

Emergency Cranial Irradiation Effects in Adult Leukemia with Extremely High Leukocytosis

Seoung-Ho Park, M.D., Moon-June Cho, M.D. and Samyong Kim, M.D.*

Department of Radiology, Department of Internal Medicine, College of Medicine
Cancer Research Institute, Chungnam National University, Daejeon, Korea*

We have treated adult acute leukemia 64 patients between January 1990 and October 1991 at the Chungnam National University Hospital. They were examined for the impact of presenting WBC count on the initial course and from them we have chosen twenty patients whose leukocyte count is over one hundred thousands per cubic millimeter. We divided the twenty patients into 4 groups on the base of treatment modalities: conservative therapy only, chemotherapy only, cranial irradiation only, and chemotherapy with cranial irradiation.

Early sudden death rate is lower in cranial irradiation with/without chemotherapy groups than the conservative only or chemotherapy only patients. Also the remission rate is high in cranial irradiation with chemotherapy patients. Therefore we suggest that the rapid intervention of cranial irradiation in adult acute leukemia could be helpful in reducing the early sudden death rate and perhaps in increasing the remission rate.

Key Words: Emergency cranial irradiation, Adult leukemia, Extremely high leukocytosis

INTRODUCTION

About 75% of new acute leukemia cases are adults. Generally, extremely high leukocytosis at the time of diagnosis of acute leukemia is to have a poor prognosis, in part because of a high frequency of early death associated with it. This is often due to fatal intracranial hemorrhage secondary to intravascular leukocytosis, that is plugging of small blood vessel by immature leukocytes, with subsequent vessel rupture and hemorrhage^{1,2)}.

Rapid intervention with radiotherapy combined with chemotherapy had been said to be effective in decreasing the incidence of early sudden death due to CNS hemorrhage³⁻⁵⁾. The main purpose of this report is to analyze the effects on the early sudden death rate and remission rate when the emergency cranial irradiation with/without chemotherapy was applied to the patients who had acute leukemia with extremely high leukocyte count at initial diagnosis⁶⁾.

MATERIALS AND METHODS

From January 1990 to October 1991, 64 patients were admitted to department of Internal Medicine,

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Chungnam National University Hospital, with acute leukemia. Of these 64 patients, 20 patients were chosen. These twenty patients had high leukocyte count over 100,000/mm³ -we refer the above count as "extremely high leukocytosis"^{2,4)}. These twenty patients were divided into 4 groups based on the therapeutic modalities; 5 patients had only conservative management without any intensive methods; 3 patients had only chemotherapy; 5 patients had only radiotherapy; 7 patients had radiotherapy with chemotherapy. We compared these 4 groups with each other in their treatment response and early sudden death rate and evaluated the clinical features and laboratory findings⁷⁾. The 12 patients of radiotherapy group received emergency cranial irradiation with 6 MV Linac, daily with dose from 150 to 200 cGy for 2 or 3 times, total 300 to 600 cGy. In addition to the above therapies, we had applied hydroxyurea and leukapheresis to the patient^{1,2,8)} (Table 1).

RESULTS

From January 1990 to October 1991, we observed 64 patients who were diagnosed with acute leukemia. Of these 64 patients, 20 patients (31.2%) had extremely high leukocyte count over 100,000/mm³. Age ranged from 15 to 64 years of age. Male to female ratio was 3 to 2 and 12 patients (60%) were under age of 30 years (Table 2).

Table 1. Leukapheresis and Hydroxyurea Cases as a Supportive Therapy

	Group A (5)	Group B (3)	Group C (5)	Group D (7)	Total (20)
Leukapheresis	3	3	4	7	17
Hydroxyurea	3	—	4	2	9

Note: Group A represents the patients who has no definitive treatment. Group B—chemotherapy only. Group C—radiotherapy only. Group D—radiotherapy with chemotherapy

Table 2. Clinical and Laboratory Findings of 20 Adult Leukemia with Extremely High Leukocytosis Patients

