

BLUE URTICARIA: IMMEDIATE HYPERSENSITIVITY REACTION FOLLOWING PATENT BLUE DYE INJECTION FOR IDENTIFICATION OF SENTINEL LYMPH NODE IN BREAST CANCER: A CASE REPORT**¹Benchakroun Khadija, ^{2*}Benali Saad, ³Babahabib Abdellah, ⁴Kouach Jaouad and ⁵Moussaoui Rahali Moulay Driss**^{1,2}Service Gynécologie Obstétrique Hôpital Militaire D'instruction Mohamed V Rabat Maroc.³Faculté de Médecine et de Pharmacie de Fès Service Gynécologie Obstétrique Hôpital Militaire D'instruction Mohamed V Rabat Maroc.^{4,5}Service Gynécologie Obstétrique Hôpital Militaire D'instruction Mohamed V Rabat Maroc.***Corresponding Author: Dr. Benali Saad**

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ABSTRACT

Introduction: The patent blue dye is often used for identification of sentinel lymph node while cancers surgery. The immediate hypersensitivity reactions of this colouring agent consisting of : blue urticaria, angioedema, bronchospasm and anaphylactic shock are not rare (0.8-2.8%). **Case presentation:** A 46 year old women, presented diffuse blue urticaria with eyelid edema without bronchospasm nor hypotension, 10min after patent blue dye sub-cutaneous injection for localisation of sentinel lymph node while breast surgery. **Discussion:** The immediate hypersensitivity reactions due to patent blue dye occur in 0.24 to 2.2% interventions. These reactions are sometimes severe with numerous cases of anaphylactic shock reported in literature.

KEYWORDS: The patent blue dye is often used for identification of sentinel lymph node while cancers surgery.

1- INTRODUCTION

The patent blue dye « E 131 » is « azo dye » frequently used in food, cosmetic, textile and pharmaceutical industries.

It's often used alone or associated to isotopic agent for sentinel lymph node identification while sentinel cancers surgery.^[1]

The immediate hypersensitivity reactions due to patent blue dye are not uncommon and estimated at 0.24 to 2.2%.^[2]

We report the case of immediate hypersensitivity following blue dye injection while breast cancer intervention to identify a sentinel lymph node.

2- CASE REPORT

It's a 46 years old women, with history of allergic rhinitises and asthma as well as a rheumatoid arthritis acute at childhood treated, an amygdallectomia under general anesthesia and two caesarians under spinal anesthesia without any incident.

The patient had a conservative surgery for a nodule of the supero-external quadrant of the left breast with sentinel lymph node. Induction of anesthesia was done

with Fentanyl, Propofol and curarisation with Atracurium.

After surgical installation, 15min after the induction, 2ml of patent blue V sodic at 2.5% (Guerbet, Roissy Charles-de-Gaulle France) diluted in 5cc of salted serum 0.9% was injected in subareolar and at the supero-external quadrant of the left breast.

Ten minutes after the injection, the patient presented an anaphylactic reaction grade 2 in the point of injection extending gradually to the neck and the upper limb (bluish papulo erythematous lesion without respiratory signs and without hemodynamic impact).

The surgery was not interrupted and the treatment consisted on injection of 120mg of methylprednisolone.

At the end of the intervention, blue urticaria was generalized on all the body with edema of eyelids, lips and neck as well as the trunk and the lower limbs.

The patient was transported to the post-interventional monitoring room, one hour later she was transferred in intensive care for monitoring.

Clinical progression was favourable. Diffuse edema declined gradually during 24 hours.



3- DISCUSSION

two dyes are the only used for the procedure of detection of sentinel lymph node in breast cancer.^[3] The patent blue (patent blue V sodic at 2,5%, Guerbet laboratory, Aulnay-Sous-Bois, France) used in France and its isomer isosulfan blue, frequently used in USA for which similar immediate hypersensitivity reactions were reported in literature.

Patent blue is found in many textile, ink, paintings, cosmetics, detergent and food industry (chocolat and chewing-gums) as well as common products of hand sanitizing (Sterilium® for example).

