Altered Biodistribution of Gallium-67 in a Patient with Aluminum Toxicity Treated with Desferoxamine

Steven J. Brown, Walter J. Slizofski, and Simin Dadparvar

Department of Radiation Oncology and Nuclear Medicine, Division of Nuclear Medicine, Hahnemann University Hospital and School of Medicine, Philadelphia, Pennsylvania

Markedly altered biodistribution of [^{67}Ga]citrate was observed in a 66-yr-old hemodialysis patient imaged at 48 hr postinjection. A review of the patient's hospital records revealed toxic serum levels of aluminum, treated with the chelating agent desferoxamine. Based on what is known about the biologic interactions between gallium, aluminum, transferrin, and desferoxamine, we believe that both toxic serum aluminum levels and desferoxamine therapy may cause altered biodistribution on [^{67}Ga]citrate scintigraphy.

J Nucl Med 1990; 31:115–117

Altered gallium biodistribution has been observed in a wide variety of circumstances. Many investigators have tried to modify the uptake of gallium in an attempt to improve target-to-nontarget ratios, or reduce the radiation burden to the patient (*1–3*). Others have suggested that altered iron metabolism might interfere with gallium-67 (^{67}Ga) scanning (*4*). However, altered biodistribution on [^{67}Ga]citrate images in the presence of serum aluminum toxicity and/or desferoxamine therapy has not, to the author's knowledge, been described. A case is presented here in a patient with aluminum toxicity treated with desferoxamine (DFO).

CASE REPORT

A 66-yr-old man with end stage renal disease was admitted with profound lethargy. He had been anuric and on hemodialysis for the past 16 yr. Past medical history was remarkable for hypertension, congestive heart failure, atherosclerotic vascular disease, and chronic anemia. Prior surgery included a right sided, below the knee amputation. Medications on admission included aluminum hydroxide, 1800 mg orally, three times daily. Admission tests revealed a hemoglobin of 8.1 g/100 ml with a mean corpuscular volume of 76 fl.

The initial workup of the patient's change in mental status was negative except for a serum aluminum level of 45 mcg/l (normal 3–10 mcg/l). A subsequent challenge with DFO, 2 g i.v., revealed pre- and post-DFO serum aluminum values of 74 and 428 mcg/l, respectively.

The patient received no DFO therapy over the next 2 wk. Hemodialysis was continued four times weekly. During this time a left knee effusion developed along with fevers to 101° Fahrenheit. A whole-body gallium scan was ordered to look for occult infection.

The patient was dialyzed and then given DFO, 1.5 grams i.v. Twenty-four hours later he was dialyzed, and then injected with 10.41 mCi of [^{67}Ga]citrate, intravenously. After 2 days the patient was again dialyzed and given DFO. This was followed by gallium imaging, 48 hr postinjection.

The 48-hr gallium images reveal diffuse gallium activity throughout the entire body. There is minimal organ localization and an altered biodistribution of gallium (Fig. 1).

DISCUSSION

Although poorly understood in the past, much has been learned about the metabolism of gallium and similar ions in recent years (*5–12*).

Studies have shown that tracer amounts of gallium in blood are exclusively bound and transported by transferrin (*12*). Furthermore, transferrin binding sites are saturable by gallium and similar ions (*4,7,9*). Once bound, these ion-transferrin complexes are not dialyzable; hemodialysis does not interfere with gallium scintigraphy (*10–13*). The cellular uptake of gallium occurs by incorporation of the gallium-transferrin complex (*7,14*). Although the exact mechanism is not known, uptake is essentially complete by 24 hr after gallium injection (*8*).

Aluminum is a metal that has chemical and biologic properties very similar to gallium (*11*). After i.v. injection aluminum and gallium bind rapidly with transferrin, occupying the same binding sites (*15*). At concentrations commonly found in dialysis patients, aluminum readily displaces tracer amounts of gallium from transferrin (*9,10*).

In recent years, aluminum has been implicated in the etiology of a number of diseases (*11*). Two of these, dialysis encephalopathy and microcytic anemia, were present in our patient. Serum aluminum levels are

Received Feb. 27, 1989; revision accepted Sept. 20, 1989.

For reprints contact: Steven J. Brown, MD, Hahnemann University Hospital, Div. of Nuclear Medicine, Mail Stop # 309, Broad and Vine St., Philadelphia, PA 19102.

