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Letter to the Editor

Urinary Excretion of Monoacetyl Polyamines in Patients with Non-Hodgkin's Lymphoma[1]

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ABSTRACT

The pretreatment concentrations of polyamines were determined in the 24-hr urine of 14 patients with widespread non-Hodgkin's lymphoma. In ten of 14 patients, the ratio of N^1-acetylspermidine to N^8-acetylspermidine was significantly higher than the mean for normal subjects. These results confirm our previous observations that the urinary excretion of N^1-acetylspermidine is increased in some patients with lymphoma and suggest that the determination of urinary acetyl polyamines may be useful in conjunction with other procedures in the diagnosis of lymphoma.

The ratio of N^1-acetylspermidine to N^8-acetylspermidine in the postchemotherapy 24-hr urine was 25 in one patient who had diffuse histiocytic lymphoma. This is the highest ratio ever reported. The patient responded well to chemotherapy, and rapid lysis of lymphoma lesion was observed. The potential utility of the rapid increase in the ratio of N^1-acetylspermidine to N^8-acetylspermidine as a criterion of tumor lysis is of interest and is currently under further investigation.

Recently, Seiler *et al.* (9) reported the results of some elegant studies on the urinary excretion of free and acetylated polyamines in hepatoma-bearing Buffalo rats during the period of linear growth of the tumor mass. Based on these results, as well as the results of previous studies on rats bearing mammary tumors and the data from only 2 melanoma patients (10), the authors concluded that the determination of the ratio of N^1-acetylspermidine to N^8-acetylspermidine in urine may be of only limited value as an indicator for the presence of tumors. However, the authors pointed out, and it should be emphasized again, that the results obtained with hepatoma-bearing rats may not be directly applicable to humans with cancer, since the profile of urinary polyamines in rodents is significantly different from that in humans. Furthermore, in humans, the urinary excretion of total polyamines and the ratio of the monoacetylspermidines may vary with the type of cancer.

The polyamines putrescine and spermidine are excreted in human urine in the form of the monoacetyl conjugates (3). The isomeric monoacetyl derivatives of spermidine, *i.e.*, N^1-acetylspermidine and N^8-acetylspermidine, are excreted in approximately equal amounts in the 24-hr urine of healthy volunteers. Examination of the urinary profiles of polyamines in a small sample of patients with cancer indicated that the amount of monoacetylputrescine and the ratio of N^1-acetylspermidine to N^8-acetylspermidine were elevated in these patients (4, 5). This suggested that the determination of urinary monoacetyl polyamines may provide a more precise marker for the presence of cancer than the total urinary polyamines.

We report results of some of our studies on the evaluation of the urinary polyamines as markers for non-Hodgkin's lymphoma and present sequential observations on one patient to discuss the potential utility of these measurements in monitoring response of the neoplastic disease to treatment.

We determined the pretreatment concentrations of polyamines in the 24-hr urine of 14 patients with widespread non-Hodgkin's lymphoma. The patients were admitted in the Medical Oncology Service of the Masonic Memorial Cancer Center of the University of Minnesota Hospitals to receive chemotherapy. Urine samples were collected in polyethylene bottles under toluene and kept refrigerated during collection. The volume of urine was measured, and aliquots were stored at −20° until analyses. The acetyl polyamines were determined, in duplicates, using high-pressure liquid chromatography of the dansyl derivatives according to a published procedure (1).

In 10 of 14 patients (Table 1), the ratio of N^1-acetylspermidine to N^8-acetylspermidine was significantly higher ($p < 0.01$) than the mean for normal subjects. These results confirm our previous observations that the urinary excretion of N^1-acetylspermidine is increased in some patients with lymphoma and suggest that the determination of urinary acetyl polyamines may be useful in conjunction with other procedures in the diagnosis of lymphoma.

