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Allergic Reaction to Patent Blue Violet during Lymphography

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Summary

A case of an allergic reaction to Patent Blue Violet dye used for the purpose of lymphangiography is reported. The clinical findings were urticarial reaction, edema of the eyelids and lips, and hypotension. Previous sensitization to triphenylmethane dyes, in drugs and other chemicals was likely, but not proven. Such commonly used compounds have been compiled in a Table. History of a previous hypersensitivity reaction to these compounds is not a contraindication for lymphangiography but should call for emergency planning and possible premedication.

Patent Blue Violet was first used in 1933 by *Hudach* and *McMaster* (1) to outline the superficial lymphatics of human skin. In 1954, *Kinmonth* (2) stated that Patent Blue Violet would be useful diagnostically to study the lymphatics in the leg, arm, viscera, and testes. He injected 2 to 2.5 ml of an 11 % aqueous solution of the dye subcutaneoulsy between the toes. In order to minimize the pain of injection, Patent Blue Violet was mixed with a local anesthetic. Since then, the dye has been commonly used to visualize the lymphatic trunk. Patent Blue Violet is a triphenylmethane dye. Alphazurine 2G, frequently used in the United States, has also been listed as identical to Patent Blue Violet.

Complications to the dye in man have been manifested by skin reactions, i.e., generalized and transient blueish discoloration of the skin. However, generalized allergic reactions to the blue dye have been reported. *Kopp* (3) reported that 2 patients had anaphylactic reactions to Alphazurine 2G during lymphangiography. Skin testing demonstrated anaphylaxis to this and to 2 other triphenylmethane dyes. Severe allergic reactions to Patent Blue Violet were reported by *Mortazavi* and *Burrows* (4). The patients demonstrated cardiovascular collapse, urticarial reaction, and edema of the eyelids, pharynx, and lips. The authors reported an incidence of hypersensitivity of 2.5 %. *Sieber* (5) gave an incidence of hypersensitivity of less than 1 % (4/500). The reactions in his series were mostly mild. From a survey of individuals performing lymphography, *Koehler* (6) compiled the incidence of complications associated with the examination. He reported incidence of 1:600 (57/32,000) hypersensitivity reactions to the vital blue dye. Of these, 50 (1:640) were attributed to Patent Blue Violet (Alphazurine 2G). The reactions ranged from hives to angioneurotic edema with or without laryngospasms to vasomotor collapse. In many instances a local anesthetic was mixed with the vital blue dye. Since these complications also occurred in patients who had negative skin reactions to the local anesthetic, it was suggested that the vital blue was the allergic component.

Thus, it appears that adverse reactions to the blue dye are infrequent. However, one should be aware that complications may occur. This is emphasized by the present paper that describes the occurrence of a nonfatal reaction to Patent Blue Violet during lymphography.

Case Report

A 27-year-old white male was referred for lymphography following excision of a left testicular mixed seminoma and embryonal cell carcinoma. Prior to the examination, it was reconfirmed that the patient did not have a previous history of allergy. He denied previous exposure to cold remedies, simple purgatives, laxatives or suppositories. He never noted any adverse reactions against stains, inks (marking or stamping), or shoe polish. He also denied any reaction to local anesthetics at regular dental visits.

One ml of a 10 % solution of Patent Blue Violet (Sigma) was mixed with 9 ml of Lidocaine 1 % (Elkins-Sinns, Inc.). Five-tenths ml of that mixture was injected between 3 toes of each foot. The total amount of the dye solution was 3 ml. Five to ten minutes following injection, the patient developed a marked generalized urticaria, edema of the eyelids and lower lip. The blood pressure was 65/40 mm Hg. His sensorium remained intact. The patient was given 50 mg. Benadryl (Parke-Davis) and 4 mg. Decadron (Merck, Sharpe & Dohme) intramuscularly. The patient improved subsequently over a period of 30 minutes but the urticaria and swelling of the face and of both feet persisted. The patient's status was stabilized in about one hour. The blood pressure at that time was 90/55 mm Hg. The symptoms subsided slowly. The steroid therapy was continued and the blood pressure remained about 100 mm Hg systolic. The day after the examination, the blood pressure was stable and there were no symptoms except some dorsal pedal edema. The dye was still present in subcutaneous tissues, but there was no evidence of infection or reaction to foreign bodies.

Comments

There is confusion concerning the chemical composition, structure, and purity of Patent Blue dyes (9). The dye administered to our patient may more adequately be described as the sodium salt of Alphazurine 2G (Acid Blue 1) having color index (C.I.) 42045. The structure of this dye appears in Figure 1.

The dye was received in purified form (approximately 90 %) from the manufacturer as a 10 % solution. Although confusion may exist concerning the description of the dye administered with respect to that investigated by *Hiranaka* et al. (9), we have been informed by the manufacturer (10) that the 11 % dye solution is no longer available and that the currently available 10 % solution contains the dye as shown in Figure 1.

The adverse reactions stated above, as well as in previously reported cases, appeared immediately after the injection of the vital blue dye which indicated an allergic type of reaction.