Distribution	No. of patients (%)	Symptoms	No. of patients (%)
Sex			
Male	12 (60)	fever & cough	20 (100)
Female	8 (40)	respiratory distress	6 (30)
Age (years)		headache	12 (60)
15~30	12 (60)	bone pain	5 (25)
~45	3 (15)	abdominal pain	11 (55)
~60	1 (5)	petechia	15 (75)
>60	4 (20)		
WBC ($\times 10^4$)		Blast (7~99%)	
10~25	12 (60)	7~64	4 (20)
~40	5 (25)	~94	8 (40)
~60	—	~99	8 (40)
>60	3 (15)		

From first symptom to diagnosis, duration was from 2 to 80 days and average duration was 25 days. All 20 patients complained fever and cough like coryza symptoms. Among them, 9 patients presented with splenomegaly and 7 out of these patients had associated hepatomegaly.

Initial leukocyte counts ranged from 100,500/mm³ to 950,000/mm³. Peripheral blood was nearly all replaced by blast cells in 16 patients (80%). Hemoglobin level ranged from 4.07 to 14.3 g/dl and one case had severe anemia, whose hemoglobin level was below 5.0 g/dl. Thrombocytopenia was not prominent. The thrombocyte count ranged from 22,000 to 508,000/mm³ (Table 2).

Of 5 patients who had no intensive therapy, 3 patients expired with intracranial hemorrhage within 15 days, and 1 patient was discharged hopelessly, and the last 1 patient was transferred to other

Table 3. Early Sudden Death and Remission Rate on Each Treatment Modality

Total case	Group A	Group B	Group C	Group D
Total case	5	3	5	7
Case of early sudden death	3	0	1	0
Case of remission	—	2	—	7

Note: Group A represents the patients who has no definitive treatment. Group B—chemotherapy only. Group C—radiotherapy only. Group D—radiotherapy with chemotherapy

hospital and suddenly expired in the course of following up. Among 3 patients who managed only with antileukemic agents, 2 patients achieved complete remission, but recurred in the course of following up. Of these 2 patients, one was discharged in the hopeless state and the other discharged because of economic causes. The rest 1 patient remained with no remission state and expired with intracranial hemorrhage after 7 months.

Among 5 patients who had received emergency cranial irradiation without chemotherapy, 1 patient died of intracranial hemorrhage at the next day of irradiation. 1 patient had discharged 2 days after irradiation in the aggravated state. 1 patient transferred himself to other hospital. 1 patient discharged at fifteenth day in the aggravated state. The last 1 patient expired with sepsis at the 45th day after irradiation.

The rest 7 patients who received radiotherapy combined with chemotherapy have achieved complete remission. Among them, 1 patient remained no evidence of disease state. 1 patient achieved complete remission but lost to follow up. Five patients recurred. Among them, 2 patients were managed with antileukemic agent and expired; one died of intracranial hemorrhage at 6 months after complete remission and the other died of sepsis in medical care refusing state. The rest patients were discharged hopelessly.

DISCUSSION

The extremely high WBC count at the time of diagnosis of acute leukemia is a poor prognostic factor^{2,4,5,9}. That is due to fatal intracranial hemorrhage secondary to plugging of small blood vessel by immature leukocyte with subsequent vessel rupture and hemorrhage. In addition, alveolar-

capillary oxygen exchange may be obstructed by leukemic infiltration of the lung, which may result in respiratory decompression¹⁰). Within 2 weeks of treatment, early sudden death rate was high because of these fatal complications. Therefore the initiation of definitive treatment including aggressive intervention with cranial irradiation and/or leukapheresis and/or hydroxyurea is highly recommended in the early state. Leukapheresis reduces the blood viscosity by rapid eradication of peripheral lymphoblast. Lowenthal et al reported a good result by using leukapheresis in chronic myelocytic leukemia patients⁸). And Hoagland et al reported good result with leukapheresis in adult acute leukemia²). But this method is not effective in extremely high leukocyte count and cannot prevent or alter the lymphoblastic leukocytosis at intracranial blood vessel.

Hydroxyurea was known as an effective treatment modality in case of stable metabolic state. Its effect is correction of metabolic disorder such as hypocalcemia or uremia. In acute leukemia, the fact that administering hydroxyurea after prednisolone is effective in decreasing the blast has already reported, however it is not accepted as a general treatment modality²).

