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## **Anaphylactic shock associated with technetium ( $^{99m}\text{Tc}$ )-labelled albumin macroaggregates**

### **Introduction**

Technetium ( $^{99m}\text{Tc}$ )-labelled albumin macroaggregates (Maasol<sup>®</sup>) have been approved for marketing in the Netherlands for the use in diagnostic lung perfusion scans and venoscintigraphy. The Dutch Summary of Product Characteristics (SPC) mentions in its section on undesirable effects the *occurrence of local allergic reactions and 'hypersensitivity-like' reactions such as chest pain, rigor and collapse*[1]. This description suggests that an anaphylactic shock is not likely to occur since the SPC does not explicitly mention allergic or anaphylactic shock. Nevertheless, the Netherlands Pharmacovigilance Centre received two reports of an allergic shock associated with the use of  $^{99m}\text{Tc}$ -labelled albumin macro-aggregates. As suggested by the MEB, a closer examination of our reports might clarify the nature of these 'hypersensitivity-like' reactions.

### **Reports**

Patient A is an 18-year-old female who received 140 MBq  $^{99m}\text{Tc}$ -labelled albumin macroaggregates (Maasol<sup>®</sup> 55ml) intravenously for a diagnostic lung perfusion scan because of suspicion of pulmonary embolism. Two minutes post injection she began experiencing shortness of breath, started coughing and manifesting red colouring of the skin (arms, face and abdomen). Her blood pressure was 90/60 mm Hg and her pulse rate was accelerated (90/min). Her lips turned blue and she subsequently lost consciousness. The patient was given 4 mg clemastin, 25 mg prednisolone, and saline, after which she fully recovered.

Patient B is a 71-year-old female who underwent a diagnostic lung perfusion scintigraphy. Immediately following administration of 140 MBq  $^{99m}\text{Tc}$ -labelled albumin macroaggregates she experienced hot flushes, which condition developed into an anaphylactic shock. She was treated with clemastin intravenously and oxygen 5 litres/min, after which she recovered. Blood pressure was not reported, nor whether adrenaline had been administered.

### **Other sources of information**

#### *Literature*

Macroaggregates, microspheres and the colloidal forms of albumin are associated with hypersensitivity-type reactions like dyspnoea, hypotension, chest discomfort, nausea and vomiting. There are some earlier reports describing cases of cardiovascular collapse following injection of radioactive macro-aggregated albumin particles for a lung perfusion scan in patients with advanced pulmonary disease. However, these cases all occurred prior to 1975, when it was still common to use high doses[2]. The two patients in the Lareb reports were not known to have advanced pulmonary disease and they had received the standard dose of  $^{99m}\text{Tc}$ -labelled albumin macroaggregates.

In order to determine the prevalence of adverse reactions to radiopharmaceuticals and to nonradioactive drugs used in interventional nuclear medicine, a 5-year prospective study was performed in 18 institutes in the United States. In this study, a mere 18 adverse drug reactions were reported with an overall reported incidence of 0.0023% of which only one report, describing a case of rash, was associated with  $^{99m}\text{Tc}$ -labelled albumin macroaggregates[3]. This may indicate that in general radiopharmaceuticals have an excellent safety record and anaphylactic reactions are rare.

#### *Databases*

The database of the WHO Collaborating Centre for Drug Monitoring contained ten reports on Maasol<sup>®</sup> on July 9<sup>th</sup> 2002, of which only a single report specified the occurrence of an anaphylactic shock. On Macrosalb  $^{99m}\text{Tc}$  (human albumine macroaggregates) 165 reports had been submitted, of which 4 concerned a anaphylactoid reaction. The database of the Netherlands Pharmacovigilance Centre has two reports on Maasol<sup>®</sup>, which cases have been described above. One was sent directly to Lareb by the reporting physician, the marketing authorisation holder of Maasol<sup>®</sup> submitted the other report.

### *Mechanism*

Anaphylaxis is an immediate (type I) hypersensitivity reaction to an allergen, caused by the allergen's rapid cross-linking with specific IgE on tissue mast cells and peripheral blood basophils. For an anaphylactic shock to occur, previous exposure to the foreign antigen is required. An anaphylactoid reaction, however, is not an IgE mediated response but, similarly, involves inflammatory mediators to be released from mast cells and basophils. This activation of immune cells may occur both directly (e.g. radiocontrast media) and as the result of disturbances in arachidonic acid metabolism (e.g. NSAIDs) and immune complex-mediated activation of complement<sup>1</sup>. These non-IgE mediated reactions, or anaphylactoid reactions, do not require previous exposure<sup>[4,5]</sup>. It is not clear whether an allergic mechanism is involved in the cases mentioned in our reports or if the reactions described are caused by an anaphylactoid reaction, i.e. a non-immunologically mediated reaction.

### **Conclusion**

Although rare, <sup>99m</sup>Tc-labelled albumin macroaggregates may cause anaphylactoid or anaphylactic reactions that require intervention. The Dutch SPC mentions the occurrence of 'hypersensitivity-like' reactions. Based on the evaluation of the two cases in our database, we recommend that the description 'hypersensitivity-like reactions' be more closely defined and is replaced by the terms anaphylactoid and anaphylactic reactions.

### References

1. Dutch summary of product characteristics of Maasol<sup>®</sup> (version 7-8-1996). [www.cbg-meb.nl](http://www.cbg-meb.nl)
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4. Murrant T, Bihari D. Anaphylaxis and anaphylactoid reactions. *Int J Clin Pract* 2000;54(5):322-8.
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