 3). Serum specific IgE antibody to fluorescein performed by enzyme linked immunosorbent assay was not detectable on the patient and control subjects.

DISCUSSION

Sodium fluorescein is a low-molecular-weight highly water-soluble compound with fluorescent properties. Because these physical properties, fluorescein angiography has become an essential guideline technique in medical and laser treatment of numerous chorioretinal diseases. Nevertheless, several side effects following the intravenous administration have been reported in about 5% of the tests.² Yanzuzi et al^{3,6} proposed a classification for these adverse reactions based exclusively on their severity; however, no reference was made to their possible pathogenic mechanisms.

Mild adverse reactions are the most frequent (2% to 10%). This group is described as a transient effect, requiring no treatment with a rapid and complete resolution. Among the mild adverse reaction to fluorescein nausea and vomiting, sneezing and pruritus have been described.⁸ Drug extravasa-

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Figure 1. Prick test to fluorescein (200 mg/mL).

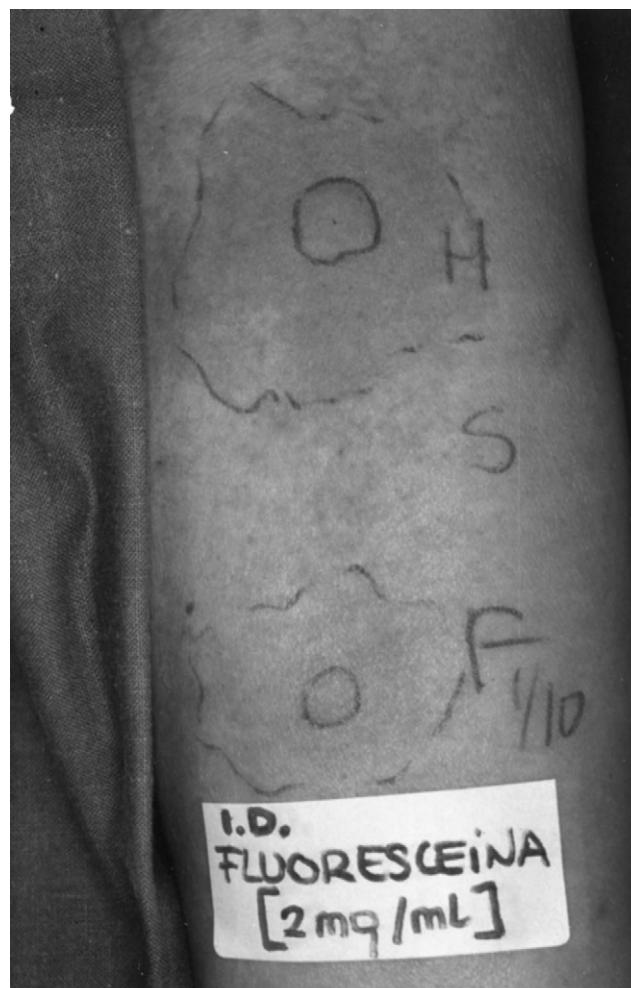


Figure 2. Intradermal skin test to fluorescein (2 mg/mL).

tion and accidental intraarterial injection may also cause mild reactions.

A reaction is considered moderate if, despite its transient nature, resolution is more gradual and occasionally requires medical intervention. A moderate reaction is not considered to be life-threatening. These reactions include skin eruptions, syncope, local

tissue necrosis,⁹ thrombophlebitis, fever and nerve palsy and are estimated to occur in 1.5% patients undergoing fluorescein angiography.

Severe adverse reactions (0.05%) have prolonged effects, requiring intensive treatment. These reactions may comprise a substantial threat to the patient's condition. They include life-threatening cardiovascular, respiratory and neurologic complications (cardiovascular shock, myocardial infarction,¹⁰ laryngeal edema, bronchospasm, . . .). Although severe adverse effects are less common with oral fluorescein administration,¹¹ anaphylactic reactions have been reported.¹² The estimated risk of death has been reported as 1 per 222,000 fluorescein angiographies.⁶

Patients with previous reactions have a 48% incidence of adverse effects for the next test.² Some authors propose premedication with antihistamines and corticosteroids before subsequent angiographies,^{13,14} although it does not always prevent all symptoms.

Pathogenic mechanisms of these adverse effects may be multiple. Allergy evaluation has not been performed in any of these patients although some of the symptoms may be similar to typical allergic reactions. The incidence of true allergic reactions is unknown. It will be important to distinguish allergic reactions from other reactions because different approaches should be taken for premedication and management of reactions.

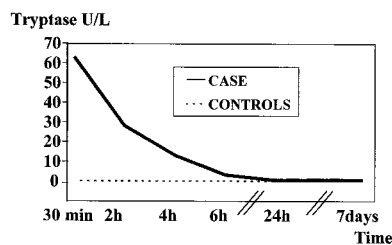


Figure 3. Serum tryptase levels after fluorescein angiography in the patient (solid line) and four control subjects.

When true allergic reactions occur with a test, it may be at times too dangerous even with pretreatment and a different form of evaluation should be considered. Prick tests have been found useful to diagnose fluorescein anaphylactic reactions.¹⁵ The positive skin tests and intense mast cell activation detected in our patient strongly support an IgE-mediated mechanism. The skin tests are not standardized but the negative results in 15 controls suggest no irritant effect. Allergy evaluation should be considered in patients with adverse reactions to fluorescein so that preventive measures can be taken in subsequent procedures.

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