Thymic Concentration of Radiolabeled Octreotide

TO THE EDITOR: A radioactive agent that would help distinguish between anterior mediastinal neoplasia and normal or hyperplastic thymic tissue would be of considerable value in pediatric patients. I was, therefore, interested in the recent report in which Lastoria et al. (*1*) documented ^{111}In-labeled octreotide concentration by malignant thymic tumors (mainly thymomas) but not by the hyperplastic thymuses of the adult patients included in their study. These findings corroborated earlier reports of lack of thymic uptake of this agent in humans (*2,3*) but are inconsistent with the autoradiographic demonstration of high densities of somatostatin receptors in the medulla of the normal thymus in both adults and children (*2*).

I reviewed the images of 11 children, ages 5 mo to 11 y, who underwent octreotide scintigraphy to evaluate abdominal or pelvic neuroblastoma (*4*). None of the patients had mediastinal masses but 9 patients had abundant thymic tissue demonstrated on chest CT scans obtained within 1–13 d of nuclear imaging.

Three of the patients (ages 4, 5 and 16 mo) had thymic activity visible on planar images obtained 2–4 h and 24 h after administration of [^{111}In-diethylenetriamine pentaacetic acid-D-Phe^1]-octreotide (Octreoscan; Mallinckrodt, Inc., St. Louis, MO). This activity was generally more conspicuous on the delayed scans. No histologic examination of mediastinal tissue was warranted in these 3 patients because anterior mediastinal involvement due to neuroblastoma is exceedingly rare and, in each case, the CT appearance of the chest was normal with an anterior mediastinal configuration typical of thymus.

It is difficult to explain the difference between our results and those reported by the previous investigators. Tracer dose and technical considerations relating to small infants may play a role. Because thymic activity was detected in 3 of our youngest patients, it is also possible that thymic somatostatin receptor expression or binding affinity is greater in this age group. Regardless, our findings suggest that uptake of radiolabeled octreotide is not a specific indicator of mediastinal disease in infants and that these scintigrams should be interpreted with caution because of potential false-positive results in this patient population.

Our work was supported in part by the National Cancer Institute, Cancer Center Support (CORE) grant P30CA21765, and by the American Lebanese Syrian Associated Charities.

REFERENCES

1. Lastoria S, Vergara E, Palmieri G, et al. In vivo detection of malignant thymic masses by indium-111-DTPA-D-Phe^1-octreotide scintigraphy. *J Nucl Med.* 1998;39: 634–639.
2. Reubi JC, Waser B, Horisberger U, et al. In vitro autoradiographic and in vivo scintigraphic localization of somatostatin receptors in human lymphatic tissue. *Blood.* 1993;82:2143–2151.
3. Rettenbacher L, Galvan G. Differentiation between residual cancer and thymic hyperplasia in malignant non-Hodgkin's lymphoma with somatostatin receptor scintigraphy. *Clin Nucl Med.* 1994;19:64–65.
4. Fletcher BD, Kauffman WM, Santana VM, Bowman LC, Furman WL. Preliminary evaluation of octreotide scintigraphy in children with neuroblastoma [abstract]. *Radiology.* 1996;201(P):243.

Barry D. Fletcher
St. Jude Children's Research Hospital
Memphis, Tennessee

Conventional Treatments for Non-Hodgkin's Lymphoma: The Need for New Therapies

TO THE EDITOR: We read with interest the article by Moskowitz (*1*). We were concerned, however, that Table 12 entitled "Studies of Radiolabeled and Immunotoxin-Conjugated Monoclonal Antibodies" confuses the results of our current experimental radioimmunotherapy for non-Hodgkin's lymphoma, IDEC-Y2B8, with earlier data on our murine ^{90}Y-labeled anti-idiotype monoclonal antibodies (*2*). Thus, the row in Table 12 labeled "White et al. (*82*)" is incorrect.

IDEC-Y2B8 is a highly specific murine anti-CD-20 monoclonal antibody covalently linked to MXDTPA which securely chelates ^{90}Y. As such, IDEC-Y2B8 combines the advantages of the target nonmodulating, nonshedding antigen CD-20 with the advantages of the high-energy pure β-emitting ^{90}Y. Table 12 should be corrected to read as follows:

Reference	Indication	Treatment	No. of patients	Response rate (%)	Complete response (%)	Partial response (%)	Duration of response
Wiseman et al. (*3,4*)	Relapsed/refract: low/int mantle	IDEC-Y2B8 (anti-CD20)	51	67	25	41	10.5+ mo (8.1–13.5+ mo)
	Low grade		34	82	27	56	N/A
Grillo-López et al. (*5*)	Relapsed/refract B-cell NHL	IDEC-Y2B8 (anti-CD20)	17	64	28	36	7.4+ mo (5.9–14.8 mo)
White et al. (*2*)	B-cell NHL	^{90}Y anti-Id	9	33	22	11	4 mo (1.5–12 mo)

Considering these above studies, IDEC-Y2B8 has an overall response rate comparable with other anti-CD20 products such as ^{131}I-B1 reported by Press et al. (*6*) and Kaminski et al. (*7*) in the original article.

