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Case report

Hodgkin Lymphoma in a Female with Long-Standing Systemic Lupus Erythematosus

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Abstract
Systemic lupus erythematosus (SLE) is associated with an increased risk of malignancies, particularly lymphomas. While non-Hodgkin lymphoma is more frequently reported, Hodgkin lymphoma (HL) represents a less common but clinically significant complication. We report a 48-year-old woman with an 18-year history of SLE who presented with pleuritic chest pain, dyspnea, fever, weight loss, and progressive lymphadenopathy. Imaging revealed left pleural effusion, splenomegaly, and widespread lymphadenopathy. Pleural biopsy was negative for malignancy. Excisional lymph node biopsy confirmed classical Hodgkin lymphoma, Ann Arbor stage III. The patient received BEACOPP followed by ABVD chemotherapy, achieving complete metabolic remission on PET-CT. Her treatment course was complicated by manageable neutropenia and mild anemia, which were addressed with supportive care. Close multidisciplinary monitoring by rheumatology and hematology ensured that her underlying SLE remained stable during chemotherapy. At follow-up, she reports good functional status and no recurrence of lymphoma symptoms. She remains in remission after 18 months of follow-up, with stable SLE on hydroxychloroquine and low-dose corticosteroids. This case highlights the critical importance of maintaining a high index of suspicion for malignancy in SLE patients who present with constitutional "B-symptoms" or rapidly progressive lymphadenopathy. It underscores the need for prompt investigation and tissue diagnosis to ensure appropriate oncological management in this high-risk population.
Keywords. Systemic Lupus Erythematosus, Lymphoma, Autoimmunity, Immunosuppression.

Introduction

Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease characterized by immune dysregulation and autoantibody production. Patients with SLE have a well-documented increased risk of various malignancies, including lymphomas – particularly non-Hodgkin lymphoma (NHL) and, less commonly, Hodgkin lymphoma (HL). The association between SLE and lymphoma is complex, involving chronic immune stimulation, impaired immune surveillance, and genetic factors [1].

Hodgkin lymphoma is a cancer of lymphocytes characterized by Reed–Sternberg cells. Its presentation in SLE patients can be challenging because symptoms such as fever, fatigue, weight loss, and lymphadenopathy are common to both conditions [2]. Therefore, a high index of suspicion is crucial when an SLE patient develops new or worsening constitutional symptoms or persistent lymphadenopathy that does not respond to conventional SLE therapy.

The pathogenesis of lymphoma in SLE is multifactorial. Chronic B-cell activation increases the risk of lymphoproliferative disorders. Immunosuppressive therapies such as cyclophosphamide and azathioprine, while essential for disease control, may impair immune surveillance and induce DNA damage. Epstein–Barr virus (EBV) has also been implicated, and SLE patients may have altered immune responses to viral infection [3]. Diagnosis typically requires a lymph node biopsy to identify Reed–Sternberg cells and classify the HL subtype [4]. Treatment follows standard oncological protocols, but the choice of regimen must be individualized to minimize SLE exacerbation and manage toxicities. Close monitoring for both lymphoma recurrence and SLE flare is essential.

The underlying mechanisms for this increased risk include chronic antigenic stimulation [2], immunosuppressive therapy [1], viral oncogenesis [5], and genetic predisposition [6]. We present a case of HL arising in a woman with longstanding SLE to illustrate this serious association.

Case Presentation

A 48-year-old woman presented with fever, pleuritic chest pain, dyspnea, and unintentional weight loss. Her clinical timeline is summarized in Figure 1 (proposed: timeline from SLE diagnosis at age 30 to presentation, diagnosis, treatment, and follow-up).

