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Case Report

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Transformation to BCR ABL1 Positive Chronic Myeloid Leukemia Following Salvage DHAP Therapy in Relapsed Refractory Classical Hodgkin Lymphoma: A Rare Case Report

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Abstract

Objective: To describe an exceptionally rare occurrence of chronic myeloid leukemia developing in the setting of relapsed refractory classical Hodgkin lymphoma following multi line chemotherapy, and to highlight the associated diagnostic challenges, therapeutic limitations, and evidence-based management considerations. ***Design:*** Single patient observational case report. ***Subjects/Patients:*** A 22 year old male with nasopharyngeal classical Hodgkin lymphoma of mixed cellularity subtype who achieved initial complete metabolic remission but subsequently developed relapsed refractory disease and a concurrent myeloproliferative neoplasm. ***Methods:*** Detailed clinical history, treatment chronology, laboratory data, histopathologic findings, cytogenetic and molecular analyses including fluorescence in situ hybridization, and radiologic imaging were systematically reviewed and interpreted in accordance with CARE guideline recommendations and current international practice guidelines. ***Results:*** Initial combination chemotherapy resulted in complete metabolic response. The patient later developed metabolically active bilateral tonsillar disease refractory to multiple salvage regimens including cyclophosphamide etoposide dexamethasone hydroxyurea and dexamethasone high dose cytarabine cisplatin. Progressive leukocytosis led to bone marrow evaluation demonstrating marked myeloid hyperplasia with breakpoint cluster region Abelson murine leukemia viral oncogene homolog one rearrangement in ninety nine percent of cells, confirming chronic myeloid leukemia. ***Conclusion:*** This case illustrates an extremely rare coexistence of chronic myeloid leukemia in relapsed refractory classical Hodgkin lymphoma, emphasizing the need for comprehensive hematologic evaluation in refractory disease and supporting early integration of targeted therapies guided by molecular diagnostics.

Keywords: ***Chemotherapy, Combination; Hodgkin Disease; Leukemia, Myelogenous, Chronic, BCR-ABL Positive; Salvage Therapy; Stem Cell Transplantation; Tyrosine Kinase Inhibitors.***

Introduction

Classical Hodgkin lymphoma is a highly curable malignancy in young adults, with standard combination chemotherapy achieving long term remission in the majority of patients. However, a subset develops relapsed or refractory disease requiring salvage chemotherapy and consideration for autologous stem cell transplantation. Secondary hematologic malignancies are a recognized late complication, particularly therapy related to acute myeloid leukemia or myelodysplastic syndromes. In contrast, chronic myeloid leukemia arising after Hodgkin lymphoma treatment is exceedingly rare, with only isolated case reports in the literature. The emergence of a breakpoint cluster region Abelson murine leukemia viral oncogene homolog one driven myeloproliferative neoplasm in the context of refractory Hodgkin lymphoma poses significant diagnostic ambiguity regarding therapy related leukemogenesis versus clonal evolution or coexistence. This report details a rigorously documented case and reviews current evidence and guideline aligned management considerations.

Methods

Clinical history, treatment timelines, laboratory parameters, histopathologic findings, cytogenetic analyses including fluorescence in situ hybridization, and radiologic imaging were systematically reviewed. Data were analyzed in accordance with CARE guideline recommendations for case reporting.

Patient Information

A 22-year-old male student with no significant occupational exposures presented initially in January 2023 with nasal obstruction and epistaxis. There was no relevant family history of hematologic malignancy. He had no known chronic medical illnesses prior to presentation.

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Clinical Findings

On current admission in January 2026, the patient presented with progressive bilateral cervical lymphadenopathy, tonsillar ulceration, weight loss, abdominal distension, cough, vomiting, dark colored urine, and dyspnea. Examination revealed bilateral cervical lymph nodes measuring up to six to seven centimeters, painless and soft to firm in consistency, right inguinal lymphadenopathy, bilateral tonsillar enlargement with whitish slough and ulceration, tense abdomen with ascites, bilateral pitting pedal edema, and bilateral pulmonary crepitations. He was conscious, oriented, and hemodynamically stable.

