

LETTER TO THE EDITOR

## **Anaphylaxis reaction of a breast cancer patient to methylene blue during breast surgery with sentinel node mapping**

ALI JANGJOO<sup>1</sup>, MOHAMMAD NASER FORGHANI<sup>2</sup>, MOSTAFA MEHRABIBAHAR<sup>1</sup> & RAMIN SADEGHI<sup>3</sup>

<sup>1</sup>Surgery Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran, <sup>2</sup>Cancer Research Center, Omid Hospital, Mashhad University of Medical Sciences, Mashhad, Iran and <sup>3</sup>Nuclear Medicine Research Center, Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

### **To the Editor**

Sentinel node biopsy is the standard method for axillary staging of the early stage breast cancer patients [1,2], which is usually performed by the aid of radiotracers and blue dyes in combination or alone [3,4]. With more availability of nuclear medicine facilities, sentinel node biopsy for breast cancer patients is increasing [5–7]. Despite its proven benefit for the patients, sentinel node mapping using blue dyes has some fatal complications; such as anaphylaxis reaction [8].

### **Case presentation**

A 56-year-old woman with early stage breast cancer was referred for breast surgery as well as sentinel node biopsy. <sup>99m</sup>Tc-Antimony sulfide colloid was injected superficially the day before surgery for sentinel node mapping using gamma probe during operation. After induction of anesthesia, 2 ml methylene blue was injected in the subdermal fashion in the peri-areolar region of the index quadrant of the breast. Two minutes post-blue dye injection the patient developed severe hypotension, tachycardia, bronchospasm, as well as hypoxia. The main surgery was not conducted and resuscitation started with oxygen, epinephrine, mechanical ventilation and intravenous fluid. Histamine receptor blockers as well as high dose corticosteroid were also started. The patient was transferred to ICU. Chest x-ray showed diffuse pulmonary edema. The patient's condition gradually improved and after couple of days she was discharged.

The patient did not have any history of atopic disorders; however she reported history of food allergy (to melon and eggplant) in her family (herself and her father). She was referred for allergy testing and prick tests with diluted anesthetic drugs (which were used for the patient during surgery), latex, and methylene blue were done. Histamine and normal saline were used as positive and negative control respectively. The prick test with methylene blue was positive (20×30 mm wheal was raised) and the patient developed urticaria.

Breast surgery with sentinel node biopsy mapping (using radiotracers and surgical gamma probe) was performed for the patient two months later without blue dye injection.

### **Discussion**

Several kinds of blue dyes are in use for sentinel node mapping of early stage breast cancer patients such as Patent blue V [9], isosulfan blue [10], and methylene blue [11].

Methylene blue is a compound with widespread use in medicine [12]. This dye has been used for sentinel node biopsy mapping since 2001 with favorable results [11,13]. However it has several reported adverse reactions such as interference with pulse oximetry [14], and skin complications (necrosis) [15–17].

It is usually stated that methylene blue is safer and cheaper than other dyes using in sentinel node biopsy [12,18]. Despite its widespread use in medicine,

anaphylaxis to methylene blue has been very rarely reported in medical literature [19,20]. To the extent of our knowledge, there is only one report of pulmonary edema after methylene blue injection for sentinel node biopsy [21]. Our case is the second in this regard and underscores the importance of considering the possibility of anaphylactic reaction to methylene blue while performing sentinel node biopsy.

In conclusion, although methylene blue is considered safer than other kinds of blue dye which are currently in use for sentinel node mapping (with almost the same accuracy), anaphylaxis can occur with this compound and facilities to treat this fatal condition should always be in hand.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