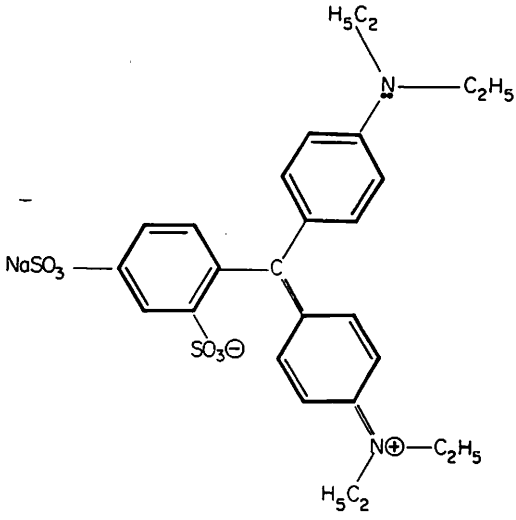

Fig. 1: Structural formula of Patent Blue Violet (Alphazurine 2G)

It is true that the vital blue was mixed with a local anesthetic (Lidocaine 1 %, Elkins-Sinns, Inc.) but a similar type of reaction has been

Table 1 Commonly occurring compounds that may sensitize for Patent Blue Violet (7)

A. Non-Prescription Drugs	Sensitizing Component
1. Cold Remedies	Yellow Phenolphtalein
2. Simple Purgative	Phenolphthalein
3. Laxative (Tablet, Capsules)	Yellow Phenolphthalein
4. Suppositories	Gentian Violet
B. Stains, penetrating or wiping, wood fillers	Aniline Dye
C. Paint, Ink (marking or stamping)	Triphenylmethane Dye
Blue (various colors)	Triphenylmethane Lakes
Green	Malachite Green
Violet	Triphenylmethane Dye
Magenta	Triphenylmethane Dye
Methyl Violet	Triphenylmethane Dye
D. Shoe Polish	
Paste	Aniline Dye
Suede Polish	Aniline Dye
E. Antifreeze	Trace quantities of dye

Compounds similar to Patent Blue Violet (Triphenylmethane) (8)

Bromosulfonphthalein
Phenolsulfonphthalein
Gentian Violet

reported in cases in which no local anesthetic was administered (6). Therefore, the possibility exists that this represents a natural allergic reaction to the blue dye in this patient. How this patient became sensitized is unknown. Exposure to triphenylmethane dyes was not revealed in the above reported case and there was no history of ingestion of phenolphthalein laxatives or of injection of phenosulfonphthalein or sodium sulfobromophthalein, the structures of which are related to those of the triphenylmethane dyes. However, very many of the compounds used in industrial work, as well as in everyday life, contain triphenylmethane or closely related structures (Table 1). It is, therefore, probable that possible sensitization to these chemicals can occur and may not be detected by history. It has been shown (11) that in hospitalized patients the incidence of a second hypersensitivity after primary exposure and reaction is 34 % of the reported hypersensitivity to drugs. The incidence of hypersensitivity in patients with previous exposure and no reaction is not known. It is well documented that pretesting is of no significant value. A proven reaction to previous exposure to triphenylmethane dyes is not a contraindication to the examination but particular vigilance for reactions should be maintained in such cases. Epinephrine should be instantly available and pretreatment with antihistamines or corticosteroids should be considered.

References

1 *Hudach, S.S., P.D. McMaster:* The lymphatic participation in human cutaneous phenomenon. J. Exp. Med. 57 (1933) 751-772
2 *Kinmonth, J.B., R.K. Harper, G.W. Taylor:* Lymphangiography by radiologic methods. J. Fac. Radiol. 6 (London) (1955) 217-223
3 *Kopp, W.L.:* Anaphylactics from Alphazurine 2G during lymphography. J.A.M.A. 198 (1966) 200-201
4 *Mortazavi, S.H., B.D. Burrows:* Allergic reaction to Patent Blue dye in lymphangiography. Clin. Radiol. 22 (1971) 389-390
5 *Sieber, F.:* Incidence after the subcutaneous installation of Patent Blue (Patent Blau) for lymphography. Med. Bild 11 (1968) 102-103
6 *Koehler, P.R.:* Complications of lymphography. Lymphology 1 (1968) 116-120
7 *Gosselin, R.E., H.C. Hodge, R.P. Smith, M.N. Gleason:* Clinical toxicology of commercial products, acute poisoning, 4th ed. Williams and Wilkins, Baltimore, 1976
8 *Wilson, C.D., O. Gisvold, R.T. Doerge:* Textbook of organic medicinal pharmaceutical chemistry, 6th ed. J.B. Lippincott Co., Philadelphia, 1971
9 *Hiranaka, P.K., L.M. Kleinmann, E.A. Sokoloski, H.M. Fales:* Chemical structure and purity of dyes used in lymphograms. Am. J. Hosp. Pharm. 32 (1975) 928-930
10 *Stern, W.:* Personal communication. Sigma Chemical Company, St. Louis, Missouri, USA
11 *Hurwitz, N.:* Predisposing factors in adverse reactions to drugs. Brit. Med. J. 1 (1969) 536-539

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