Section: Radiation Oncology

Case Report

CNS INVOLVEMENT IN CLASSICAL HODGKIN LYMPHOMA: A RARE CASE REPORT AND MULTIDISCIPLINARY MANAGEMENT APPROACH

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ABSTRACT

Central nervous system (CNS) involvement in classical hodgkin lymphoma (cHL) is an exceptionally rare clinical entity, occurring in less than 0.5% of cases. Owing to its infrequency, there is limited evidence guiding optimal management, and outcomes have historically been variable. We report the case of a 40-year-old male diagnosed with stage IVB cHL who achieved a complete systemic metabolic response following standard ABVD chemotherapy but subsequently developed isolated CNS relapse. Neuroimaging revealed a solitary frontal lobe lesion, which was surgically excised and histologically confirmed as classical hodgkin lymphoma. The patient was further treated with adjuvant whole brain radiotherapy (WBRT), resulting in complete radiological remission and resolution of neurological symptoms. This case underscores the importance of vigilance for neurological symptoms in lymphoma patients and highlights the effectiveness of a multimodal therapeutic strategy.

Keywords: Classical hodgkin lymphoma, CNS relapse, WBRT, ABVD chemotherapy, case report, multimodal therapy.

INTRODUCTION

Hodgkin lymphoma (HL) is a unique B-cell derived lymphoid malignancy characterized histologically by the presence of Reed–Sternberg cells within a reactive inflammatory background. Classical Hodgkin lymphoma (cHL) represents approximately 90–95% of all HL cases and is considered one of the most curable hematological malignancies, particularly in early stages, with survival rates exceeding 80–90% following contemporary treatment protocols. Despite excellent systemic control, extranodal involvement may occur in advanced stages. However, involvement of the central nervous system (CNS) remains exceedingly uncommon, with an incidence estimated between 0.2% and 0.5%. CNS manifestations can include parenchymal lesions, leptomeningeal disease, or dural infiltration, often presenting during relapse or refractory disease. Due to the rarity of CNS involvement in cHL, there is a lack of consensus regarding optimal management strategies. Most available evidence is derived from isolated case reports and small case series. Herein, we describe a rare presentation of isolated CNS relapse following systemic remission and discuss the role of multimodal treatment in achieving favorable outcomes.

CASE PRESENTATION

A 40-year-old male presented with constitutional B symptoms, including persistent high-grade fever, unintentional weight loss, and drenching night sweats over a period of several months. Clinical evaluation and imaging raised suspicion for a lymphoproliferative disorder. An excisional lymph node biopsywas performed. Histopathological examination revealed classical Reed–Sternberg cells in a mixed inflammatory background. Immunohistochemical analysis showed positivity for CD15, CD30, and PAX5, along with Epstein–Barr virus latent membrane protein-1 (EBV/LMP1),

confirming the diagnosis of classical Hodgkin lymphoma.

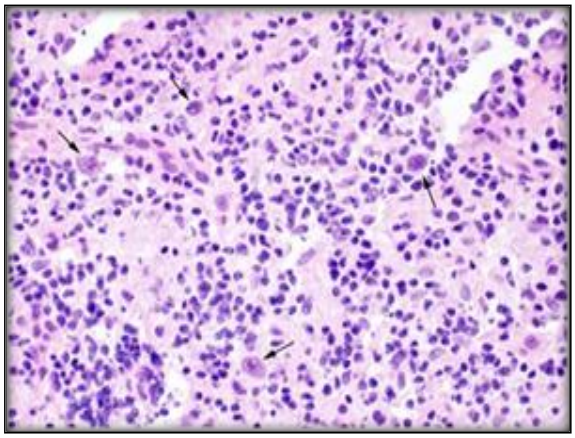

Figure 1: Arrow showing reed–sternberg cells

A baseline fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) scandemonstrated extensive disease involvement, including lymphadenopathy above and below the diaphragm, bilateral pulmonary nodules, hepatic and splenic lesions, pleural deposits, and skeletal involvement. Based on these findings, the disease was staged as stage IVB. The patient was initiated on standard ABVD chemotherapy, consisting of Adriamycin, Bleomycin, Vinblastine, and Dacarbazine, administered on days 1 and 15 of each cycle. He completed five cycles of chemotherapy after which interim & post-treatment FDG PET-CT indicated a near-complete metabolic response. Approximately one month after completion of chemotherapy, the patient developed new-onset generalized seizures accompanied by weakness in the left upper limb. There was no prior history of neurological disease. Contrast enhanced magnetic resonance imaging (CEMRI) of the brain with contrast revealed a well-defined lesion in the right anterior frontal lobe measuring approximately 1.4 × 1.3 × 2 cm. The lesion exhibited heterogeneous enhancement, areas of hemorrhage, and surrounding vasogenic edema. Cerebrospinal fluid (CSF) analysis obtained via lumbar puncture did not reveal malignant cells.