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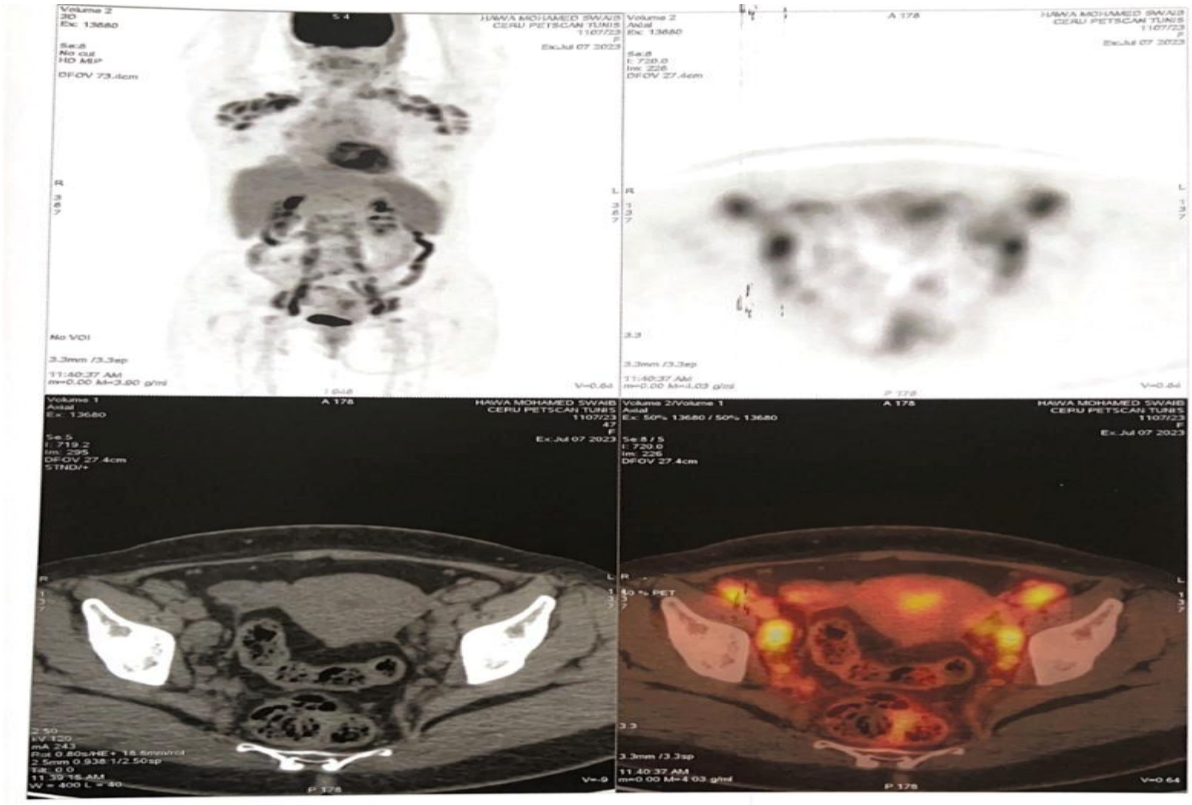

Figure 1. Initial PET-CT scan (Coronal and Axial views) showing intense FDG uptake in the pelvic and abdominal regions, indicating active lymphadenopathy.

The patient had been diagnosed with SLE 18 years earlier based on malar rash, oral ulcers, weight loss, positive ANA (1:1280, homogeneous), and anti-dsDNA antibodies. Her disease course was moderately active, with intermittent flares primarily affecting the skin. She had no history of lupus nephritis or neuropsychiatric involvement. Her maintenance regimen included weekly subcutaneous injections (for one year, specific agent not recalled), daily prednisone 7.5 mg, and hydroxychloroquine 400 mg daily.

Over the month prior to presentation, she developed persistent left-sided pleuritic chest pain, progressive dyspnea, low-grade fever, anorexia, and 5 kg weight loss. These symptoms did not improve with her usual SLE therapy, raising concern for an alternative or concurrent pathology.

She had no smoking, alcohol abuse, or radiation exposure. There was no family history of hematologic malignancies or autoimmune diseases other than SLE. Current medications: prednisone 7.5 mg daily, hydroxychloroquine 400 mg daily, calcium, and vitamin D supplements.

Vital signs: temperature 38.0°C, pulse 102 bpm, blood pressure 125/80 mmHg, oxygen saturation 95% on room air. General appearance: fatigued and pale. Lymph nodes: firm, fixed, non-fluctuant, tender mass in the left subclavicular and axillary regions. Abdomen: palpable splenomegaly (2 cm below the costal margin). Chest: decreased breath sounds at the left base. No active malar rash, oral ulcers, or arthritis.

