

원발성 중추신경계 림프종의 치료전략

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= Abstract =

Treatment Strategies for Primary Central Nervous System Lymphoma

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Objective : We have currently changed treatment strategies to methotrexate(MTX) - based preirradiation chemotherapy with subsequent planned radiation for the initial therapy of primary central nervous system lymphoma (PCNSL). The aim of this study was to evaluate the results of treating PCNSL with chemotherapy plus radiotherapy (CRT) or radiotherapy(RT) alone.

Method and Material : This study involved 10 females and 3 males patients with a mean age of 54.2 years. All patients underwent surgery, open(8 cases) or stereotactic biopsy(5 cases) for histological diagnosis. Eleven tumors were diffuse large B - cell lymphomas. Tumor volume change in the follow - up images and survival time were evaluated in patients treated with CRT and RT alone.

In the beginning, two patients received ProMACE - Cytabom chemotherapeutic regimen, but did not complete the course and died of progressive tumor 8 and 9 months after diagnosis, respectively. One patient died at 6 months before chemotherapy. These three were excluded from the survival analysis. Five patients(RT group) completed full courses of cranial irradiation with or without boost. For the current combined modality treatment, high - dose MTX - based chemotherapy(systemic and intrathecal MTX, IV vincristine, and oral procarbazine) followed by whole brain irradiation to 45Gy to tumor was introduced in 5 patients of CRT group.

Result : A complete response was achieved in three of five who received RT only and in all of five who received CRT. All patients in CRT groups are in disease free status at a mean 23 months following therapy. The RT group patients refused any additional salvage therapy at tumor relapse and survived at mean 20 months from diagnosis. The Karnofsky performance status improved in eight of ten patients with treatment. The treatment toxicity included leukoencephalopathy in RT group and severe leukopenia, transient hepatitis, avascular necrosis of femoral head, hearing loss, and amenorrhea in CRT group, respectively.

Conclusion : The combined modality therapy of MTX - based chemotherapy plus radiotherapy for PCNSL may enhance tumor response and improve patient survival. The patients who received CRT should be carefully followed up because of the higher risk of treatment - induced late neurotoxicity.

KEY WORDS : Primary central nervous system lymphoma · Cranial irradiation · Chemotherapy · Methotrexate · Survival.

