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Metachronous and Synchronous Presentation of Acute Myeloid Leukemia and Lung Cancer

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Abstract

Smoking is associated with both acute myeloid leukemia (AML) and lung cancer. We therefore searched our database for concomitant presentation of AML and lung cancer. Among 775 AML cases and 5225 lung cancer cases presenting to Roswell Park Cancer Institute between the years January 1992 and May 2008 we found 12 (1.5% of AML cases; 0.23% of lung cancer cases) cases (seven metachronous and five synchronous) with AML and lung cancer. All but one patient were smokers. There were no unique characteristic of either AML or lung cancer in these patients. Nine patients succumbed to AML, one died from an unrelated cause while undergoing treatment for AML, one died of lung cancer and one patient is alive after allogeneic transplantation for AML. In summary, this study supports the need for effective smoking cessation programs.

Keywords

Acute myeloid leukemia; lung cancer; smoking

Introduction

Smoking is associated with both acute myeloid leukemia (AML) and lung cancer. Case-control and cohort studies [1–3] revealed that smoking was associated with an increased risk for AML, and the risk correlated with amount and duration of smoking. In two studies [1,3] smoking was associated with increased risk for AML with maturation and in several studies [1,4–7] smoking

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Contributions: Dr. Varadarajan collected the data and wrote the manuscript; Mrs. Ford constructed the database; Drs. Sait and Block performed the cytogenetic analyses; Dr. Barcos oversaw the pathological diagnoses; Dr. Wallace oversaw the flow cytometry analyses; Drs. Ramnath and Wang contributed patients and Dr. Wetzler contributed patients, oversaw data collection and contributed to the manuscript preparation.

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was more common among patients with specific chromosome abnormalities (e.g., -7 or $7q-$, $+8$, $t(8;21)$, $+13$, $-Y$). Therefore, in 2004, the Surgeon General of the United States [8] and the International Agency on Research in Cancer of the World Health Organization concluded that cigarette smoking caused AML. Similarly, smoking is clearly associated with lung cancer [9]. Although tobacco smoking induces all histological types of lung cancer, the strongest associations are with squamous cell and small cell carcinoma; the risk ratio for adenocarcinoma is four-to-fivefold lower than for the other histological types [10]. In this case series we examined whether patients with the diagnoses of both AML and lung cancer possessed common disease and/or clinical characteristics and what the overall outcomes were.

Patients and Methods

The Roswell Park Cancer Institute (RPCI) Tumor Registry was searched for patients with the diagnosis of both AML and lung cancer. The medical records of these patients were reviewed and clinical data and outcome were collected. This analysis was approved by RPCI's Scientific Review Committee and the Institutional Review Board.

Results

Among 775 AML cases and 5225 lung cancer cases presented to RPCI between January 1992 and May 2008 we identified five male and seven female patients with both AML and lung cancer (1.5% of AML cases; 0.2% of lung cancer cases). Of these twelve patients, seven patients presented with AML and lung cancer at different time points (metachronous group) and five patients presented concomitantly (synchronous group). Eleven of the twelve (92%) patients ever smoked as compared to 434 of 775 (56%) AML patients at RPCI. The median age at the respective diagnoses was 65 (range 58–85) years for AML and 66 (range 53–79) years for lung cancer.

Metachronous group

Lung cancer preceded AML in six patients by a median interval of eight (range five–14) years, while AML preceded the diagnosis of lung cancer in one patient by three years. The disease characteristics of patients who had metachronous lung cancer and AML are shown in Table 1A and 1B. Table 1C shows their treatment and outcome. Of the five people who were treated for AML, two achieved complete remission, two had primary refractory disease and one patient died during induction. The median survival for lung cancer was 65 (range 22–120) months. The median survival since AML diagnosis was less than one (range <1–105) month.

Synchronous group

The disease characteristics of the five patients who presented with synchronous diagnoses are shown in Table 2A and 2B. Their treatment and outcome are summarized in Table 2C. All five patients were treated initially for AML. Of these, two achieved complete remission, two had refractory disease and one patient had prolonged cytopenia. The median survival was five (range three–21) months.