On day 2, laboratory studies showed hemoglobin 11 g/dL (normocytic, normochromic), normal white blood cell count, C-reactive protein 59 mg/L, normal liver function tests, normal coagulation profile, negative tuberculin skin test, and negative tumor markers (CA19-9, CA125, ACE). Pleural fluid analysis (day 2) revealed a clear, lymphocyte-predominant effusion with normal glucose, high protein, alkaline pH; AFB negative, PCR for tuberculosis negative, and routine cultures negative.

On day 3, chest X-ray showed left pleural effusion with left lower lobe collapse. Thoracic CT angiography excluded pulmonary embolism and confirmed a moderate left pleural effusion (see Figure 2, proposed: chest imaging showing effusion).

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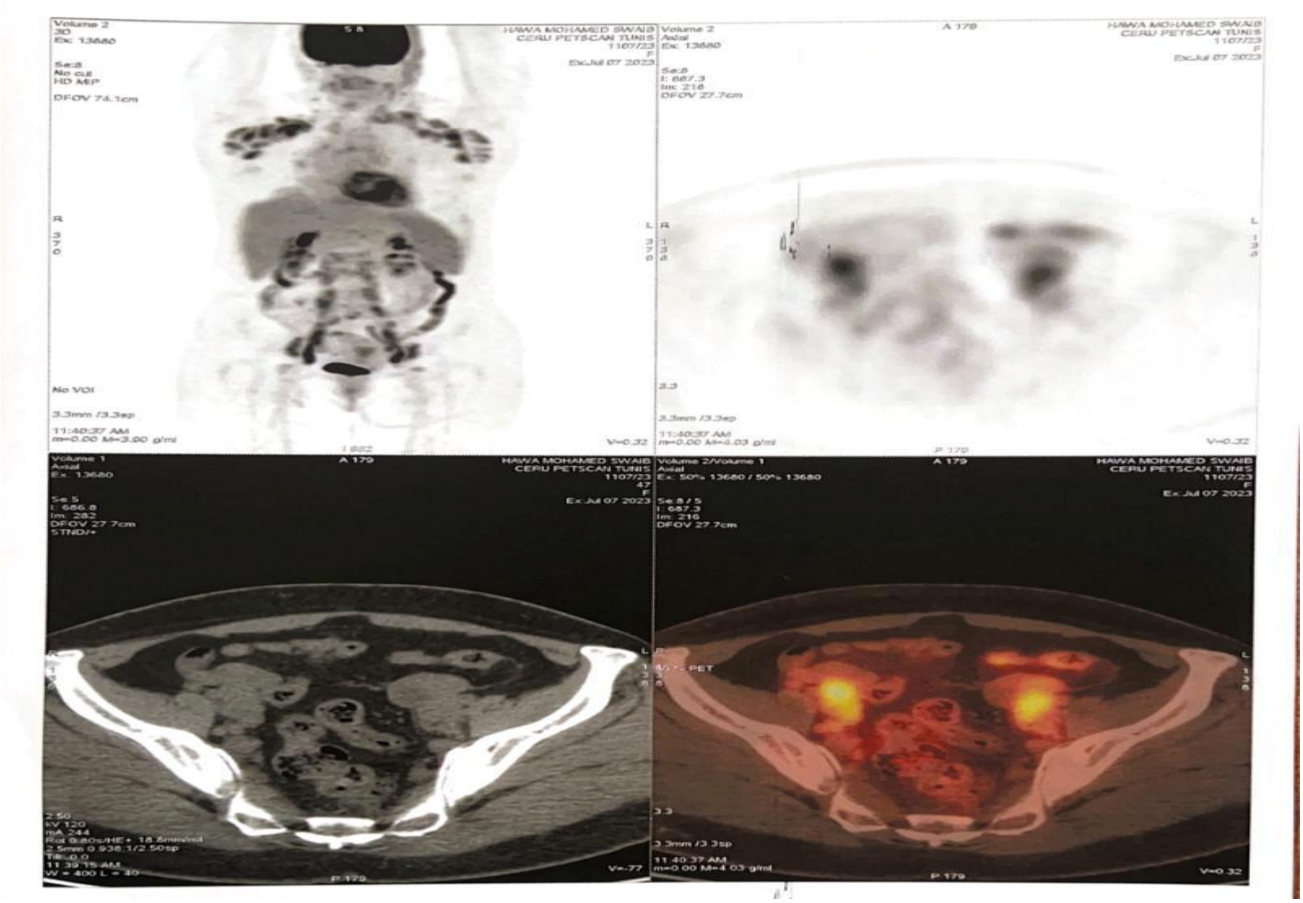

Figure 2. PET-CT imaging highlighting significant FDG-avid nodes in the iliac and inguinal stations.