It appears in industry under the reference E 131. The patent blue might be responsible for mild undesirable effects like bluish coloring of the seed coat and urine veering to yellow and then to green and disappearing in 24 to 48 hours. This coloring can persist several days or even months in the injection site.^[4] Immediate hypersensitivity reactions due to patent blue are not rare, estimated between 0.24% and 2.2% of procedures.^[2] They are more common than anaphylactic reactions due to general anesthesia, estimated between 1/5000 and 1/13000.^[5]

Clinical allergy manifestations due to patent blue are various, from general urticaria until anaphylactic shock. These reactions can be severe because some cardiac failures have been reported.^[6] However, no deaths were reported to date. The largest series reported by Barthelmes and al, including 7917 patients who had a search of sentinel lymph node with the patent blue associated to radio isotope.^[7] In this series, we found 0.3% of reactions grade 1, 0.2% of reactions grade 2 and 0.06% of severe reactions grade 3. That risk associated

with the use of patent blue, was recalled in 2008 as a result of a national survey of drug monitoring, by French Agency of Sanitary Security for Health Products (AFSSAPS) and by the laboratory trading the product.

In fact, 77 reactions due to patent blue with a delay average of 37mn were recorded between 1991 and 2006 including 47 anaphylactic shocks.^[8] In literature, the deadline of reaction to patent blue is often retarded of an average of 30 mn and makes etiologic diagnosis difficult, especially when the reaction occurs in the recovery room.^[9]

This deadline contrast with that of anaphylactic reactions related to anaesthetics which is less than 10mn.

This is probably explained by the subcutaneous injection and not intravenous of the dye thereby confirming the criminalization of the product in our case.

Two mechanisms are probably intricate: an allergic reaction IgE mediated is evoked by the majority of authors because of the existence of severe responses, the response time sometimes very short, the near-constant elevation of tryptase when it's dosed in the acute stage, suggesting a massive degranulation mast cell and finally positive allergy skin tests to strong dilutions.^[10]

Furthermore, (Wöhrle et al.) have demonstrated by technique ELISA, IgE specific of patent blue.^[6] All of these reactions IgE mediated require a prerequisite awareness, which is probably formed via numerous food industrial products containing the dye.

Moreover, a non-specific histamine releasing phenomenon is also envisaged because of some delayed

responses, normal tryptase assays and positive skin tests sometimes only to high concentrations.



The interest of skin tests with patent blue was highlighted by Mertes and al. who published the most important serial of patientes tested with patent blue with 14 cases.^[5]

All patients had an anaphylactic reaction during general anesthesia in which patent blue was used. 3 tryptase values of 9 collected (33%) and 6 histamin values of 8 (75%) were subnormal.

All patent blue skin tests were positive. 8 non diluted pricktests (0,025g/ml) of 13 and 11 IDR were positive with dilutions from 1/1000 to 1/10. Some skin tests with same concentrations performed in 9 control patients were negative, highlighting non-irritating character of patent blue at these concentrations.^[11] No predictive factor during the pre-anesthetic consultation suspects the occurrence of these accidents.

Glucocorticoids and antihistaminic premedication would probably reduce the severity of accident but not the incidence.^[5] The methylene blue which is considered less sensitizing and with different chemical structure, was sometimes suggested as alternative to identifie sentinel lymph node but it can induce skin necrosis at the injection site.^[9] The existence of co-awareness to patent blue and methylene blue seems to be fortuitous^[10] but encourage for caution.

Our case provides to insist on the gravity of reactions due to patent blue. Skin tests represent a simple method reliable for diagnosis of these accidents, they should be done during the pre-anesthetic evaluation with precaution, starting with pricktests and then IDR strongly diluted. This allergenic aspect of patent blue has

encouraged to the development of other methods to detect sentinel lymph node.

The lymphoscintigraphie with radioisotope for detection of sentinel lymph node in case of patent blue allergy, requiring a probe for detection of gamma radiation in surgical room ; tracking technologies combining both methods colorimetric and isotopic; and the use of indocyanine green which requires infrared camera in the surgical room, are safe methods but more expensive.

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