Discussion

We describe the first series of metachronous and synchronous AML and lung cancer. The synchronous presentation of AML and lung cancer is somewhat surprising. The lungs are known to receive a high concentration of tobacco by inhalation while the bone marrow is exposed to smoke-containing mutagens present in the blood and body fluids [14]. Thus, tobacco's genotoxic effect would be expected to be lower on bone marrow cells as compared to the lung parenchyma explaining a longer latency for AML development as compared to lung

cancer in our patients. However, other toxins [15,16] and polymorphism related to detoxifying enzymes [4] may have contributed to the earlier development of AML and thus the synchronous presentation of both malignancies in some individuals.

Four of the patients with metachronous presentation examined here underwent chemotherapy and/or radiation treatment for lung cancer prior to development of AML. Prior chemoradiation for non small cell lung cancer has been shown to represent a known risk factor for secondary AML [17]. However, the lack of prior therapy in two of our patients with AML following lung cancer suggests that this factor alone does not account for the development of AML in all the patients. This suggests a potential role of prior tobacco use as a common carcinogenic risk factor.

Further, three patients in the metachronous group had preceding myelodysplastic syndrome (MDS). Lung cancer preceded MDS and AML in two of these three patients though these two patients underwent only surgical intervention for their lung cancer without exposure to chemotherapy or radiation. This suggests that smoking with or without additional genetic events may underlie both malignancies in these patients. These findings are consistent with studies showing alteration of tumor suppressor genes in chromosome 11 both in solid tumors and hematologic malignancies [11–13].

To date we could not find any literature on the management of patients with concurrent AML and lung cancer. However, instead of expecting larger series with these two malignancies, we hope that this report will highlight the need for enforcing smoking cessation.

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Table 1

Table 1A. Metachronous AML disease characteristics						
Patient No.	Age at diagnosis	WBC count ^d at diagnosis	Hgb ^b at diagnosis	Plt count ^d at diagnosis	Immunophenotype	Karyotype
1	77	264	12.1	95	CD13+, 14+, 33+, 34+, 56+, 64+, CD34-	Normal
2	71	0.6	9.8	56	CD13+, 33+, 34+, CD14-, 56-, 64-	Normal
3	59	81.1	11.4	111	CD13+, 4(p)+, 33+, CD34-, 56-	Normal
4	85	3.74	6.4	28	CD13+, 33+, 34(p)+, 64(p)+; CD14-, 56-	Complex
5	81	8.52	10.3	14	CD13(p)+, 33+, 34(p)+; CD14-, 54-, 56-	Complex
6	64	17.7	8.5	20	CD13+, 14(p)+, 33+, 34(p)+, 64(p)+; CD56 -	Complex
7 ^c	58	2.68	9.7	487	CD13+, 34+; CD14-, 33-, 56-, 64-	Normal

Table 1B. Metachronous lung cancer characteristics

Patient	Age at diagnosis	Ever smokers (packs/year) ^e	Staging	Type
1	74	+ (50)	I	NA
2	68 & 71 ^d	+ (NA)	I, I	Adenocarcinoma
3	53	+ (NA)	III	Adenocarcinoma
4	79	+ (NA)	IIB	Squamous
5	71	-	NA	NA
6	56	+ (40)	III	Small cell
7 ^c	61	+ (NA)	IB	Adenocarcinoma

Table 1C. Metachronous AML and lung cancer treatment and outcome

Patient No.	AML treatment	Lung cancer treatment	Lung cancer survival ^e	AML survival ^e	Cause of death	Notes
1	7 + 3 ^f	RL Lobectomy	37	<1	AML	2 nd AML d/t MDS
2	7 + 3 + 3 ^g and PSC-833 ^h	LU & RU Lobectomy	60 & 22	12	AML	2 nd AML d/t MDS for 2 years; AML relapse 1 year after remission

Table 1C. Metachronous AML and lung cancer treatment and outcome

Patient No.	AML treatment	Lung cancer treatment	Lung cancer survival ^e	AML survival ^e	Cause of death	Notes
3	HiDAC/Ida ⁱ	Definitive Chemoradiation; Brain mets 2 years later- RT with no recurrence	64	2	SVC rupture	Death due to complication from line placement
4	7 + 3 + 3 ^g	RU Lobectomy followed by RT	72	<1	AML	Primary refractory AML
5	None	LU Lobectomy followed by Chemotherapy	120	<1	AML	No Rx for AML due to comorbidities
6	None	Chemoradiation	96	<1	AML	No Rx for AML due to comorbidities
7 ^c	7 + 3 + 3 ^g	RU Lobectomy; Brain mets 2 years after- Rx with surgery+RT- Chest wall recurrence Rx with RT with no recurrence	66	105	Alive	2 nd AML from MDS; Primary refractory AML, followed by 6/6 sibling matched allotransplant with a complete remission