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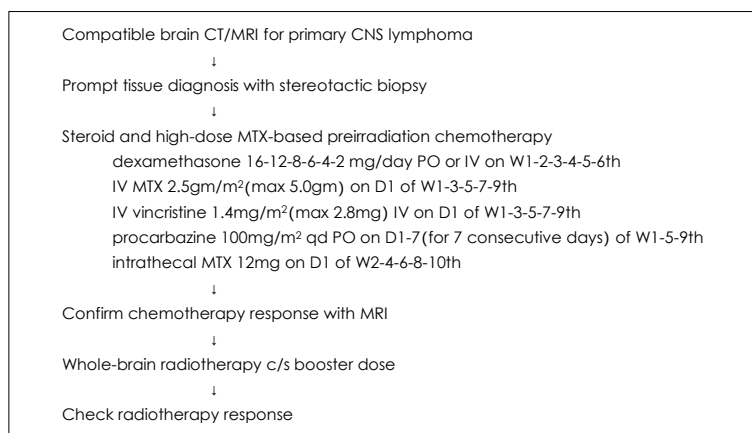
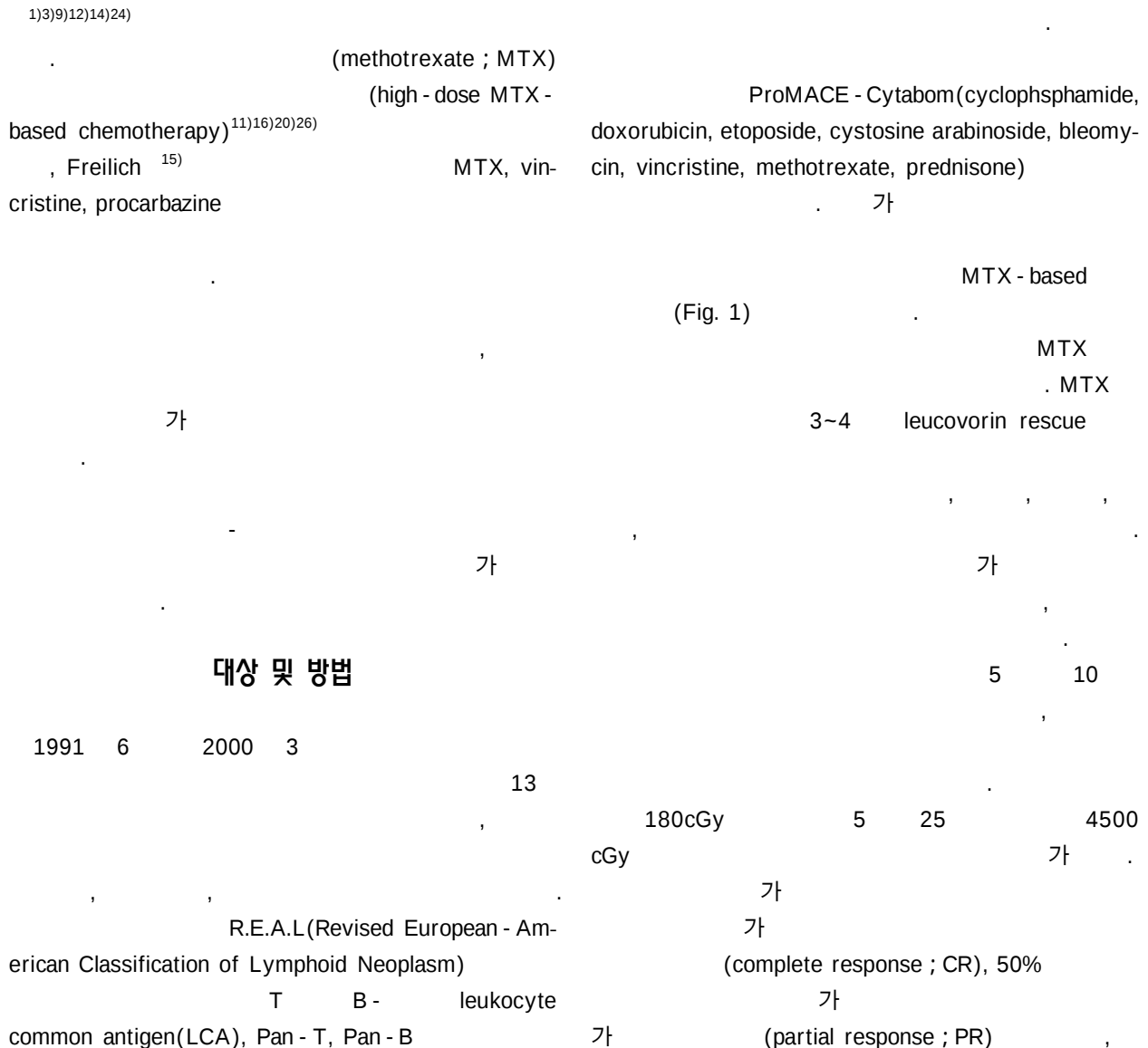


Fig. 1. Outline of treatment protocol for primary central nervous system lymphoma.

*Abbreviations : MTX ; methotrexate, D1 ; the first day of each week of chemotherapy schedule, W1 ; the first week, c/s ; with or without

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Table 1. Pretreatment of characteristics of 13 patients with primary CNS lymphoma

Characteristic	No. of cases
Age	Mean 54.2 years(22 - 72)
Sex	Male : female 3 : 10
Duration of symptoms	Mean 3.1 months(1 - 10)
Initial KPS score	Median 70(range 60 - 90)
Tumor multiplicity	
Solitary/multiple	8/5
Lesion location(N=24)	
Supratentorial/infratentorial/spine	20/3/1
Immunohistopathology	
B cell/unclassified	12/1
Diffuse large cell/diffuse small cell	11/2
CSF cytology	
Positive/negative/undocumented	1/7/5

*Abbreviations : CNS=central nervous system
 KPS=Karnofsky Performance Scale
 CSF=cerebrospinal fluid

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Table 2. Comparison of treatment results between radiation (RT) alone group and chemotherapy plus radiotherapy(CRT) group

Factor	RT group(N=5)	CRT group(N=5)
Tumor response		
Complete	3	5
Partial	2	
Toxicity	Leukoencephalopathy (N=1)	Leukopenia, hepatitis, deafness femur head AVN, ammenorrhea(N=5)
Changes of KPS		
Improved	4	4
Stationary	1	1
Current status	All died at mean 20 M	All alive, disease free at mean 23 M F/U
Dx. procedures		
Resection	4	
Biopsy	1	5

*Abbreviations : AVN=avascular necrosis
 KPS=Karnofsky Performance Scale
 M=month ; F/U=follow-up ; Dx=diagnosis