Timeline

1. January 2023: Initial presentation with nasal obstruction and epistaxis; nasopharyngeal biopsy diagnosed classical Hodgkin lymphoma mixed cellularity subtype.
2. November 2023 to March 2024: Six cycles of combination chemotherapy administered.
3. June 2023 and June 2024: Positron emission tomography imaging demonstrated complete metabolic response.
4. November 2024: Development of bilateral tonsillar enlargement.
5. December 2024: Positron emission tomography showed no metabolically active disease.
6. Early 2025: Two cycles of cyclophosphamide etoposide dexamethasone and hydroxyurea administered.
7. February 2025: Three cycles of dexamethasone high dose cytarabine and cisplatin completed.
8. July 2025: Imaging revealed metabolically active bilateral tonsils and leukocytosis.
9. June 2025 to January 2026: Treated with imatinib therapy.
10. January 2026: Admission with progressive disease and multisystem involvement.

Diagnostic Assessment

Histopathologic review of nasopharyngeal biopsy demonstrated diffuse CD45 positivity, CD30 positive large, atypical cells, scattered CD19 and CD20 positivity, CD5 and CD10 negativity, BCL6 and cyclin D1 negativity, and scattered MUM1 positivity consistent with classical Hodgkin lymphoma mixed cellularity subtype.

Hematologic evaluation revealed neutrophilic leukocytosis ranging from seventeen thousand to twenty two thousand per cubic millimeter with marked left shift, anemia, and mildly elevated platelets. Bone marrow biopsy showed ninety to ninety five percent cellularity with marked myeloid hyperplasia and left shifted maturation. Fluorescence in situ hybridization demonstrated breakpoint cluster region Abelson murine leukemia viral oncogene homolog one rearrangement in ninety nine percent of analyzed cells. Molecular testing for Janus kinase two, calreticulin, and myeloproliferative leukemia mutations was negative.

Radiologic evaluation demonstrated diffuse lymphadenopathy, gross ascites, bilateral pleural effusions, mild splenomegaly, and pulmonary consolidations with halo sign suggestive of invasive fungal pneumonia. Ascitic fluid analysis showed high serum ascites albumin gradient consistent with portal hypertensive ascites.

Previous PET-CT done on 07/12/2024 was reviewed and compared. Bilateral faucal tonsils demonstrated increased FDG uptake (SUVmax 13.76 vs previously 6.84) consistent with metabolically active enlargement, while no other sites of abnormal FDG avidity were observed in the head and neck, thorax, mediastinum, abdomen, pelvis, or skeleton. Mild diffuse bone marrow FDG uptake was noted, likely reactive. Overall, PET-CT findings indicate stable disease with localized metabolically active tonsillar involvement as shown in Figure 1, Figure 2 & Figure 3.

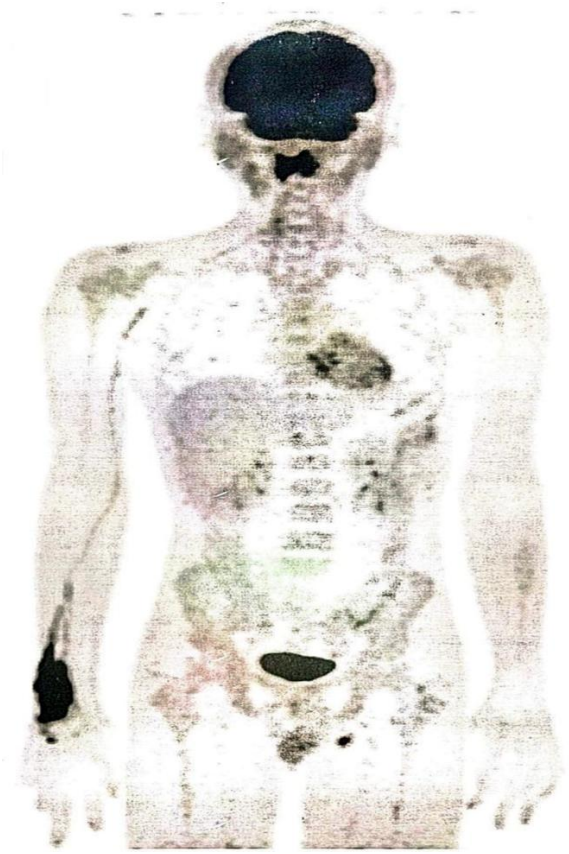

Figure 1: This whole-body FDG PET-CT maximum intensity projection demonstrates normal physiological radiotracer uptake in the brain, myocardium, liver, spleen, bowel, kidneys, and urinary bladder. In the head and neck region, there is metabolically active enlargement of the