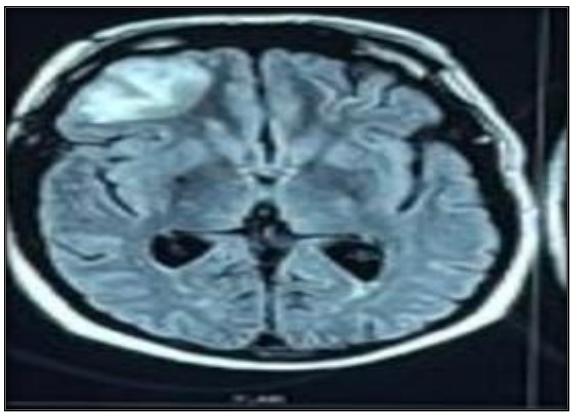

Figure 2: Baseline CEMRI Brain

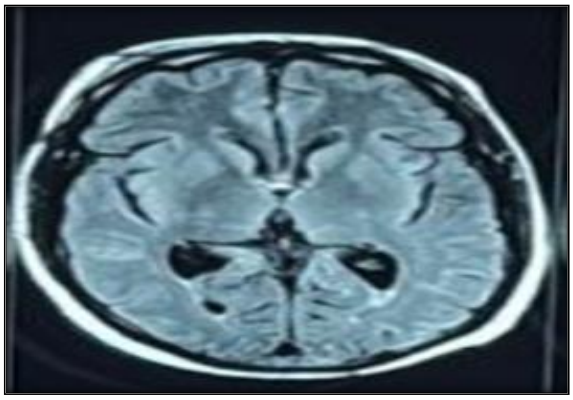

Figure 3: Follow-up CEMRI Brain

Given the diagnostic uncertainty, including the possibility of a second primary brain tumor, the patient underwent a right fronto-parietal craniotomy with near-total excision of the lesion and duraplasty in March 2025.Histopathological evaluation of the resected specimen demonstrated features consistent with classical Hodgkin lymphoma. Immunohistochemistry confirmed expression of CD15, CD30, and PAX5, thereby establishing CNS involvement of cHL. Following neurosurgical intervention, the patient was referred for adjuvant radiotherapy. Whole brain radiotherapy (WBRT) was delivered to a total dose of 41.4 Gy in 23 fractions (1.8 Gy per fraction, five fractions per week) using a three-dimensional conformal radiotherapy (3DCRT) technique over a period of approximately five weeks. The treatment was well tolerated, with no significant acute toxicities reported.

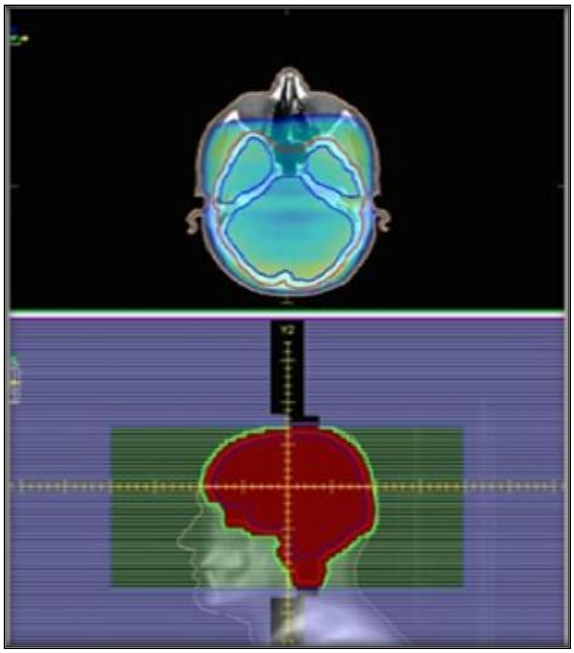

Figure 4: WBRT planning isodose distribution

After 3 months, post-treatment CEMRI demonstrated complete resolution of the intracranial lesion with no evidence of residual or recurrent disease. A follow-up PET-CT scan confirmed sustained systemic

remission. Clinically, the patient experienced complete resolution of seizures and neurological deficits. At four months of follow-up, the patient remained disease-free with good functional status.