The postchemotherapy urinary polyamines in one patient who had diffuse histiocytic lymphoma were determined (Table 2). Prechemotherapy 24-hr urine sample was obtained immediately after admission. Chemotherapy began on Day 12 of hospitalization and continued for 5 days. On Day 19, a 24-hr urine sample was obtained. The patient responded well to chemotherapy, and rapid lysis of lymphoma lesion was observed. However, he developed a coagulopathy; his serum phosphorus, blood urea nitrogen, and creatine increased; and his serum calcium decreased. The patient developed pneumonia and died from respiratory complications on Day 22. The ratio of N^1-acetylspermidine to N^8-acetylspermidine in the postchemotherapy 24-hr urine was 25 and is the highest ever reported. The highest ratio reported previously was 10 and was observed in the 24-hr urine from a patient with hepatoma obtained a few days before her death (5). The potential utility of the rapid increase in the ratio of N^1-acetylspermidine to N^8-acetylspermidine as a criterion of tumor lysis is of interest and is currently under further investigation. This will address the

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Table 1

Pretreatment concentrations of polyamines in the 24-hr urine of patients with non-Hodgkin's lymphoma

Patient	Polyamine concentration (μmol/24 hr)				
	AC-PUT[a]	N^1-AC-SPD	N^8-AC-SPD	Total[b]	Ratio[c]
R. B.	8.0	4.9	1.7	24.6	2.9
J. C.	17.4	9.1	1.7	28.2	5.4
W. C.	37.2	4.5	1.8	43.5	2.5
F. E.	4.6	1.1	0.9	6.6	1.3
E. F.	9.7	5.5	1.6	16.8	3.4
L. H.	7.2	1.7	1.5	10.4	1.1
B. J.	26.0	2.0	17.0	45.0	0.1
G. K.	15.2	5.6	2.1	22.9	2.7
N. L.	3.6	0.8	0.8	5.3	1.0
R. L.	16.4	6.3	3.1	25.8	2.0
E. L.	19.4	3.5	1.4	24.3	2.5
R. R.	4.7	0.9	0.7	6.3	1.8
M. T.	17.2	4.4	1.7	23.3	2.6
C. W.	22.0	5.2	2.5	29.7	2.1
	11.7 ± 1.5[d]	2.9 ± 0.6	2.8 ± 0.5	17.4	0.9

[a] AC-PUT, monoacetyl putrescine; N^1-AC-SPD, N^1-acetylspermidine; N^8-AC-SPD, N^8-acetylspermidine.
[b] Total represents the sum of the 3 monoacetyl derivatives.
[c] Ratio of N^1-acetylspermidine to N^8-acetylspermidine.
[d] Normal mean (± S.E.).

Table 2

Pretreatment and postchemotherapy concentrations of the monoacetyl polyamines in the 24-hr urine of a patient (J. C.) with diffuse histiocytic lymphoma

	Polyamine concentration (μmol/24 hr)				
	AC-PUT[a]	N^1-AC-SPD	N^8-AC-SPD	Total[b]	Ratio[c]
Pretreatment	17.4	9.1	1.7	28.2	5.4
Postchemotherapy	5.4	9.9	0.4	15.7	24.8

[a] AC-PUT, monoacetyl putrescine; N^1-AC-SPD, N^1-acetylspermidine; N^8-AC-SPD, N^8-acetylspermidine.
[b] Total represents the sum of the 3 monoacetyl derivatives.
[c] Ratio of N^1-acetylspermidine to N^8-acetylspermidine.

question of whether urinary acetyl polyamines may have potential utility as an early criterion of the response of the tumor to chemotherapy.

The observation that the urinary excretion of N^1-acetylspermidine is elevated in some patients with cancer is undoubtedly of great interest. However, the biochemical events which result in this increase are not well understood. Recently, a number of laboratories reported on the metabolism of the monoacetyl polyamines in animal tissue (2, 6–10). We (2) as well as others (6–10) have examined the changes in acetylpolyamine concentration in proliferating tissues after treatment with a variety of agents. The results of these studies indicate that, in rapidly proliferating tissues, the concentration of N^1-acetylspermidine increases significantly while the concentration of N^8-acetylspermidine is not significantly changed. Consequently, the ratio of N^1- to N^8-acetylspermidine in rapidly proliferating tissues is much greater than unity.

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