2018

Saudi Clinical Practice Guidelines for Diagnosis, Treatment and Follow-up of Primary Central Nervous System Lymphoma

National Cancer Center

(NCC)

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Primary Central Nervous System Lymphoma: Saudi Clinical Practice Guidelines for Diagnosis, Treatment and Follow-up

Overview

Primary central nervous system lymphoma (PCNSL) is a rare variant of aggressive extranodal non-Hodgkin Lymphoma (NHL) of the diffuse large b-cell type that confined to the brain, leptomeninges, spinal cord, eyes without evidence of systemic disease. It estimated to account for up to 1% of all lymphomas, 4-6% of all extra-nodal lymphoma, and about 3% of all CNS tumors.[1] Presenting symptoms vary with the neuroanatomical localization of the tumor in the CNS. Most patients present with focal neurological symptoms, neuropsychiatric symptoms or symptoms of increased intracranial pressure with seizures that is relatively uncommon and may have visual symptoms associated with vitreous involvement.[2] The risk of development of PCNSL is highly associated with immunodeficiency status either congenital or acquired as HIV infection. Likewise, the incidence continues to rise for patients aged>65 years who represent most of immunocompetent patients.[3,4,5] Very few population studies have been published about PCNSL in Saudi Arabia. However, recent studies showed that there are slightly more female are diagnosed with PCNSL. The mean age at diagnosis was 50.4 years (ranged between 20 to 60 years and above) for all patients. [6,7]

1. Diagnosis

1.1. Magnetic resonance imaging (MRI) with contrast should be performed in all PCNSL suspected cases to define site and extension of the disease.

1.2. Fluid-attenuated inversion recovery (FLAIR) and T1 weighted sequences before and after contrast injection is the method of choice for diagnosis.

1.3. The diagnosis of PNCSL needs to be confirmed pathologically according to the WHO classification. [1]

1.4. Stereotactic needle brain biopsy is the optimal method to obtain a histopathological diagnosis; therefore, surgical resection of PCNSL is not recommended. [8]

1.5. Steroids should be withheld at least 7-10 days prior to biopsy to minimize lymphocytotoxic effect of steroids on histological diagnosis.[9,10]

1.6. Required immunohistochemical markers for lymphoma cell characterization should include pan B-cell antigens (i.e. CD19, CD20, CD22, CD79a), BCL6, MUM1/IRF4, BCL2, and CD10.[11,12,13]

2. Staging Workup

2.1 Pathology review (essential for all referral cases).

2.2. Complete history (Age, comorbidities, B-symptoms, ECOG, neurological and neuropsychiatric symptoms, hepatitis or HIV risk factors, medications, allergy to contrast or drugs, social and family history).

2.3 Physical examination

2.3.1 Full neurological examination (i.e, Mini –mental status exam).

2.3.2 Assessment of Lymph nodes, Waldeyer's ring, spleen, liver and skin.

2.4. CBC, Diff, LFT, Cr, LDG, electrolytes, calcium.

2.5. Hepatitis serology (HBV, HCV).

2.6. HIV antibody test.

2.7. Whole brain MRI (contrast-enhanced).

2.8. CT neck and CAP. [14]

2.9. Bone marrow biopsy. [14]

2.10. Testicular ultrasonography in elderly patient is recommended.[14]

2.11. CSF examination (lymphoma cell counts, protein and glucose levels, cytology, flow cytometry, and IgHV gene rearrangement studies). [15,16,17,18,19,20]

2.12. Ophthalmologic assessment.

2.12.1 Slit-lamp examination should be carried out to investigate possible ocular movement.

2.12.2 Indirect ophthalmoscopy.

2.12.3 Ophthalmic ultrasonography.

2.13. ECHO.

2.14. Pregnancy test for woman at childbearing age.

3. Prognostic Factors

3.1 International Prognostic score for PCNSL.[2]

3.1.1. Age >60 years.

3.1.2. Eastern Cooperative Oncology Group (ECOG) PS >1.

3.1.3. Elevated serum level LDH.

3.1.4. Elevated CSF protein concentration.

3.1.5. Tumor localization within the deep regions of the CNS.

3.2 Risk classification score: 0-1, low risk; 2-3, intermediate risk; 4-5, high risk.[2]

4. Management of PCNSL

4.1. Treatment of PCNSL is based on the age, performance status and response to initial steroid therapy. [2,14,21,22,23,24,25,26,27,28,29]

4.2. High dose MTX ($\geq 3 g/m^2$) is the standard of care induction therapy to cross the blood brain barrier and yield cytotoxic levels in the CSF. It should be delivered over 2-4 hours rapid infusion time for a minimum of 4-6 injections and at intervals that should not exceed 2-3 weeks.[30,31,32]

4.3 Infusions of HD MTX require pre and post-hyperhydration, urine alkalinization, leucovorin rescue, and MTX concentration monitoring.