^a × 10⁹/L

^b g/dL

^c AML preceding lung cancer

Abbreviations: Hgb, hemoglobin; NA, not available; neg, negative; No, number; p, partial; Plt, platelet; pos, positive; WBC, white blood cell

^d Two primary lung tumors

^e Patients quit smoking after or just before the lung cancer diagnosis (Pt 7 resumed smoking after AML diagnosis and quit only after lung cancer diagnosis)

Abbreviations: NA, not available;

^e in months

^f Cytarabine 100 mg/m² continuous infusion over 7 days, daunorubicin 60 mg/m² daily for 3 days

^g Cytarabine 100 mg/m² continuous infusion over 7 days, daunorubicin 60 mg/m² daily for 3 days, etoposide 100 mg/m² daily for 3 days

^h PSC-833, an MDR modulator as part of CALGB 9720

ⁱ Cytarabine 1.5 g/m² every 12 hours for a total of 12 doses and idarubicin 12 mg/m² daily for 3 consecutive days

Abbreviations: AML, acute myeloid leukemia; d/t, due to; LU, left upper; plt, platelet; MDR, multi drug resistance; RL, right lower; RU, right upper; Rx, treatment; RT, Radiotherapy; mets, metastasis

Table 2

Table 2A. Synchronous AML disease characteristics						
Patient No.	Age at diagnosis	WBC count ^d at diagnosis	Hgb ^b at diagnosis	Plt count ^d at diagnosis	Immuno phenotype	Karyotype
1	66	2.6	7.5	25	CD13+, 33+, 34+, CD14-, 56-	Complex
2	72	3.07	10.3	15	CD13+, 33+, 34+, CD14-, 56-	No growth
3	59	96.2	9.5	75	CD13(p)+, 14+, 33+, CD34-	Normal
4	60	17.5	NA	NA	NA	del(5q)
5	64	7.8	6.1	16	CD13(p)+, 33+, 34(p)+, CD14-, 54-, 56-	Normal

Table 2B. Synchronous lung cancer characteristics			
Patient	Age at diagnosis	Ever smokers (packs/year)	Type
1	66	+ (100)	IIIB Squamous
2	72	+ (NA)	IA Adenocarcinoma
3	59	+ (NA)	IA Adenocarcinoma
4	60	+ (NA)	IB and II ^c Adenosquamous
5	64	+ (150)	IV Squamous

Table 2C. Synchronous AML and lung cancer treatment and outcome				
Patient No.	AML treatment	Lung cancer treatment	Survival ^d	Notes
1	7 + 3 ^e	Palliative radiation	4	Delayed count recovery after induction and discharged to hospice
2	HIDAC/Ida ^f	None	3	Disseminated aspergillosis after induction
3	HIDAC/Ida	VATS-wedge resection	6	6/6 related donor BMT-relapsed on D +50; Death due to Clostridium difficile colitis
4	HIDAC/Ida	RU & LU Lobectomy; Recurrence 1 year later	21	Primary refractory; Re-induction, consolidation then autotransplant-Remission with no recurrence

Table 2C. Synchronous AML and lung cancer treatment and outcome

Patient No.	AML treatment	Lung cancer treatment	Survival ^d	Cause of death	Notes
5	7 + 3	None	5	AML	Low platelet count

^a × 10⁹/L
^b g/dL
Abbreviations: Hgb, hemoglobin; NA, not available; Neg, negative; No, number; p, partial; Plt, platelet; Pos, positive; WBC, white blood cell
Abbreviations: NA, not available;
^c Right upper lobe and left upper lobe, respectively
^d in months
^e Cytarabine 100 mg/m² continuous infusion over 7 days, daunorubicin 60 mg/m² daily for 3 days
^f Cytarabine 1.5 g/m² every 12 hours for a total of 12 doses and idarubicin 12 mg/m² daily for 3 consecutive days
Abbreviations: AML, acute myeloid leukemia; LU, left upper; RU, right upper; VATS, video-assisted thoracoscopic surgery