bilateral faucal tonsils with increased FDG uptake compared to prior imaging, while the nasopharynx, oropharynx, hypopharynx, larynx, thyroid, salivary glands, and cervical or supraclavicular nodal stations show no abnormal FDG avidity. The thorax and mediastinum reveal no FDG-avid pulmonary parenchymal lesion, pleural disease, or mediastinal, hilar, or axillary lymphadenopathy. The abdomen and pelvis show no abnormal FDG uptake in the liver, spleen, pancreas, adrenal glands, kidneys, bowel loops, or abdominopelvic lymph nodes, with no ascites or peritoneal deposits identified. The musculoskeletal system demonstrates no FDG-avid lytic or sclerotic skeletal lesions, with mild diffuse bone marrow uptake in the axial and proximal appendicular skeleton, likely reactive in nature.

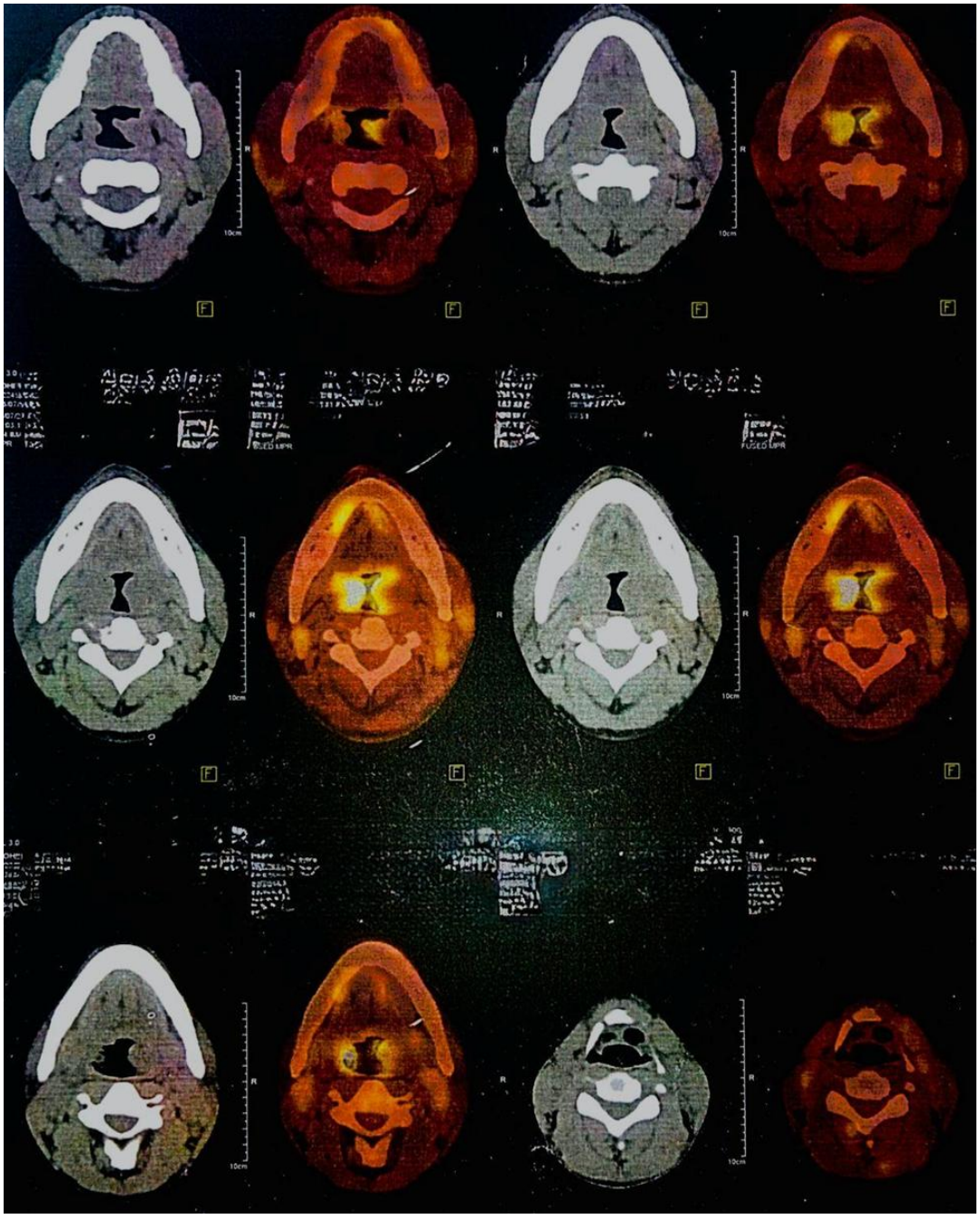

Fig. 2: These axial CT, PET, and fused PET-CT sections through the head and neck demonstrate structurally preserved upper aerodigestive tract anatomy with intense FDG uptake localized to the bilateral faucal tonsillar region, corresponding to enlarged tonsils seen on CT and appearing hypermetabolic on fused images. The degree of uptake is markedly higher than background musculature, consistent with the reported elevated SUVmax, while the surrounding nasopharynx, oropharynx beyond the tonsillar pillars, hypopharynx, larynx, salivary glands, thyroid, cervical soft tissues, and parapharyngeal spaces show no abnormal focal FDG avidity. No FDG-avid cervical lymphadenopathy is identified at these levels. The pattern of focal tonsillar hypermetabolism in the absence of nodal or distant FDG-avid disease supports a localized process, with differential considerations including active inflammation or localized lymphomatous involvement, requiring clinicopathologic correlation.