On day 5, an ultrasound-guided pleural biopsy was performed; histopathology showed no malignant cells. On day 10, an excisional biopsy of a left cervical lymph node was performed. Histology revealed effacement of normal nodal architecture by a diffuse infiltrate of large, atypical lymphoid cells with prominent nucleoli and a high mitotic rate. Immunohistochemistry confirmed classical Hodgkin lymphoma.

PET-CT on day 15 revealed widely scattered hypermetabolic lymph nodes above and below the diaphragm and splenic involvement, consistent with Ann Arbor stage IIIAb. The pre-treatment scan demonstrated abnormal FDG uptake in retroperitoneal lymph nodes, as detailed in Figure 3, while Figure 4 illustrates the extensive mediastinal and axillary lymphadenopathy with the left-sided effusion seen earlier. An overview of the widespread disease distribution is provided in the Maximum Intensity Projection image (Figure 5). Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Confidentiality and anonymity were strictly maintained.

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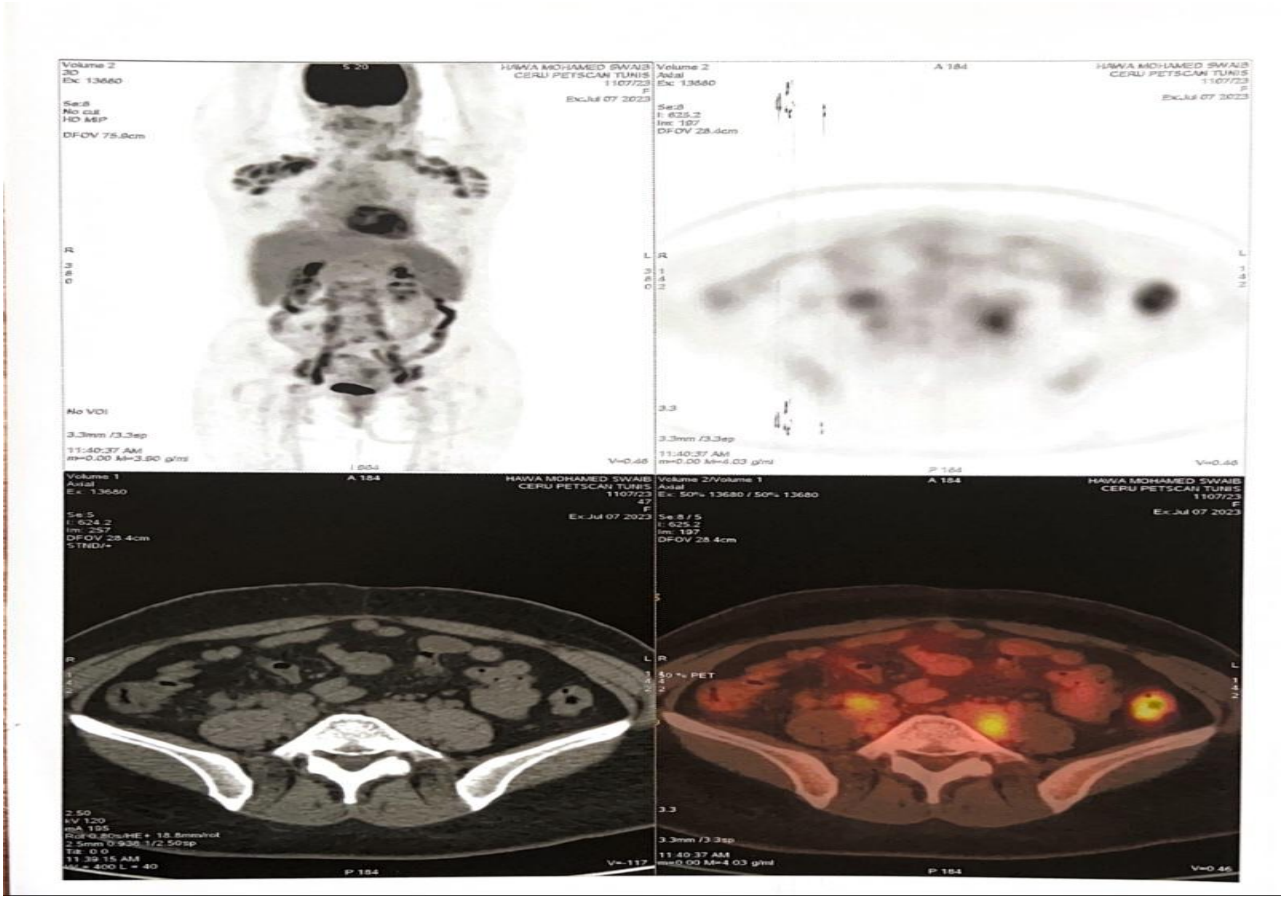

