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LETTER TO THE EDITOR

Grade 3 anaphylactic shock after administration of [^{99m}Tc]-labeled nanocolloidal albumin (Nanocoll®) for sentinel node scintigraphy

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Dear Sir,

Adverse effects due to radiopharmaceuticals are very rare, and only sporadic reports have been published. However, in some cases these effects can be life-threatening. The main cause of anaphylactic reaction is the pharmaceutical carrier, not the radiation itself [1]. Furthermore, radiopharmaceuticals are used in tracer quantities; thus there should be no dose–response relationship. Various national reports have been published about the occurrence of adverse effects in nuclear medicine departments after radiopharmaceutical administration [2–4]. In general, the prevalent signs are rash, nausea and vomiting, and the most frequent agents are diphosphonates, colloids and albumin [1]; incidence is less than 1 per 10^4 cases of diagnostic administration [2–4].

A 50-year-old woman was recently admitted to our nuclear medicine department for sentinel node scintigraphy before surgery on a right breast ductal carcinoma. Ultrasonography and mammography showed a 12-mm nodule in the upper-outer quadrant, BIRADS [Breast Imaging Reporting and Data System] 5. A biopsy of the lesion showed a Scarff-Bloom-Richardson grade 1 carcinoma, with the presence of high levels of estrogen and progesterone receptors (100%), without significant expression of human epidermal growth factor receptor 2.

The day before surgery, nanocolloidal albumin was reconstituted under sterile conditions within the radiopharmacy unit, according to the manufacturer's instructions, and labeled with technetium-99m. The patient was administered 37 MBq of [^{99m}Tc]-labeled nanocolloidal albumin (Nanocoll®) by subdermal injection in the peri-areolar region in the same quadrant as the tumor, according to international guidelines [5].

Latex-free gloves were used for the injection. Since the patient had not reported any side effects after disinfection using povidone-iodine (Betadine), e.g. before biopsy, the same product was used for disinfection prior to radionuclide injection.

Roughly 10–15 min after the injection, the patient showed itchiness, hives, dizziness and malaise. Desloratadine 5 mg was administered orally, with no significant reduction in signs and symptoms. Approximately 1 h later, she showed systolic blood pressure of 72 mmHg, bradycardia 43 bpm, oxygen saturation 94%, vomiting, and diffuse rash in the upper and lower limbs as well as in the abdomen. A bolus injection of adrenaline 100 μg was administered immediately, followed by a second bolus, and then continuous administration of adrenaline 1.6 mg/h according to emergency room (ER) protocol for 3 h. After the second adrenaline bolus, blood pressure was 164/82 mmHg, heart rate was 70 bpm and oxygen saturation was 100%.

The next day, she underwent breast surgery for removal of the tumor, and the sentinel node was also removed after intraoperative gamma detection. No particular complications were observed, and a formal declaration was addressed to the national competent drug institution. According to a classification based on symptom severity, the patient reacted with grade 3 anaphylactic shock [6]. According to the algorithm proposed by Silberstein et al. [2], the probable cause of the adverse reaction was Nanocoll® administration, given the reasonable

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time sequence, the pattern of response, and the inability to explain the response based solely on the patient's clinical state.

Meanwhile, the patient was declared to be allergic to macrogols (polyethylene glycol, PEG). Macrogols have shown potential cross-reactivity with structurally related poloxamers [7], and poloxamer 238 is described in the composition of Nanocoll®.

Based on our preliminary analysis, the patient received a subdermal injection of 17 μg [^{99m}Tc]-labeled nanocolloidal albumin and 70 μg poloxamer 238 (Nanocoll®). The immunologist provided the patient with a long list of contraindicated drugs (>250) containing macrogols and poloxamers until further allergy testing. Informed consent for the publication was obtained from the patient described in this report.

In the past 15 years, three individual cases of allergic reactions to nanocolloidal albumin have been published [8–10]; however, in all cases, the reaction was grade 1, and the patient recovered spontaneously or after treatment with antihistamines or topical steroid cream. None of the case reports described a severe reaction like that observed in our patient. In 2018, however, another case was described [11] in which a reaction similar to that of our patient was observed (with similar management): grade 3 anaphylactic shock. Furthermore, in this last case, anaphylaxis due to poloxamer 238 was formally identified by skin prick and intradermal testing.

In conclusion, attention is warranted when adverse effects, although very rare, are observed after radiopharmaceutical administration, particularly in life-threatening situations, when prompt care, and perhaps ER admission, is needed. Moreover, in the case of an anaphylactic reaction to Nanocoll®, poloxamer testing should also be performed.

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Compliance with ethical standards

Conflict of interest All authors declare that they do not have a conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent for the publication was obtained from the patient described in this report.

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