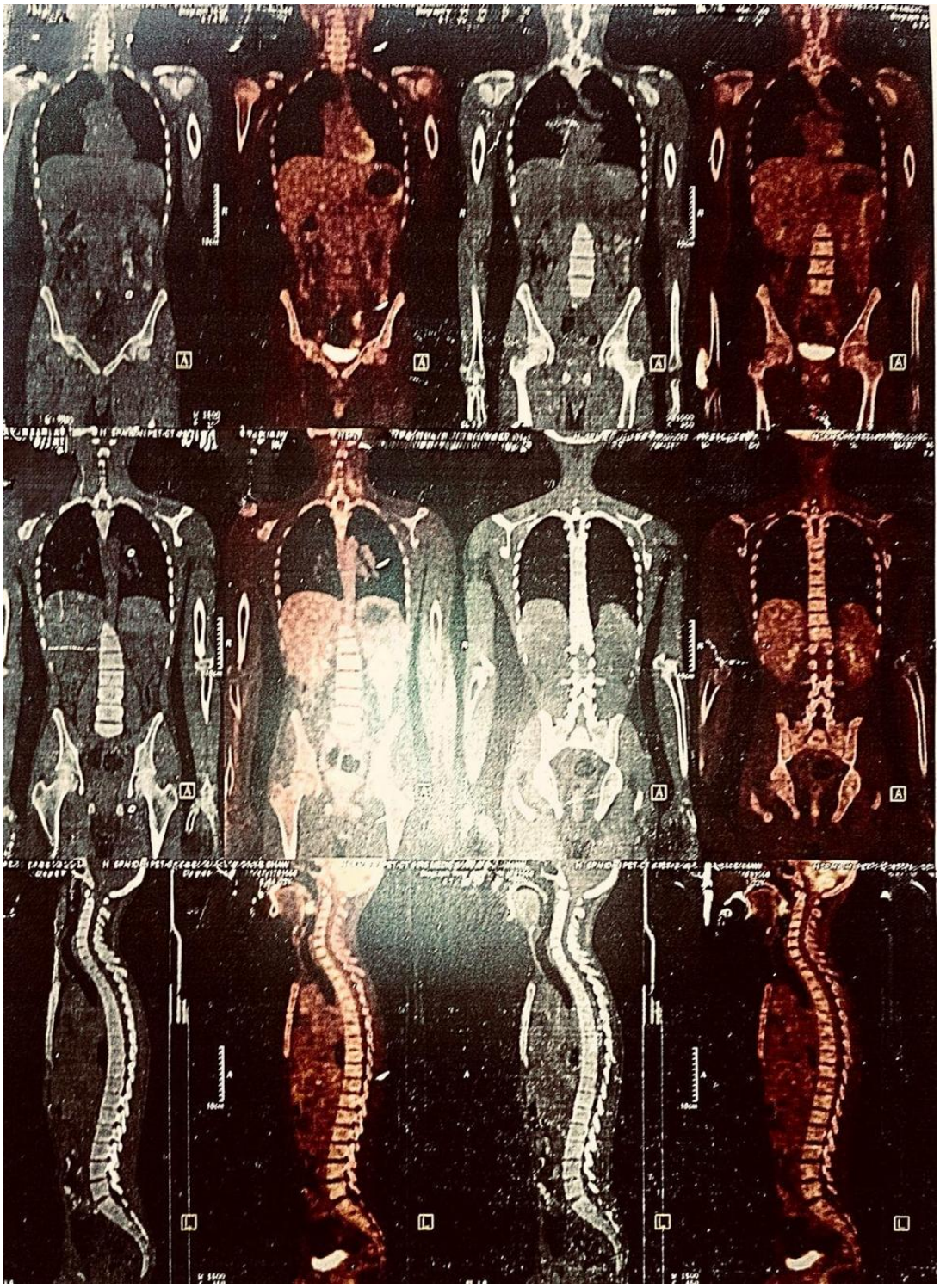

Figure 3: These coronal CT, PET, and fused PET-CT images of the whole body demonstrate preserved thoracic, abdominal, pelvic, and musculoskeletal anatomy with no focal abnormal FDG uptake in the lungs, mediastinum, liver, spleen, pancreas, adrenal glands, kidneys, bowel loops, or abdominopelvic lymph node stations. There is no evidence of FDG-avid mediastinal, hilar, axillary, retroperitoneal, or pelvic lymphadenopathy, and no metabolically active pleural or peritoneal disease is identified. The skeletal system shows no FDG-avid lytic or sclerotic lesions, with only mild diffuse marrow uptake along the axial and proximal appendicular skeleton, consistent with reactive or treatment-related marrow activity rather than infiltrative disease. Overall, apart from previously described tonsillar hypermetabolism, these coronal sections corroborate the absence of metabolically active systemic lymphoproliferative disease.

Following completion of dexamethasone, high dose cytarabine, and cisplatin therapy, the patient developed persistent and progressive leukocytosis that was disproportionate to infectious or steroid related causes. Peripheral blood smear demonstrated marked granulocytic proliferation with left shifted maturation including myelocytes and metamyelocytes, basophilia, and absence of significant dysplasia, raising suspicion for an underlying myeloproliferative neoplasm rather than reactive leukemoid response.

Bone marrow aspiration and trephine biopsy revealed a markedly hypercellular marrow with overall cellularity of approximately ninety to ninety five percent. There was striking myeloid predominance with increased myeloid to erythroid ratio, orderly but left shifted granulocytic maturation, relative erythroid suppression, and increased megakaryocytes including small hypolobated and atypical forms. Blasts were not increased. Reticulin staining did not demonstrate significant marrow fibrosis.