Figure 3. Detailed axial PET-CT sections showing hypermetabolic activity in the retroperitoneal lymph nodes.

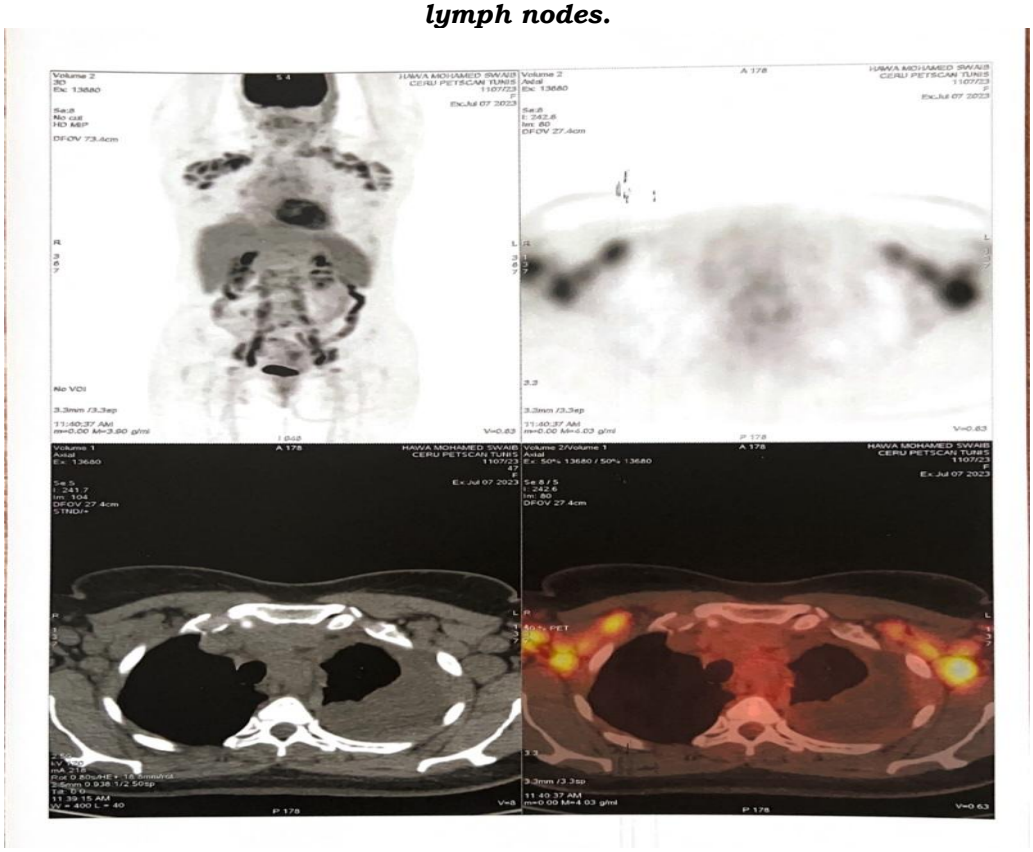

Figure 4. PET-CT scan showing extensive mediastinal and axillary lymphadenopathy, alongside a left-sided pleural effusion.