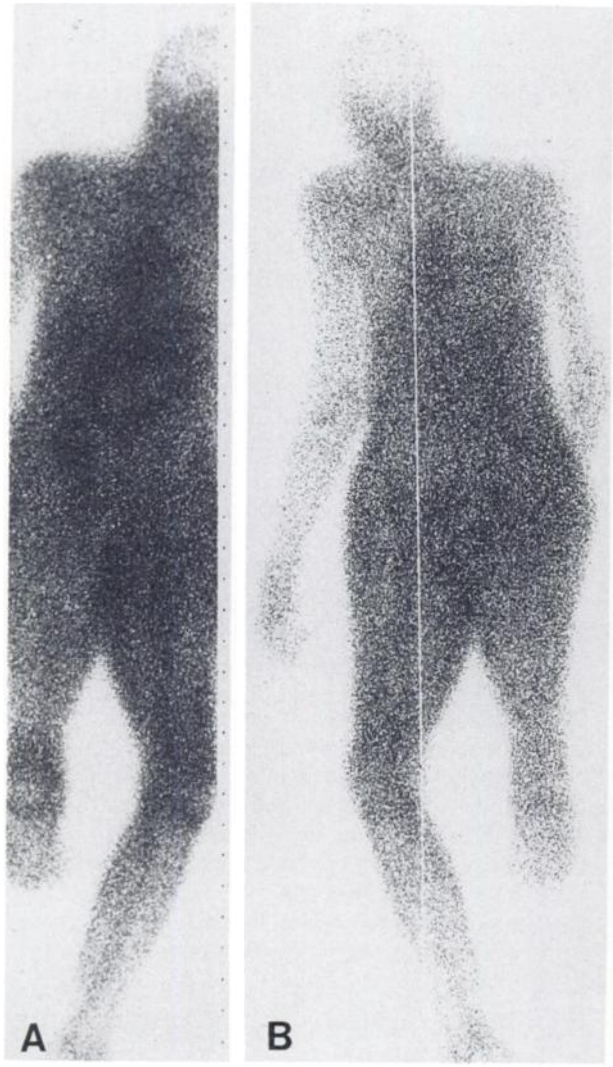


FIGURE 1
Whole-body images obtained 48 hr after gallium injection show diffuse activity and poor tissue localization with absence of the normal organ distribution of gallium. (A) anterior and (B) posterior.

elevated in many dialysis patients, due in part to the aluminum content of dialysate and the high oral intake of aluminum hydroxide used to decrease phosphate absorption (*16–19*). They are not considered toxic unless greater than 200 mcg/l or symptoms develop.

Desferoxamine, a chelating agent used primarily to reduce iron overload, is also used to treat aluminum toxicity. DFO rapidly forms a complex with aluminum that is readily dialyzable (*20*). However, DFO binds with gallium as well, forming a complex much stronger than that of gallium with transferrin (*21*). DFO given up to 24 hr after gallium injection has been shown to decrease tissue levels of gallium (*1*).

Thus, in our patient, DFO given prior to gallium injection would have bound some aluminum and been removed during dialysis. Excess aluminum could then have interfered with gallium-transferrin binding and subsequent cellular uptake, altering the biodistribution of gallium. Although a small amount of gallium could have been bound and removed during dialysis after repeat DFO therapy, DFO should have bound primarily with aluminum. These interactions could account for the high blood-pool activity and altered biodistribution of ^{67}Ga seen on the 48-hr images.

As more is learned about the biologic activity of gallium and similar ions we should develop a better understanding of gallium scan findings. It would be interesting to see if other metallic ion overload states, such as hemochromatosis, result in similar images to those presented here. Also, the potential for interference with gallium imaging by chelating agents such as DFO should be considered if recently administered.

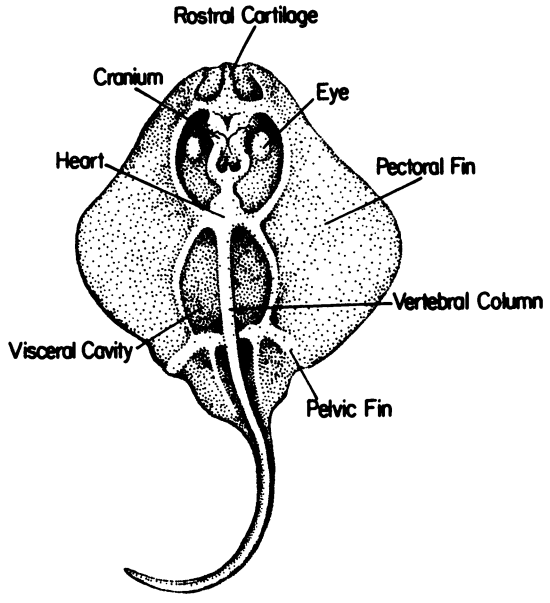
ACKNOWLEDGMENTS

The authors thank Edward P. Yeager, Jr. for photographing the illustrations for publication.