Immunohistochemical evaluation showed diffuse positivity for myeloperoxidase in granulocytic precursors, CD34 highlighting normal vascular structures without blast expansion, and CD61 highlighting increased megakaryocytes. There was no aberrant lymphoid immunophenotype. Fluorescence in situ hybridization analysis demonstrated breakpoint cluster region Abelson murine leukemia viral oncogene homolog one rearrangement in ninety nine percent of interphase nuclei, confirming the diagnosis of chronic myeloid leukemia. Molecular testing for Janus kinase two, calreticulin, and myeloproliferative leukemia mutations was negative, excluding alternative myeloproliferative neoplasms.

The temporal emergence of these findings after salvage chemotherapy strongly supported a diagnosis of chronic myeloid leukemia arising during treatment for relapsed refractory classical Hodgkin lymphoma rather than a reactive marrow process.

Therapeutic Interventions

Initial therapy consisted of six cycles of combination chemotherapy resulting in complete metabolic response. Upon relapse, the patient received two cycles of cyclophosphamide, etoposide, dexamethasone, and hydroxyurea followed by three cycles of dexamethasone, high dose cytarabine, and cisplatin with intent for autologous stem cell transplantation. Due to lack of durable response and emergence of chronic myeloid leukemia, imatinib therapy was initiated. During the current admission, voriconazole was started for probable invasive pulmonary aspergillosis, and supportive management was provided for hyponatremia, ascites, and cardiac dysfunction.

Follow up and Outcomes

During hospitalization, the patient exhibited persistent leukocytosis and progressive disease burden with multisystem involvement. Infectious complications and metabolic derangements were managed with partial improvement. Definitive oncologic management was deferred pending completion of histopathologic and cytogenetic evaluation. After multidisciplinary discussion and counseling, the family opted to continue care at a tertiary referral center. The patient was discharged in stable condition with ongoing antifungal therapy, supportive measures, and planned follow up.