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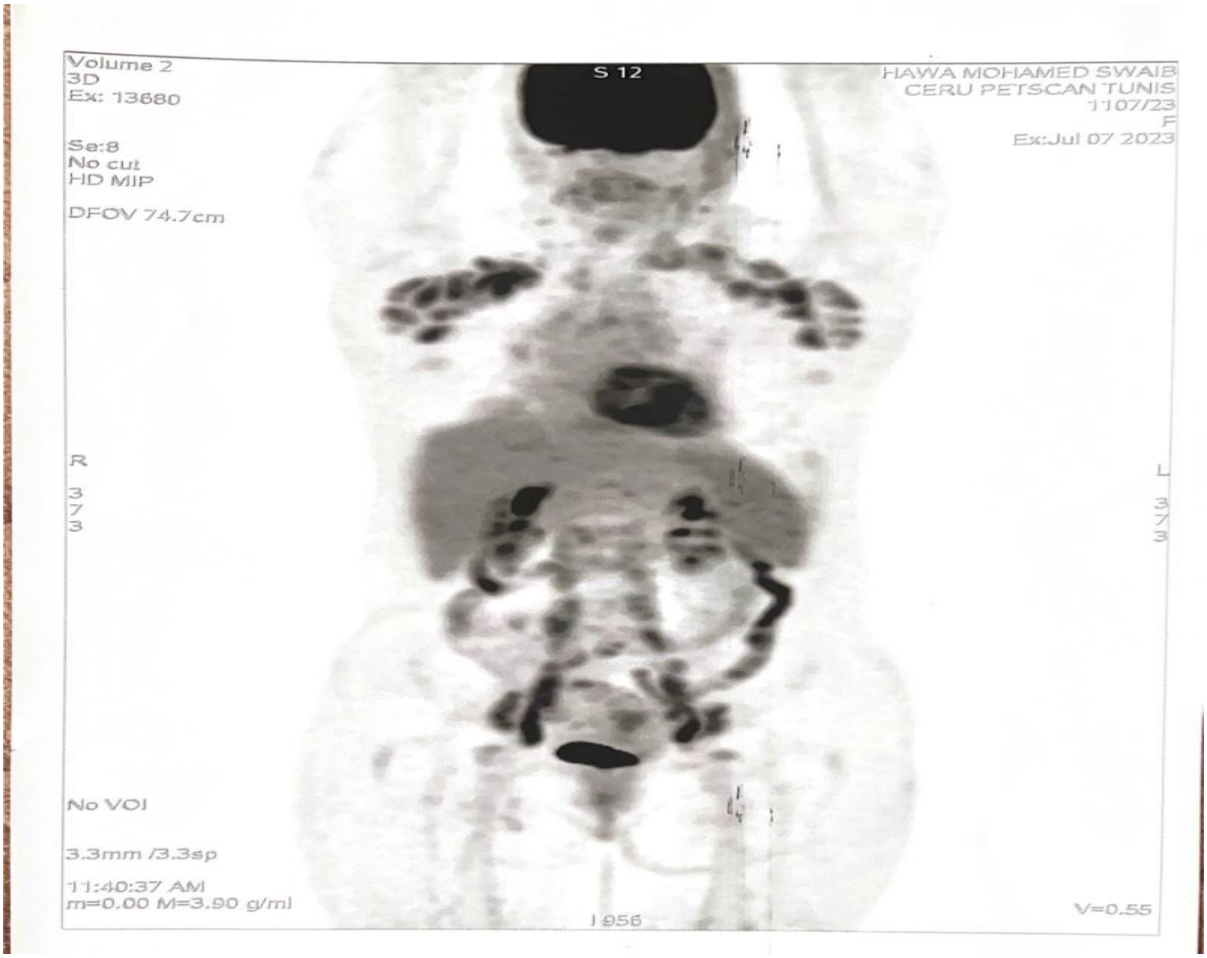

Figure 5. Maximum Intensity Projection (MIP) image of the initial PET-CT showing the widespread distribution of the Hodgkin Lymphoma at diagnosis.

