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Histopathologic Findings of Lung Cancer in Navajo Men: Relationship to U Mining†

(Received 8 July 1985; accepted 6 March 1986)

Introduction

THIS study reports the histopathologic findings in 26 cases of lung cancer occurring between 1969 and 1982 in Navajo men, 21 of whom had documented history of U mining. Eight cases were small-cell undifferentiated (SCUC) cancer, 10 were squamous, six adenocarcinoma, and two large cell. At least 13 of the 18 non-SCUC cases were far advanced at presentation. Only one patient currently survives. Of the 20 cases with smoking information available, 12 had smoked cigarettes but averaged less than five daily. Radon daughter exposure was quite variable among the known miners. The distribution of lung-cancer cell types was not different from that of lung cancer in the general population. Neither the predominance of SCUC seen in white U miners, many with a considerable smoking history, nor the predominance of adenocarcinoma reported for nonsmokers was seen in this small group of men. The average age of these men was much lower than that of lung cancer patients in the general population. We conclude that, if smoking is minimal, radon daughter exposure dose not result in a large excess of SCUC.

Lung cancer is an uncommon malignancy in American Indians of the Southwest (Sa80). While few studies have examined risk factors for lung cancer in this population, the available data indicate that cigarette smoking is uncommon (Si68; De79). In Navajo males, who are predominantly non-smokers, we have recently shown that the majority of lung cancer cases were attributable to U mining (Sa84). In other studies of U miners with higher smoking prevalence, small-cell lung cancer occurred in greatest excess, though the occurrence of all major cell types increased with the dose of radon daughters (Ar74; Ho77). Of the 32 cases of clinical lung cancer in Navajo males included in our recent

investigation, 23 occurred in U miners and 28 were pathologically confirmed. This report provides the histopathological findings for 26 of the 28 cases and examines the relationships among cell type, cigarette smoking, and U-mining experience.

Since 1969, the New Mexico Tumor Registry (NMTR), a member of the National Cancer Institute's Surveillance, Epidemiology and End Results Program, has recorded all incident cancer cases in the Navajo population of Arizona, New Mexico and Utah (Yo81). Thirty-two cases of non-carcinoid primary lung cancer among Navajo males were diagnosed between 1 January 1969, and 31 August 1982. Of these, 28 had been confirmed pathologically, two were diagnosed by chest radiograph, and two were classified on clinical grounds as reported on the death certificates. Diagnostic microscopic material and pathology reports were obtained in 26 of the 28 cases. In 23, the specimens were surgically obtained, either by biopsy or lung resection. Autopsy, bronchial washing or sputum cytology material was available for the remaining cases.

The manner in which epidemiologic information was obtained for these cases has been detailed previously (Sa84). Briefly, U.S. Public Health Service (PHS) records of Colorado Plateau miners, maintained since the 1950s, were the principal source of occupational and smoking data. Because all but one of these men have died, death certificates were another source of occupational information. In addition, NMTR abstracts provided relevant occupational information. The clinical stage at initial diagnosis was available for 17 non-small cell cases from NMTR records. Radon daughter cumulative exposures‡ were available from the PHS records for 13 miners. Smoking information was available for 20 of the cases.

The slides were reviewed by each of three pathologists (CB, WCB, CK) without knowledge of clinical or epidemiologic data. After this initial individual review, differences on histological classification were settled by consensus. The neoplasms were classified as small-cell undifferentiated carcinoma (SCUC), large-cell undifferentiated carcinoma (LCUC), squamous carcinoma, or adenocarcinoma. Criteria for diagnosis included conventional, predominantly nuclear, criteria for SCUC (Ma81), and are similar to those of the World

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‡ Radon daughter exposure is measured in working-level months (WLM), where one WLM represents exposure at one working level (WL) for a 170-h month. The WL is any combination of radon daughters in 1 L of air that ultimately releases 1.3×10^5 MeV of α energy during decay.

Health Organization, as discussed by Yesner (Ye81). Mucin stains were unavailable in most cases, so scanty mucin production may have gone unrecognized. Small admixtures of one cell type were found in a few neoplasms that were predominantly of another type. In no case was a small-cell carcinoma the lesser proportion of the neoplasm; therefore, all neoplasms containing small-cell carcinoma were diagnosed as such. If squamous or adenocarcinoma were dominant, the neoplasm was diagnosed as such. If large-cell carcinoma was admixed in any proportion, even a predominant one, with another cell type, the neoplasm was diagnosed as the other type.

The men ranged in age from 31 to 78 y at diagnosis; the median age was 50.5 and the mean 51.1. Of the 26 cases, 21 had documented U mining experience. Unfortunately, smoking histories were unavailable for the five non-miners and for one miner (see Table 1). However, the tobacco consumption of the 12 miners with a positive smoking history was low, averaging three to four cigarettes per day and not exceeding eight; this pattern of consumption is consistent with other reports concerning cigarette smoking among Navajos (Si68; De79).

There was sufficient information available to assess the clinical stage at initial diagnosis in 15 of the 18 cases which were not SCUC. (SCUC cases were ex-

cluded from staging consideration because it was assumed that they were disseminated on discovery.) Of the 15, two were Stage II and 13 were Stage III (ATS83).

