Classical Hodgkin Lymphoma as De Novo B-Cell Malignancy After Treatment of Multiple Myeloma in the Pre-Lenalidomide Era

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Clinical Practice Points

- During the past decade, introduction of the novel agents in treatment of multiple myeloma disease resulted in a significant improvement in response and an increase in progression-free and overall survival.
- In myeloma patients, an increased incidence for secondary primary malignancies is described as caused by intrinsic immunosuppression by the disease itself and additional effects of the applied chemotherapeutic treatment. Recently, occurrence of rare B-cell malignancies have been reported for the first time in myeloma patients after high-dose melphalan treatment and lenalidomide maintenance.
- Here, we show a case of Hodgkin's lymphoma in a patient with complete remission of multiple myeloma as a de novo B-cell malignancy. Hodgkin's disease was diagnosed 22 months after termination of thalidomide maintenance and applying high-dose melphalan treatment. Hodgkin's disease presented with an unusual manifestation pattern but classical histopathology. Clonal analyses revealed a de novo B-cell malignancy. Chemotherapeutic treatment resulted in complete remission.
- Treating physicians should be aware of potential secondary B-cell malignancies in myeloma patients. Early histopathological examination of enlarged lymph nodes is recommended.

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Introduction

Multiple myeloma (MM) is a hematological malignancy that is caused by proliferation of neoplastic monoclonal plasma cells in bone marrow. MM comprises approximately 1% of all types of cancer and 10% of all hematologic malignancies.[1] Clinical characteristics of MM result from proliferation of malignant plasma cells in the bone marrow, which interact with the surrounding environment and cause the replacement of normal bone marrow and the destruction of bone tissue.[2,3] Hodgkin lymphoma (HL) is a B-cell–derived malignancy and typically presents as painless lymphadenopathy, which is frequently cervical or supraclavicular with a predominance in patients younger than 30 years of age. The annual incidence of HL is approximately 1 in 25,000 people, and the disease accounts for slightly less than 1% of all cancers worldwide.[4,5]

It is known that MM patients have an increased incidence of secondary cancers as a result of continuous immunosuppression because of the malignant B-cell clone and chemotherapeutic treatment. These cancers mainly consist of acute myeloid leukemia, myelodysplastic syndromes, and solid tumors.[6] Recently, an increased awareness for secondary primary malignancies (SPM) in myeloma patients arose because of a reported imbalance of secondary cancers in treatment arms of clinical trials in which lenalidomide was combined with melphalan or given immediately after high-dose melphalan treatment.[7] Attal et al[8] reported for the first time an increased incidence of HL and acute lymphoblastic leukemia among myeloma patients who had received induction therapy

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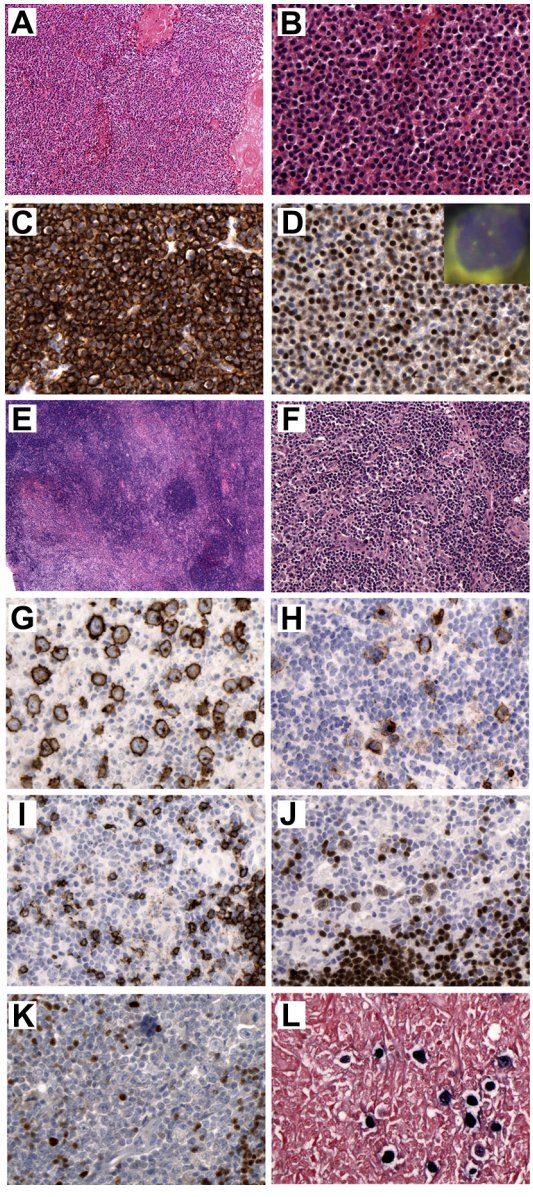
Figure 1 Medullary Manifestation of Plasmacytoma (A-D) and Nodal Manifestation of Classical Hodgkin Lymphoma (E-L). (A) Light Microscopic Examination Showed Dense Infiltrations of Plasma Cells (H & E; Original Magnification ×100). (B) Plasma Cells are Arranged in Sheets (H & E; Original Magnification ×400), and (C) Show Strong Membrane Staining for CD138 (CD138 Immunoperoxidase; Original Magnification ×400). (D) Cyclin D1 is Expressed With a Heterogeneous Nuclear Pattern (Cyclin D1 Immunoperoxidase; Original Magnification ×400) Because of a Copy Number Gain With up to 4 Copies of the Cyclin D1 Gene Without a Detectable Break in the FISH Analysis (Insert). (E) Light Microscopic Examination Showed a Partly Effaced Lymph Node Architecture (H & E; Original Magnification ×25). (F) The Infiltrate Consists of Large Blasts With Characteristic Hodgkin and Reed-Sternberg Cell Morphology. There is a Background Infiltration by Small Lymphocytes, Histiocytes, and Aggregations of Plasma Cells (H & E; Original Magnification ×200). (G) Blastic Tumor Cells Show Consistent Strong Expression of CD30 (CD30 Immunoperoxidase; Original Magnification ×400). (H) CD15 is Coexpressed in a Weaker Intensity (CD15 Immunoperoxidase; Original Magnification ×400). (I) Staining for the B-cell Marker CD20 Highlights the Reactive Small B-Cells in the Infiltrate, but Remains Mostly Negative in the Tumor Cells (CD20 Immunoperoxidase; Original Magnification ×400). (J) PAX5 is Expressed in the Tumor Cells With Significant Less Intensity Compared With the Reactive B-Cells (PAX5 Immunoperoxidase; Original Magnification ×400). (K) OCT2, a Transcription Factor, is not Expressed in the Tumor Cells, in Accordance With the Concept of a Defective B-Cell Programming in Hodgkin Lymphoma (OCT2 Immunoperoxidase; Original Magnification ×400). (L) EBV RNA is Detectable in the Tumor Cells (in Situ Hybridization of EBV-Encoded RNA; Original Magnification ×400)



Abbreviations: EBV = Epstein-Barr virus; FISH = fluoresence in situ hybridization; H & E = hematoxylin and eosin stain; OCT2 = octamer binding protein-2; PAX = transcription factor paired box 5.