As a result, cranial irradiation rapidly but transiently kill the blasts in the vessel, and hydroxyurea and additional chemotherapy rapidly reduce the peripheral blast to prevent reaccumulation in the vasculature of the brain⁵). Wiernik et al in 1975 reported a good result of early prophylactic cranial irradiation, when applied to acute leukemia patients who had leukocytes over 150,000/mm³ at the time of diagnosis^{3,11}). They recommend all leukemia patients who has blast crisis over 100,000/mm³ leukocyte count to receive the early prophylactic cranial irradiation.

Dearth et al reported the good results by performing prophylactic cranial irradiation to the acute lymphocytic leukemia patients who had high leukocytosis over 100,000/mm³ 1,3,12). Choi et al in 1982 reported prophylactic cranial irradiation is more effective than early antileukemic agents in preventing early sudden death of acute lymphocytic leukemia patients who has extremely high leukocyte count⁴). Janice P et al in 1987 reported cranial irradiation with chemotherapy is effective in reducing the risk of the CNS hemorrhage who has extremely high leukocytosis over the 100,000/mm³ 5).

The results of this report for adult leukemia suggest that the prophylactic cranial irradiation

should be immediately performed at the time of diagnosis and could consider the leukapheresis and hydroxyurea. It is said that chemotherapy alone cannot help in reducing intracranial hemorrhage at the early time of disease¹¹). Therefore we applied the emergency cranial irradiation to 12 out of 20 patients who had extremely high leukocyte counts over the 100,000/mm³ and we had good results that only one patients had early sudden death. 9 out of 20 patients had achieved complete remission. The 7 patients who had cranial irradiation with chemotherapy have all achieved complete remission. 2 out of 3 patients who had chemotherapy only achieved complete remission. Although the number of cases was not sufficient, we could suggest that cranial irradiation have an effect on the improvement remission rate (Table 3).

CONCLUSION

This study had analyzed the effects on the early sudden death and remission rate when the emergency cranial irradiation is applied to adult leukemia patient who has extremely high leukocyte count at the time of diagnosis, daily with dose from 150 to 200 cGy for 2 or 3 times, total 300 to 600 cGy.

Of the 8 patients who had no definitive treatment or had chemotherapy only, 3 patients (37.5%) suffered early sudden death. But among the 12 patients of the radiotherapy only or radiotherapy with chemotherapy, only 1 patient (8.3%) suffered early sudden death. And 2 out of 3 patients who had chemotherapy only achieved complete remission. But the 7 patients who had cranial irradiation with chemotherapy have all achieved complete remission. Therefore we suggest that the radiotherapy could be effective in reducing the early sudden death rate and in increasing the remission rate.

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국문초록 =

극심한 백혈구 증다증이 동반된 성인 백혈병에 있어서 응급 두개부 방사선 조사의 효과

충남대학교 의과대학 방사선과학교실, 내과학교실* 및 암 공동연구소

박 승 호 · 조 문 준 · 김 삼 용*

성인의 급성 백혈병 환자 64예를 1990년 1월부터 1991년 10월 사이에 충남대학교 병원에서 치료하였다. 극심한 백혈구 증다증이 동반된 20예를 선별하여 네가지 각기 다른 방법으로 치료하였으며 이 치료양상에 따른 급성 사망율과 완해율에 관하여 조사하여 보았다. 응급 두개부 방사선 조사 단독 또는 항암제 약물요법을 병행한 경우에 있어서 단지 보조적 요법만을 시행한 경우나 항암제 약물요법만을 시행한 경우에 비하여 초기 급성 사망율이 낮았다. 또 완해율에 있어서도 응급 두개부 방사선 조사 및 항암제 약물요법을 병행한 경우에 높았다. 따라서 우리는 성인의 급성 백혈병에서 극심한 백혈구 증다증이 동반된 경우 조기 두개부 방사선 조사가 초기 급성 사망율을 낮추고 후에 완해율을 높이는 데에도 효과가 있을 것이라고 추정해보았다.