## References

- [1] Christiansen P, Friis E, Balslev E, Jensen D, Moller S. Sentinel node biopsy in breast cancer: Five years experience from Denmark. *Acta Oncol* 2008;47:561–8.
- [2] Eftekhari M, Beiki D, Fallahi B, Arabi M, Memari F, Gholamrezanezhad A, et al. Assessment the diagnostic accuracy of sentinel lymph nodes lymphoscintigraphy using Technetium-99m phytate in breast cancer. *DARU* 2009; 17:83–7.
- [3] Lauridsen MC, Garne JP, Sorensen FB, Melsen F, Lernevall A, Christiansen P. Sentinel lymph node biopsy in breast cancer—experience with the combined use of dye and radioactive tracer at Aarhus University Hospital. *Acta Oncol* 2004;43:20–6.
- [4] Ilum L, Bak M, Olsen KE, Kryh D, Berg V, Axelsson CK. Sentinel node localization in breast cancer patients using intradermal dye injection. *Acta Oncol* 2000;39:423–8.
- [5] Sadeghi R, Forghani MN, Memar B, Rajabi Mashhadi MT, Dabbagh Kakhki VR, Abdollahi A, et al. How long the lymphoscintigraphy imaging should be continued for sentinel lymph node mapping? *Ann Nucl Med* 2009;23: 507–10.
- [6] Sadeghi R, Forghani MN, Zakavi SR, Jangjoo A, Shabani GA, Kakhki VRD. The need for skin pen marking for sentinel lymph node biopsy: A comparative study. *Iran J Nucl Med* 2008;16:23–7.
- [7] Moghimi M, Ghoddosi I, Rahimabadi AE, Sheikvatan M. Accuracy of sentinel node biopsy in breast cancer patients with a high prevalence of axillary metastases. *Scand J Surg* 2009;98:30–3.
- [8] Amr D, Broderick-Villa G, Haigh PI, Guenther JM, DiFronzo LA. Adverse drug reactions during lymphatic mapping and sentinel lymph node biopsy for solid neoplasms. *Am Surg* 2005;71:720–4.
- [9] Thierrin L, Steiger D, Zuber JP, Spertini F, Brunisholz Y, Delaloye JF. Severe anaphylactic shock to Patent Blue V with cardiac arrest during breast carcinoma surgery with lymphatic mapping. *Eur J Obstet Gynecol Reprod Biol* 2008; 140:140–1.
- [10] Kaufman G, Guth AA, Pachter HL, Roses DF. A cautionary tale: Anaphylaxis to isosulfan blue dye after 12 years and 3339 cases of lymphatic mapping. *Am Surg* 2008;74:152–5.
- [11] Zakaria S, Hoskin TL, Degnim AC. Safety and technical success of methylene blue dye for lymphatic mapping in breast cancer. *Am J Surg* 2008;196:228–33.
- [12] Masannat Y, Shenoy H, Speirs V, Hanby A, Horgan K. Properties and characteristics of the dyes injected to assist axillary sentinel node localization in breast surgery. *Eur J Surg Oncol* 2006;32:381–4.
- [13] Varghese P, Abdel-Rahman AT, Akberali S, Mostafa A, Gattuso JM, Carpenter R. Methylene blue dye—a safe and effective alternative for sentinel lymph node localization. *Breast J* 2008;14:61–7.
- [14] Pinero A, Illana J, Garcia-Palenciano C, Canizares F, Canteras M, Canadillas V, et al. Effect on oximetry of dyes used for sentinel lymph node biopsy. *Arch Surg* 2004;139: 1204–7.
- [15] Stradling B, Aranha G, Gabram S. Adverse skin lesions after methylene blue injections for sentinel lymph node localization. *Am J Surg* 2002;184:350–2.
- [16] Salhab M, Al Sarakbi W, Mokbel K. Skin and fat necrosis of the breast following methylene blue dye injection for sentinel node biopsy in a patient with breast cancer. *Int Semin Surg Oncol* 2005;2:26.
- [17] Bleicher RJ, Kloth DD, Robinson D, Axelrod P. Inflammatory cutaneous adverse effects of methylene blue dye injection for lymphatic mapping/sentinel lymphadenectomy. *J Surg Oncol* 2009;99:356–60.
- [18] Nour A. Efficacy of methylene blue dye in localization of sentinel lymph node in breast cancer patients. *Breast J* 2004; 10:388–91.
- [19] Dewachter P, Mouton-Faivre C, Trechot P, Llleu JC, Mertes PM. Severe anaphylactic shock with methylene blue instillation. *Anesth Analg* 2005;101:149–50.
- [20] Rzymiski P, Wozniak J, Opala T, Wilczak M, Sajdak S. Anaphylactic reaction to methylene blue dye after laparoscopic chromopertubation. *Int J Gynaecol Obstet* 2003;81:71–2.
- [21] Teknos D, Ramcharan A, Oluwole SF. Pulmonary edema associated with methylene blue dye administration during sentinel lymph node biopsy. *J Natl Med Assoc* 2008;100: 1483–4.