DISCUSSION

Central nervous system (CNS) involvement in classical Hodgkin lymphoma (cHL) remains an exceptionally rare clinical entity, with an incidence of less than 0.5%, and is therefore poorly characterized in prospective studies.[7,8]

Unlike non-Hodgkin lymphomas, where CNS dissemination is relatively more common, cHL demonstrates a distinct biological behavior, likely related to its unique tumor microenvironment and dependence on reactive inflammatory cells.[1,8]

The pathogenesis of CNS involvement in cHL is not fully elucidated. Proposed mechanisms include hematogenous dissemination, particularly in advanced-stage disease, and direct extension from adjacent osseous structures.[6,7]

The rarity of CNS spread may be attributed to the limited expression of adhesion molecules and chemokine receptors necessary for CNS homing, distinguishing cHL from other aggressive lymphomas.[8] In our case, the presence of stage IV disease and Epstein–Barr virus (EBV) positivity likely contributed to the risk of extranodal dissemination. Several risk factors for CNS involvement have been suggested, including advanced-stage disease, multiple extranodal sites, B symptoms, and immunosuppression.[2,5]

However, unlike aggressive B-cell lymphomas, there are no validated CNS risk stratification models for cHL. This highlights a critical gap in current understanding and underscores the need for individualized clinical vigilance. Clinically, CNS involvement may present with seizures, focal neurological deficits, or signs of raised intracranial pressure, depending on lesion location.[4,9]

In our patient, new-onset seizures and focal weakness prompted timely neuroimaging. Magnetic resonance imaging (MRI) remains the modality of choice for evaluation, although imaging findings are often nonspecific and may mimic primary brain tumors, metastases, or infectious lesions.[4] Notably, cerebrospinal fluid (CSF) cytology may be negative even in confirmed cases, as demonstrated here, reinforcing the importance of tissue diagnosis when feasible.Given the absence of standardized treatment guidelines, management strategies for CNS involvement in cHL are largely extrapolated from primary CNS lymphoma and systemic lymphoma paradigms.[7,9]

Multimodal treatment approaches, including surgery, radiotherapy, and systemic therapy, are commonly employed. Surgical resection plays a dual role in establishing definitive diagnosis and achieving cytoreduction, particularly in cases with solitary, accessible lesions. Radiotherapy remains a cornerstone of treatment for intracranial disease control. Whole brain radiotherapy (WBRT) has demonstrated efficacy in achieving local control, particularly in patients with isolated CNS involvement or residual disease following surgery.[4] In the present case, adjuvant WBRT to a dose of 41.4 Gy resulted in complete radiological remission, consistent with previously reported outcomes in small case series. The role of systemic chemotherapy and intrathecal therapy in this setting remains controversial. While high-dose methotrexate-based regimens are standard in primary CNS lymphoma, their role in cHL-associated CNS disease is not well established.[7] Furthermore, the blood–brain barrier may limit the efficacy of conventional chemotherapy regimens such as ABVD in preventing CNS relapse, as observed in this patient. Importantly, this case highlights a rare phenomenon of isolated CNS relapse following complete systemic metabolic response. Such presentations emphasize the need for continued clinical vigilance even in patients achieving remission. The absence of systemic disease at relapse raises important biological questions regarding sanctuary sites and treatment resistance.

To the best of our knowledge, isolated CNS relapse after complete metabolic remission in cHL remains exceedingly rare, with only a limited number of cases reported in the literature. Our findings support the role of aggressive multimodal therapy in achieving durable remission and favorable neurological outcomes.

CONCLUSION

Central nervous system involvement in classical Hodgkin lymphoma is rare but clinically significant. Early recognition of neurological symptoms and prompt diagnostic evaluation are essential.This case highlights that a multidisciplinary treatment approach incorporating surgery and radiotherapy can result in excellent clinical and radiological outcomes. Given the lack of standardized guidelines, individualized treatment planning remains critical.

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