Although the numbers were small, the cell-type distributions did not differ between miners and non-miners, or between the 12 smokers and the eight known nonsmokers among the miners (Table 2). Overall, there were 10 cases of squamous carcinoma; eight were in miners, two of whom were nonsmokers, and two were in non-miners. There were eight cases of SCUC; seven were in miners, three of whom were non-smokers, and one occurred in a non-miner. There were six cases of adenocarcinoma, four occurring in miners, two of whom were nonsmokers (another lacked an available smoking history); two cases occurred in non-miners. The two cases of LCUC occurred in miners, one of whom was a nonsmoker.

Radon daughter exposure, as measured in working level months (WLM), was available for 13 of the miners. Exposures varied from 103 to 2698 lifetime WLM, and averaging 1334 WLM. We found no relationship between cell type and exposure in this small group of miners.

Conclusions

Interpretation of this study's results must be constrained by the small number of cases, the limitations

Table 1. Distribution of histological type in 26 Navajo men

	NO. CASES	SQUAMOUS	SCUC	ADENO	LCUC
Uranium Miners					
Smoking	12	6	4	1	1
Non-smoking	8	2	3	2	1
All miners	21*	8	7	4*	2
Non-miners	5	2	1	2	0
ALL SUBJECTS	26	10	8	6	2

*Smoking status unavailable for one miner.

Abbreviations: SCUC - Small-cell undifferentiated carcinoma
Adeno - Adenocarcinoma
LCUC - Large-cell, undifferentiated carcinoma

Table 2. Characteristics of study subjects. WLM = working level month

URANIUM MINERS	AGE	TUMOR CELL TYPE	WLM	SMOKING HISTORY
1	31	LCUC	103	none
2	33	LCUC	1450	variable, 3-6/day
3	39	SCUC	1280	variable, 3-4/day
4	39	Squamous	1474	none
5	40	Squamous	1143	variable, 3/day
6	42	SCUC	1510	none
7	42	SCUC	N/A	2/day
8	43	SCUC	1215	none
9	43	Adeno	N/A	none
10	44	SCUC	830	2-3/day
11	44	Squamous	N/A	1-2/day
12	50	Adeno	1113	none
13	53	Adeno	N/A	1-2/day
14	54	SCUC	N/A	none
15	56	Squamous	N/A	1/day
16	60	SCUC	1207	"light to moderate"
17	62	Squamous	1985	3-6/day
18	62	Squamous	2698	2-3/day
19	64	Squamous	1548	none
20	71	Squamous	N/A	4/day
21	78	Adeno	N/A	N/A
<u>NON-MINERS</u>				
22	44	Adeno		N/A
23	51	SCUC		N/A
24	58	Adeno		N/A
25	59	Squamous		N/A
26	68	Squamous		N/A

Abbreviations: LCUC - Large-cell undifferentiated carcinoma;
 SCUC - Small-cell undifferentiated carcinoma;
 Adeno - Adenocarcinoma
 WLM - Working level months of exposure;
 N/A - Not available;
 Smoking history in numbers of cigarettes

of classification of lung cancer cell type by light microscopy, and potential errors in the exposure information. While we examined only 21 cases in miners, this study is population-based and provides information on those who never smoked and those who smoked only occasionally. Information on cigarette smoking and radon daughter exposure was obtained from several different sources. For some men, the smoking histories were conflicting and for others the WLM estimates appear to have been based on incomplete work histories (Sa84). However, the classification of subjects as miners or nonminers is not suspect; the miners were labelled as smokers if they gave a positive history on one or more occasions.

We believe we have largely avoided the well-documented problems (Ye73; St81) with light microscopic classification of pulmonary carcinomas, which relate in part to the capacity for variable differentiation inherent in these neoplasms (Mc78). Consensus without dissent was reached in all cases by three pathologists. Only two cases were diagnosed as LCUC, which is potentially a "wastebasket" diagnosis in the absence of mucin stains and immunohistochemistry. Most of the material was of surgical rather than autopsy origin, so that improved fixation aided in accurate diagnosis.

Our finding that all cell types were present in a distribution similar to that in the general lung cancer population (Ca80) is at some variance with related

studies. In another report of 16 Navajo miners with lung cancer, 10 had SCUC, but apparently panel review of diagnoses was not used (Go82). In white U miners from the Colorado Plateau, who had much greater cigarette consumption, SCUC occurred with greatest excess of any cell type at all levels of radon daughter exposure (Ar74). However, one should note that the incidence of SCUC in men in the general population increases with increasing cigarette consumption, at least through the seventh decade (Au75). In contrast, adenocarcinoma is generally the predominant cell type in non-smokers (Ka84), and SCUC is very infrequent among them, less than 5% of cases (St83). In the present study, SCUC was not the most common cell type, but it was more common than anticipated from the data on non-smokers. The distribution of histopathology in the Navajo miners suggests that heavy cigarette smoking in combination with radon daughter exposure leads to the predominance of SCUC demonstrated in U miners. Radon daughter exposure in light or non-smokers may increase the occurrence of SCUC, but not to the extent observed in heavy smokers.

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