REFERENCES

1. Moskowitz CH. Conventional treatments for non-Hodgkin's lymphoma. *J Nucl Med.* 1998;39(suppl):2S–10S.
2. White CA, Halpern SE, Parker BA, et al. Radioimmunotherapy of relapsed B-cell lymphoma with yttrium 90 anti-idiotype monoclonal antibodies. *Blood.* 1996;87: 3640–3649.
3. Wiseman GA, Dunn WL, Witzig TE, et al. Non-Hodgkin's lymphoma tumor and bone marrow radiation from radioimmunotherapy with IDEC-Y2B8 yttrium-90 anti-CD20 monoclonal antibody [abstract]. *J Nucl Med.* 1998;39:69P.
4. Wiseman G, Witzig T, White CA, et al. Radioimmunotherapy of relapsed or refractory non-Hodgkin's lymphoma (NHL) with IDEC-Y2B8 [abstract]. *J Radiat Oncol.* 1998;42(1 suppl):130.
5. Grillo-López AJ, Chinn P, Morena R, et al. Treatment of non-Hodgkin's lymphoma using the 90-yttrium labeled anti-CD20 monoclonal antibody IDEC-Y2B8: a phase I clinical trial [abstract]. *Ann Oncol.* 1996;7(3 suppl):57.
6. Press OW, Eary JF, Appelbaum FR, et al. Phase II trial of ^{131}I-B1 (anti-CD20) antibody therapy with autologous stem cell transplantation for relapsed B cell lymphomas. *Lancet.* 1995;346:336–340.
7. Kaminski MS, Zasadny KR, Francis IR, et al. Iodine-131-anti-B1 radioimmunotherapy for B-cell lymphoma. *J Clin Oncol.* 1966;14:1974–1981.

Christine A. White
IDEC Pharmaceuticals
San Diego, California

Gregory Wiseman
Mayo Clinic
Rochester, Minnesota

Accuracy of Estimation of Glomerular Filtration Rate from Renography

TO THE EDITOR: The estimation of glomerular filtration rate (GFR) from measurement of the absolute uptake of activity in the kidney is a useful enhancement to radionuclide renography, allowing information obtained on the individual kidneys to be interpreted in the context of overall renal function. This process requires the depth of the kidney to be assessed, and lateral images obtained at the end of the renography acquisition have been used for this purpose (*1*). At our own center the use of lateral images has been shown to improve the precision of GFR estimation from renography compared with the use of equations (*1*), although the difference was not statistically significant. The study described in Steinmetz et al. (*2*) contains some useful new ideas on using lateral images in GFR quantification, in particular the use of the centroid of the renal region of interest. It also confirms the improvement in precision achieved through use of lateral images in determining kidney depth. However, despite this increase in precision I believe that it is wrong to conclude that this refinement brings the technique into the precision range of blood sample based methods.

The first reason that Steinmetz et al. cannot make this conclusion is that there are weaknesses in their methodology. They have compared their GFR estimates with creatinine clearance which itself is an inaccurate estimate of GFR (*3*). They also have used the correlation coefficient as the measure of agreement between their estimates of GFR which is an inappropriate statistic in this instance (*4*). SEE is a more appropriate parameter and is the one used by most previous investigators in this field. Standard errors for blood sample GFR are of the order of 3–4 mL/min (*1*). Visual interpretation of the graph showing the data of Steinmetz et al. would suggest a standard error considerably greater than this.

The second reason for rejecting their conclusion is that the errors inherent in the technique mean that it would never be expected to have a precision equal to blood sample techniques. The error of 3–4 mL/min expressed as a percentage error is around 5%–7% on a typical population of GFR measurements. Such a percentage error would not be expected in gamma camera GFR measurement for the following reasons:

1. The cumulative uptake measured at 2–3 min in renography is proportional to the average GFR over a very short period of time. By contrast blood sample GFR gives a value averaged over a period of several hours which, therefore, will be much less subject to short-term physiologic variability than the renogram measurement.
2. There is a considerable contribution to the counts obtained in the kidney region from both extrarenal and intrarenal background. Although there are methods for subtraction of both components of background counts these are not perfect and have a random error associated with them (*5*).
3. There are significant errors in performing depth measurements from lateral images obtained at the end of the dynamic phase of renography. The visual outline of the kidney region at this time may not be the same as that which would have been obtained at 2 min. This is particularly the case when there is significant hold up in a dilated pelvis. The appearance also may be confused by contribution from the contralateral kidney. Again, this will be more marked in kidneys with delayed transit. There is also difficulty in defining the posterior border, although this will be subject to less error when using a supine position as described by the authors than when using seated or semirecumbent positions. If a depth precision of ± 1 cm is achieved, the corresponding error in renal activity measurement is about 12.5%.

The combination of all these sources of error will almost certainly lead to a precision of greater than the 5%–7% achieved by blood sampling. Previous studies have shown a variety of precision, with the best results claiming SEE of approximately 11–13 mL/min (*1*), which corresponds to 18%–22%.

Although the use of absolute measurements of percentage uptake in renography and their relation to GFR is clinically useful, the method does not produce such precise values as blood sample measurements and should not be used as an alternative when an exact figure is required.

REFERENCES

1. Fleming JS, Keast CM, Waller DG, Ackery DM. Measurement of glomerular filtration rate with Tc-99m DTPA: a comparison of gamma camera methods. *Eur J Nucl Med.* 1987;13:250–253.
2. Steinmetz AP, Zwas ST, Macadziob S, Rotemberg G, Shrem Y. Renal depth estimates to improve the accuracy of glomerular filtration rate. *J Nucl Med.* 1998; 39:1822–1825.
3. Kampmann JP, Molholm Hanssen J. Glomerular filtration rate and creatinine clearance. *Br J Pharmacol.* 1981;12:7–14.
4. Campbell MJ, Machin D. *Medical Statistics: A Commonsense Approach.* Chichester, UK: John Wiley and Sons; 1990:121–122.