4.4 HDMTX in combination with Temozolmide and Rituximab improves the response rates with respect to HDMTX alone.[33]

4.5 High dose consolidation of cytarabine and etopside following HDMTX-based polychemotheraphy induction therapy is recommended.[33]

4.6. Palliative whole brain radiotherapy (WBRT) should be considered for those patients who are deemed not candidate for high dose MTX such as those unable to tolerate or relapsing after high-dose, CNS penetrating chemotherapy and not fit for further chemotherapy.

5. Follow-Up Schedule and Assessments

5.1. Every 3 months for 2 years, then every 6 months thereafter.

5.2. History and physical examination every visit.

5.3. Cognitive evaluation (e.g MMSE).

5.4. Contrast Enhanced MRI of the brain.

5.5. Ophthalmologic examination and CSF analysis if clinically indicated.

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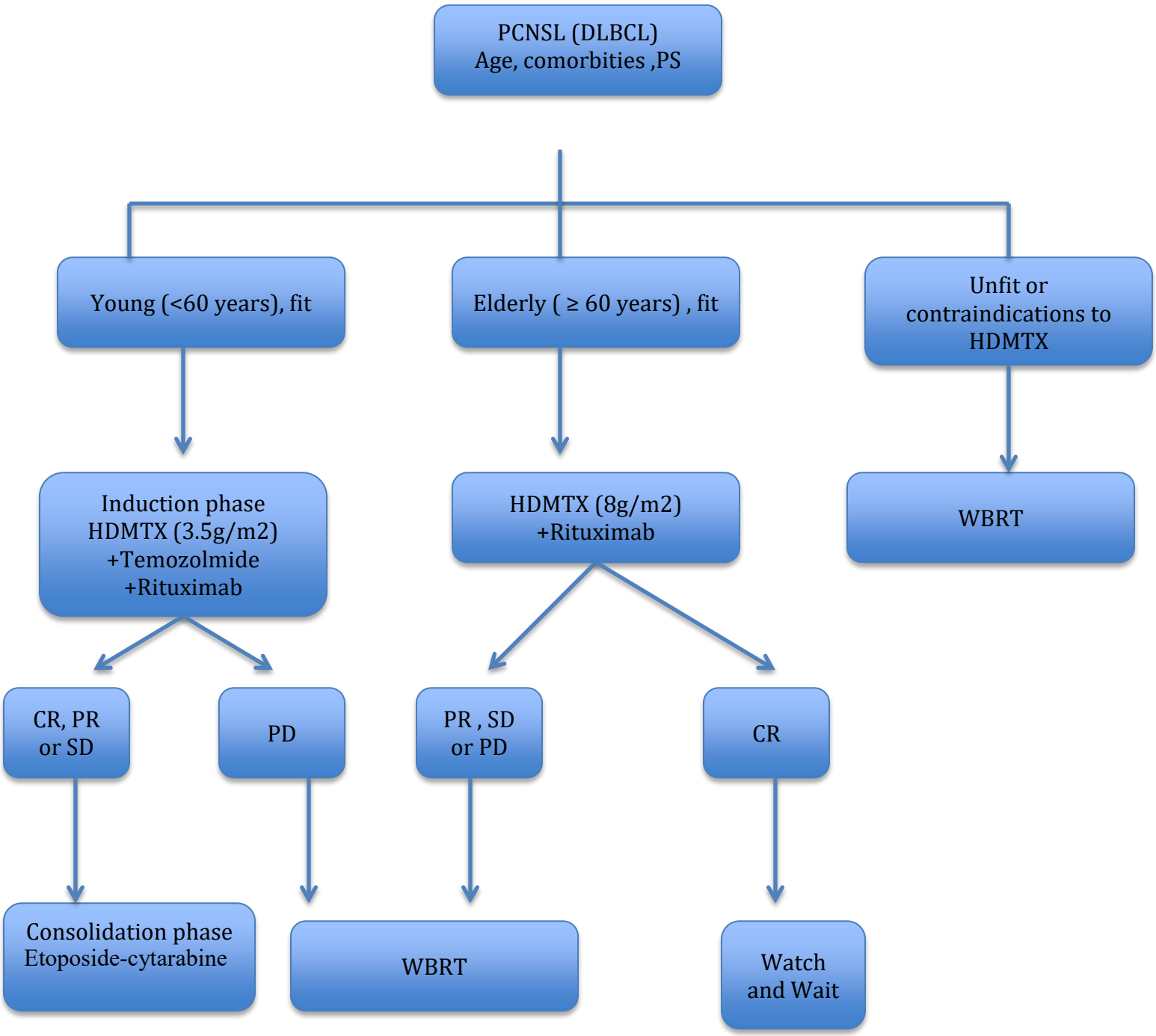
i. Appendix


PCNSL (DLBCL)
Age, comorbities ,PS
Young (<60 years), fit
Elderly (≥ 60 years) , fit
Unfit or contraindications to HDMTX
Induction phase HDMTX (3.5g/m2) +Temozolmide +Rituximab
HDMTX (8g/m2) +Rituximab
WBRT
CR, PR or SD
PD
PR , SD or PD
CR
Consolidation phase Etoposide-cytarabine
WBRT
Watch and Wait