jnm/CASE REPORT

# ANAPHYLACTOID REACTION TO HUMAN ALBUMIN MICROSPHERES

Richard L. Littenberg

*Tripler Army Medical Center, Honolulu, Hawaii*

***The first case of an anaphylactoid reaction to the intravenous administration of $^{99m}$Tc-labeled human albumin microspheres is reported.***

Technetium-99m-labeled human albumin microspheres (HAM) has become an accepted and commonly used radiopharmaceutical for the evaluation of pulmonary perfusion. No adverse effects to the intravenous administration of this agent have been previously reported. Recently, we have observed an anaphylactoid reaction in a patient given this agent.

## CASE REPORT

The patient is a 22-year-old white woman who was admitted to Tripler Army Medical Center because of left anterior chest and left upper-quadrant abdominal discomfort. This had been present since the morning of admission and was sharp, cramping, and nonpleuritic in nature. She had several episodes of vomiting productive of a small quantity of bilious material. This was followed by several bouts of diarrhea. There was no history of hemoptysis, dyspnea, palpitations, or symptoms referable to venous thrombophlebitis. The patient was taking birth control pills. She presented to an outlying dispensary where she suffered a syncopal episode and was transferred to Tripler Army Medical Center.

The patient had had mild asthma since age 12. An occasional Tedral tablet was the only therapy ever required and her last asthma episode was in early 1972. She had smoked between two and three packs of cigarettes per day since age 12. She had previously been evaluated for bifrontal headaches with a $^{99m}$Tc-pertechnetate brain scan and electroencephalogram in 1972. The headaches vanished with a change in birth control medication.

On admission she had scattered rhonchi and wheezing most marked in the region of the left upper lobe. The leukocyte count was 18,000 with a left shift. Arterial blood gases on room air were $PO_2$ of 87 mmHg, $PCO_2$ of 24 mmHg, and a pH of 7.45. Her chest x-ray film was normal.

A pulmonary perfusion scan was requested to evaluate the possibility of pulmonary embolism. She presented to the nuclear medicine laboratory in good spirits and with only minor complaints. Within 15–20 sec after the intravenous administration of 3 mCi of $^{99m}$Tc-labeled human albumin microspheres (which contained approximately 0.6 mg albumin—90,000 particles, manufactured by the 3M Co.), the patient suddenly experienced severe bronchospasm associated with striking apprehension. Her blood pressure, which had previously been 110/70, was unobtainable. Her femoral pulsations were rapid and weak. Within 1 min she demonstrated a histamine-like reaction with marked cutaneous flushing. Acro- and circumoral cyanosis became prominent.

Shortly after the intravenous administration of 0.8 mg of epinephrine, the patient responded with a marked decrease in wheezing and return of blood pressure to 120/80. Subsequent therapy after an adequate intravenous line was obtained consisted of isotonic saline, 50 mg of benadryl, and 100 mg of hydrocortisone sodium succinate. She continued to improve and the lung scan was performed approximately 1 hr after the initial intravenous injection. A small perfusion defect was noted in the left upper lobe. There were no other significant perfusion abnormalities.

The patient was discharged within 48 hr of admission. The discharge diagnoses were acute nonbacterial gastroenteritis accounting for her acute symptoms, chronic bronchitis related to cigarette smoking, and an anaphylactoid reaction to the lung-scanning agent. There was no evidence for pulmonary embolism.

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For reprints contact: Richard L. Littenberg, Nuclear Medicine Service, Tripler Army Medical Center, Honolulu, Hawaii.

The day after discharge from the hospital the patient underwent scratch and intradermal skin testing with salt-poor human serum albumin, fresh microspheres prepared 30 min prior to testing labeled with $^{99m}$Tc eluted from the same generator, and microspheres from the original suspension that had caused the systemic reaction. The pH of the latter had fallen to 3.4 over the intervening 72 hr and was titrated to 8.0 using sodium bicarbonate. Serial dilutions from 1:100,000 to full strength were negative with the exception that undiluted intradermal human serum albumin produced a 7-mm wheal and a 40-mm flare. A similar response was elicited in normal controls and was considered to be nonspecific in nature and related to chemical irritation. In order to obviate any possible influence of the administered steroids, repeat skin testing 2 weeks after discharge was performed giving identical results.

## DISCUSSION

The acute time course after injection and the clinical manifestations in this patient are most consistent with an anaphylactoid reaction. The HAM particles had been made up within 1 hr of actual intravenous administration. Both direct visual and microscopic inspection of the microspheres were unremarkable. Two patients had uneventful lung scans within the preceding 40 min using microspheres from the same vial. Routine bacteriologic examination of the microsphere suspension, which included gram staining and aerobic and anaerobic cultures, were negative. A pyrogenic, endotoxemic, or bacteriemic effect is considered to be highly unlikely since the two patients studied almost simultaneously with the patient in question showed no adverse reactivity and all bacteriologic testing proved negative. Allergy to human serum albumin is a possibility but this cannot be demonstrated with intradermal skin testing although it is well recognized that intravenous and intradermal challenging with antigens are not entirely comparable.

The general lack of adverse reactions to radiopharmaceuticals tends to de-emphasize the fact that such reactions do occur. Among these reactions approximately half are allergic or idiosyncratic and at least one immediate death has been noted after the intravenous administration of $^{131}$I-macroaggregates (*1*). Previous studies have demonstrated the lack of antigenicity of denatured albumin (*2,3*). In addition to 5 mg of human albumin the 3M Co. microsphere kit contains 3 mg thiosulfate, 67.6 mg lactose, 0.1 mg poloxalene, and 4 mg sodium benzoate. The solution used for rinsing and suspending the microspheres contains 17 mg polysorbate 80 and 270 mg benzyl alcohol. None of these components in the amounts used is known to cause adverse reactions although in this particular patient this possibility cannot be excluded.

In conclusion, it is thought that a patient has been observed who experienced an anaphylactoid reaction to the intravenous injection of $^{99m}$Tc-labeled human albumin microspheres. It is highly recommended that a physician who is equipped to handle anaphylactoid reactions and appropriate medications be immediately available when intravenous radiopharmaceuticals are administered.

## REFERENCES


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