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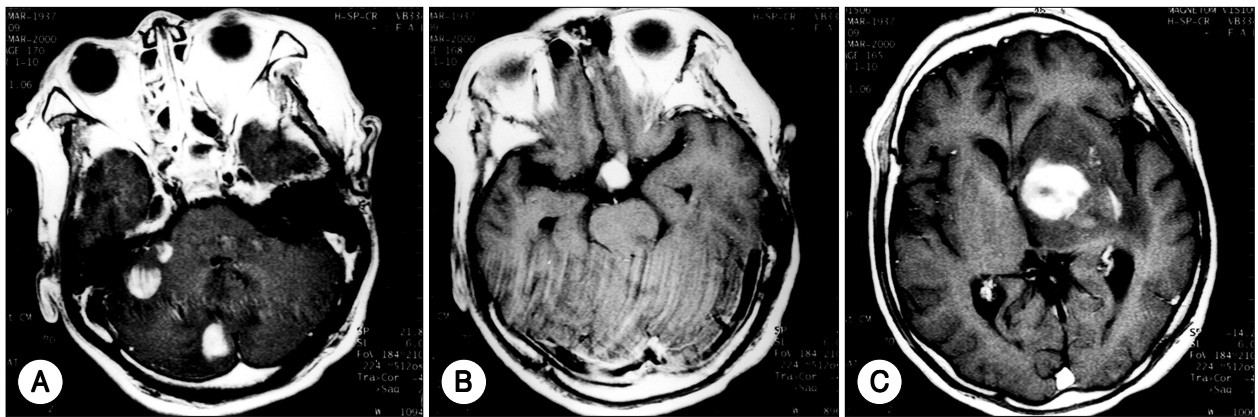


Fig. 2. A 62-year-old immunocompetent man with primary central nervous system lymphoma in the basal ganglia, suprasellar, and cerebellum. Gadolinium-enhanced transaxial T1-weighted images obtained before stereotactic biopsy showing homogenous strong enhancing multiple lesions with minimal mass effect.