The diagnostic work-up included a complete blood count showing mild normocytic anemia (hemoglobin 11 g/dL) with normal white cell counts. Inflammatory markers were elevated (CRP 59 mg/L). Routine chemistry, liver function tests, and coagulation profile were normal. Tuberculin skin test and tumor markers (CA19-9, CA125, ACE) were negative. Pleural fluid analysis was lymphocyte-predominant and negative for infection, including tuberculosis. Chest X-ray and CT angiography confirmed a left pleural effusion without pulmonary embolism. Pleural biopsy was non-diagnostic. The key diagnostic procedure was an excisional lymph node biopsy, which provided the definitive diagnosis of classical Hodgkin lymphoma. Staging PET-CT established Ann Arbor stage IIIAb.

Multidisciplinary management

The patient was managed jointly by rheumatology and hematology/oncology.

SLE management during chemotherapy

Hydroxychloroquine 400 mg daily was continued. Prednisone was tapered from 7.5 mg to 5 mg daily. No SLE flare occurred during chemotherapy.

The patient received two cycles of the BEACOPP protocol (bleomycin, etoposide, doxorubicin, vincristine, cyclophosphamide, procarbazine, prednisolone) over weeks 1–6. An interim PET-CT at week 7 showed a complete metabolic response (Deauville score 3). She then received four cycles of the ABVD protocol (Adriamycin, bleomycin, vinblastine, dacarbazine) over weeks 8–22.

She developed grade 2 neutropenia and mild anemia (hemoglobin nadir 9.5 g/dL), which were managed with granulocyte colony-stimulating factor and iron supplementation. No febrile neutropenia or severe infections occurred.

A post-treatment PET-CT at week 24 confirmed complete metabolic remission (Deauville score 1). Figure 6 provides a direct comparison between the pre-treatment and post-treatment scans, demonstrating the resolution of previously active lymph nodes. At 12- and 18-month follow-up, the patient remains in complete remission from HL. Her SLE remains quiescent on hydroxychloroquine and prednisone 5 mg daily. She has returned to full activities with no constitutional symptoms or lymphadenopathy.

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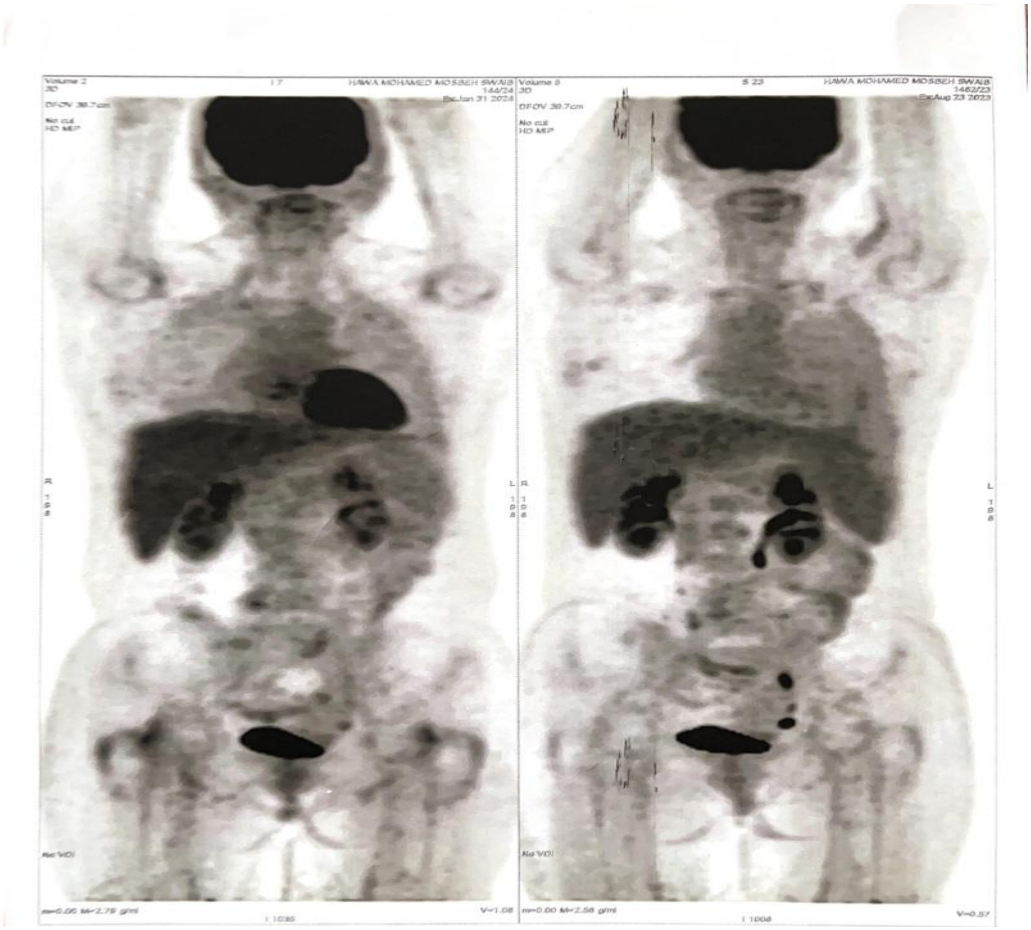