REFERENCES

1. Oster ZH, Som P, Sacker DF, Atkins HL. The effects of desferoxamine mesylate on gallium-67 distribution in normal and abscess-bearing animals: concise communication. *J Nucl Med* 1980;21:421–425.
2. Yokoyama A, Ohmomo Y, Horiuchi K, et al. Desferoxamine, a promising bifunctional chelating agent for labeling proteins with gallium: Ga-67 DF-HSA: concise communication. *J Nucl Med* 1982;23:909–914.
3. Oster ZH, Larson SM, Wagner HN Jr. Possible enhancement of ^{67}Ga-citrate imaging by iron dextran. *J Nucl Med* 1976;17:356–358.
4. Bradley WP, Alderson PO, Eckelman WC, Hamilton RG, Weiss JF. Decreased tumor uptake of gallium-67 in animals after whole-body irradiation. *J Nucl Med* 1978;19:204–209.
5. Hartman RE, Hayes RL. The binding of gallium by blood serum. *J Pharmacol Exp Ther* 1969;168:193–198.
6. Gunasekera SW, King LJ, Lavender PJ. The behaviour of tracer gallium-67 towards serum proteins. *Clin Chim Acta* 1972;39:401–406.
7. Larson SM, Grunbaum Z, Rasey JS. The role of transferrins in gallium uptake. *Int J Nucl Med Biol* 1981;8:257–266.
8. Hayes RL. The tissue distribution of gallium radionuclides. *J Nucl Med* 1977;18:740–742.
9. Cochran M, Neoh S, Stephens E. Aluminum interaction with ^{67}Ga uptake by human plasma and transferrin. *Clin Chim Acta* 1983;132:199–203.
10. Trapp GA. Plasma aluminum is bound to transferrin. *Life Sci* 1983;33:311–316.
11. Ganrot PO. Metabolism and possible health effects of aluminum. *Environ Health Perspect* 1986;65:363–441.
12. Vallabhajosula SR, Harwig JF, Siemsen JK, Wolf W. Radiogallium localization in tumors: blood binding and transport and the role of transferrin. *J Nucl Med* 1980;21:650–656.
13. Marlette JM, King WM, Shafer RB. Effect of hemodialysis on gallium-67-citrate scanning. *Clin Nucl Med* 1980;5:401–403.
14. Chan SM, Hoffer PB, Maric N, Duray P. Inhibition of gallium-67 uptake in melanoma by an anti-human transferrin receptor monoclonal antibody. *J Nucl Med* 1987;28:1303–1307.
15. Tomimatsu Y, Donovan W. Spectroscopic evidence for per-

turbation of tryptophan in Al(III) and Ga(III) binding to ovotransferrin and human serum transferrin. *FEBS Lett* 1976;71:299–302.
16. Kaehny WD, Alfrey AC, Holman RE, Shorr WJ. Aluminum transfer during hemodialysis. *Kidney Int* 1977;12:361–365.
17. Kovalchik MT, Kaehny WD, Hegg AP, Jackson JT, Alfrey AC. Aluminum kinetics during hemodialysis. *J Lab Clin Med* 1978;92:712–720.
18. Gorsky JE, Dietz AA. Aluminum concentrations in serum of hemodialysis patients. *Clin Chem* 1981;27:932–935.
19. King SW, Savory J, Wills MR. Aluminum distribution in serum following hemodialysis. *Ann Clin Lab Sci* 1982;12: 143–149.
20. Milliner DS, Hercz G, Miller JH, Shinaberger JH, Nissenson AR, Coburn JW. Clearance of aluminum by hemodialysis: effect of desferioxamine. *Kidney Int Suppl* 1986;29:S100–S103.
21. Weiner RE, Thakur ML, Goodman M, Hoffer PB. Relative stability of In-111 and Ga-67 desferrioxamine and human transferrin complexes. In: Sodd VJ, Hoogland DR, Allen DR, Ice RD, Sorensen JA, eds. *Radiopharmaceuticals II: Proceedings of the 2nd International Symposium on Radiopharmaceuticals.* Seattle: The Society of Nuclear Medicine; 1979: 331–340.



Female Little Skate *Raja erinacea*
34 cm length

FIRST IMPRESSIONS

NAME:
Peter R. Burn, PhD

INSTITUTION:
Suffolk University/Massachusetts General Hospital

INSTRUMENTATION:
Anger Camera

TRACER:
1.8. mCi ^{99m}Tc-MDP

ROUTE OF ADMINISTRATION:
Cardiac Puncture

TIME AFTER INJECTION:
21 Hours

PURPOSE:
To determine the extent of calcification of the cartilage skeleton of the little skate, *Raja erinacea* (Chonorichthyes)