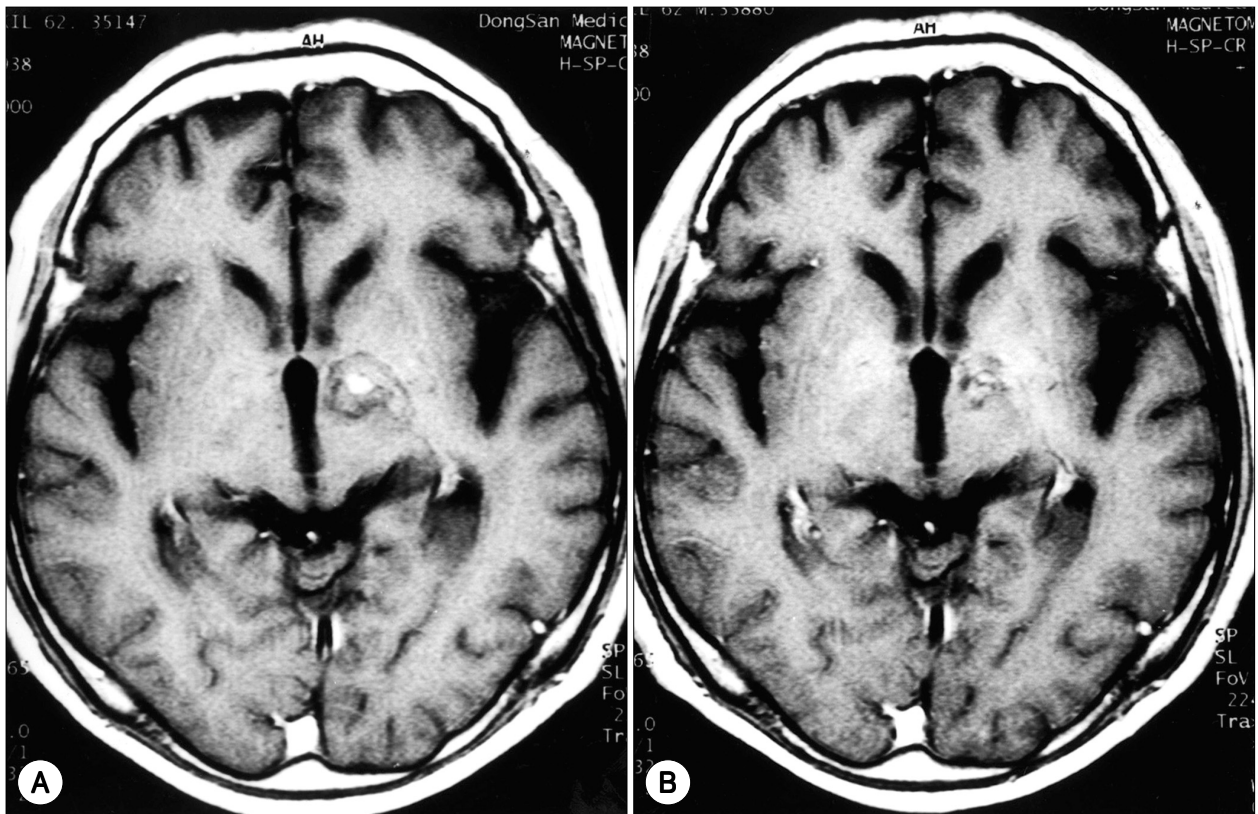


Fig. 3. Follow-up enhancing MR image after preirradiation methotrexate-based chemotherapy showed minimal residual tumor in basal ganglia on the end of the 5th week(A), but complete radiographic response was noted on the end of the 10th week(B). The suprasellar and cerebellar lesions also disappeared.

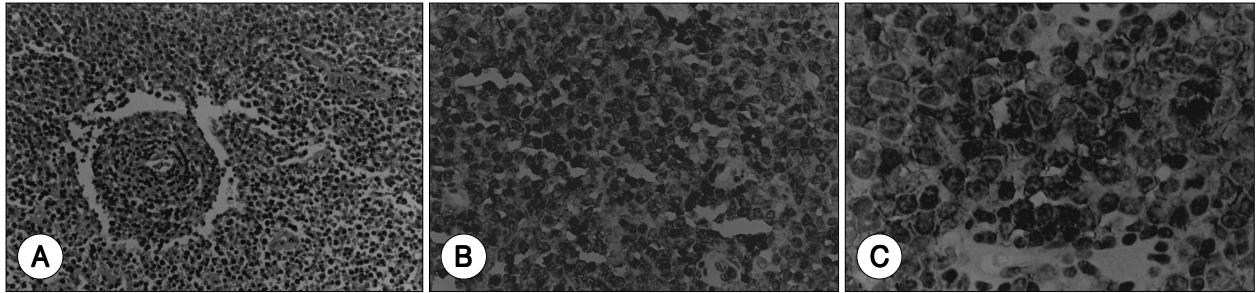


Fig. 4. Histopathological analysis of the biopsied tissue showing diffuse proliferation of large lymphoid cells without organoid pattern. The tumor cells demonstrate large, vesicular nuclei with prominent multiple nucleoli and frequent mitoses and some area of necrosis. Typical angiocentricity of tumor cells are also noted(A). Immunohistochemical stainings show membranous immunoreactive cells with leukocyte common antigen(C) and B-cell(D) immunostain.

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Table 3. Chemotherapy(CT) plus radiotherapy(RT) trials for primary CNS lymphoma

Author	Year	No. of patients	CT regimens	Timing of CT in relation to RT	Whole brain RT dose(Gy)	Median survival (months)
Gabbai	1989	13	HDMTX	pre RT	30 - 44	9.5
DeAngelis	1992	31	HDMTX+ITMTX+Ara-C	pre & post RT	40	42.5
Selch	1994	23	HDMTX + / - Ara-C or CHOP	during or post RT	10 - 46	8
Glass	1994	25	HDMTX	pre RT	30 - 44	33
Ahn	1995	8	EDAP + / - CHOP or ITMTX	unknown	30 - 60	31
Schultz	1996	52	CHOD+ / - ITMTX	pre RT	max. 41.4	16.1
Kim	1996	7	CHOP or HDMTX or ITMTX	during or post RT	50 - 60	unknown
Lee	1999	13	M-CHOD+ITMTX	pre RT	40	43
Hiraga	1999	28	HDMTX	pre RT	30 - 50	39.3
Bataille	2000	129	Doxorubicin or HDMTX or Ara-C or Doxorubicin + / - HDMTX	pre RT	max. 40	unknown

*Abbreviations : HDMTX=high-dose methotrexate ; ITMTX=intrathecal methotrexate ; Ara-C=cytosine arabinoside ; CHOP or CHOD=cyclophosphamide, adriamycin, vincristine, prednisolone or dexamethasone ; M-CHOD=methotrexate-CHOD.

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