Figure 6. Follow-up PET-CT scans comparing the initial state (right) with the post-treatment state (left), demonstrating complete metabolic remission and resolution of previously active lymph nodes.

Discussion

Patients with SLE are at increased risk of lymphomas compared to the general population [1]. Large cohort studies and meta-analyses consistently demonstrate that this risk is particularly elevated for hematologic malignancies, including both non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) [2]. Although HL is less common than NHL, pooled data indicate a standardized incidence ratio (SIR) of approximately 3.16 (95% CI, 1.63–5.51) for HL in SLE patients [3], meaning SLE patients are over three times more likely to develop HL than age- and sex-matched controls. The risk is notably higher in patients with long-standing disease (>10 years) and those previously exposed to immunosuppressive therapy [4,5]. The pathogenesis is multifactorial, involving chronic immune stimulation, viral oncogenesis, treatment-related effects, and genetic susceptibility [6–8]. Chronic immune stimulation: Persistent B-cell activation in SLE results in polyclonal expansion, increasing the likelihood of oncogenic mutations [6,7].

Viral oncogenesis: EBV infection has been implicated [7]. SLE-associated immune dysregulation can impair cytotoxic T-cell control, facilitating uncontrolled B-cell proliferation [7,8]. Higher EBV viral loads are reported in SLE-associated lymphomas [8]. Treatment-related risk: Alkylating agents and prolonged corticosteroid use may impair immune surveillance [9]. Some studies suggest medication exposure correlates with higher lymphoma incidence, while others indicate disease activity itself may be a stronger predictor [9,10].

HL in SLE frequently presents with symptoms overlapping active lupus [2]. Common features include long-standing SLE (>10 years) [4], constitutional “B symptoms” [3], progressive lymphadenopathy [2], and splenomegaly [2]. Our patient exhibited fever, pleuritic chest pain, progressive lymphadenopathy, and splenomegaly, consistent with prior reports [4,3].

Due to overlapping findings, clinicians should maintain a low threshold for tissue biopsy in patients with persistent or unexplained lymphadenopathy [2,6]. Excisional lymph node biopsy remains the gold standard, allowing identification of Reed–Sternberg cells and assessment of nodal architecture [6]. Fine-needle aspiration is often insufficient. Imaging (CT, PET-CT) is crucial for staging and monitoring [3,9].

Standard chemotherapy regimens such as ABVD or BEACOPP are effective in SLE patients when coordinated with rheumatology [3,9]. Multidisciplinary management ensures control of SLE activity, management of cytopenias, and infection prevention [9,10]. Our patient tolerated chemotherapy well,

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achieved complete metabolic remission, and remained in remission at 18 months [3,9,10], supporting that SLE does not necessarily worsen HL prognosis when treated appropriately.

Conclusion

This case emphasizes the need for a high index of suspicion for lymphoma in patients with long-standing SLE who develop new constitutional symptoms, unexplained lymphadenopathy, or organomegaly. Early excisional biopsy is essential for timely diagnosis. A multidisciplinary approach balancing autoimmune disease control with immunosuppressive chemotherapy is crucial. Modern regimens such as BEACOPP and ABVD can achieve durable remission, as demonstrated here. Vigilant monitoring and coordinated care optimize both oncological and rheumatological outcomes.

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