Discussion

Classical Hodgkin lymphoma is a highly curable malignancy, particularly in young adults, with long term survival exceeding eighty percent following first line ABVD chemotherapy. However, relapsed or refractory disease occurs in approximately ten to twenty percent of patients and represents a biologically aggressive subset associated with inferior outcomes [1]. Salvage chemotherapy followed by autologous stem cell transplantation remains the standard of care for eligible patients, with platinum based regimens such as DHAP frequently employed to achieve cytoreduction prior to transplantation [2].

Secondary hematologic malignancies are a recognized late complication of Hodgkin lymphoma therapy. Large population based studies have consistently demonstrated an increased risk of therapy related acute myeloid leukemia and myelodysplastic syndromes, typically emerging within five to ten years following exposure to alkylating agents and topoisomerase II inhibitors [3,4]. In contrast, the development of chronic myeloid leukemia following Hodgkin lymphoma is exceedingly rare, with only isolated case reports described in the literature [5]. This distinction is biologically significant, as chronic myeloid leukemia is driven by the BCR ABL1 fusion oncogene and is not classically associated with chemotherapy induced DNA damage mechanisms implicated in therapy related acute leukemias [6].

In the present case, the detection of BCR ABL1 rearrangement in ninety nine percent of cells by fluorescence in situ hybridization, together with bone marrow findings of marked hypercellularity and myeloid hyperplasia with left shifted maturation, fulfills World Health Organization criteria for chronic myeloid leukemia [7]. The absence of JAK2 CALR and MPL mutations further excludes alternative myeloproliferative neoplasms, supporting a definitive diagnosis of BCR ABL1 driven disease [7]. The temporal relationship between refractory Hodgkin lymphoma and the emergence of chronic myeloid leukemia raises important diagnostic considerations including true secondary malignancy clonal coexistence or unmasking of a pre existing myeloid clone under selective pressure from cytotoxic therapy [6].

DHAP chemotherapy remains a widely used salvage regimen in relapsed or refractory Hodgkin lymphoma, with reported overall response rates of approximately sixty to seventy percent in transplant eligible populations [2]. However, primary refractory disease extranodal involvement and early relapse are well established predictors of poor response to DHAP and inferior progression free survival following autologous transplantation [8]. The failure of DHAP to induce durable clinical remission in this patient despite transient metabolic responses underscores the limitations of conventional cytotoxic salvage in biologically aggressive Hodgkin lymphoma.

Over the past decade, therapeutic paradigms for relapsed Hodgkin lymphoma have shifted toward targeted and immune based approaches. Brentuximab vedotin, an anti CD30 antibody drug conjugate, has demonstrated high overall and complete response rates in heavily pretreated patients including those with prior salvage failure and has been successfully used as a bridge to transplantation [9,10]. Similarly, immune checkpoint inhibitors targeting programmed death one such as nivolumab and pembrolizumab exploit the unique immune evasion mechanisms of Reed Sternberg cells and have shown durable responses even in patients refractory to both chemotherapy and brentuximab [11]. Current international guidelines increasingly favor incorporation of these agents earlier in the salvage sequence rather than reliance on repeated cytotoxic regimens [10,11].

The coexistence of active Hodgkin lymphoma and chronic myeloid leukemia presents a complex therapeutic challenge. Management of chronic myeloid leukemia is well defined, with tyrosine kinase inhibitors forming the cornerstone of therapy. Imatinib has demonstrated durable long term survival benefit, while second generation agents such as dasatinib and nilotinib offer deeper molecular responses in selected patients [12]. Serial quantitative BCR ABL1 transcript monitoring is essential for assessing response and guiding therapy modification [12]. In young patients with dual hematologic malignancies, allogeneic stem cell transplantation may be considered in highly selected cases after achieving adequate disease control, although data in this specific context remain limited [12].

Conclusion

In conclusion, this case highlights the rare coexistence of relapsed refractory classical Hodgkin lymphoma and chronic myeloid leukemia. It emphasizes the importance of comprehensive diagnostic evaluation in refractory disease, the limitations of conventional salvage chemotherapy, and the need for individualized multidisciplinary management guided by molecular diagnostics and contemporary evidence.

Declarations

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NONE

Conflict of interest

NONE

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NONE

Ethical Clearance

Informed consent was taken from the patient with no obligations.

Trial details

N/A

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