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Evaluation of primary musculocutaneous Hodgkin's lymphoma with the aid of ^{18}F FDG PET/CT – a rare entity

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ABSTRACT

Introduction and aim. Primary musculocutaneous lymphoma is extremely rare and associated with poor prognosis. Here, we present a case of refractory primary muscular lymphoma with overlying cutaneous involvement with the aid of 18F-Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F FDG PET/CT) for staging and treatment.

Description of the case. We present the case of a 52-year-old man presented with musculocutaneous Hodgkin's lymphoma having swelling and discolored areas over the left leg and right arm associated with itchiness. Upon examination, there was scaling, erythema over the body with Gottron's papules on knuckles and heliotrope rash. Skin and muscle biopsy were suggestive of Hodgkin's lymphoma. This patient was had primary musculocutaneous lymphoma. His diagnosis was delayed. PET/CT was performed for staging and response to treatment, which was suggestive of refractory disease.

Conclusion. PET/CT plays a vital role in diagnosis, staging, response to therapy and helps in optimized treatment for these specific patients.

Keywords. cutaneous lymphoma, muscular lymphoma, musculocutaneous Hodgkin's lymphoma, refractory

Introduction

Lymphomas are a heterogeneous group of neoplasm derived from lymphoid cell linages that vary widely in presentation, clinical features, and prognosis. Although extra nodal involvement of lymphoma is common, involvement of muscular/ cutaneous/ musculocutaneous/ musculoskeletal lymphoma is rare

because of nodal disease spread into the adjacent structures i.e. secondary.[1-5] Hybrid imaging modalities like PET/CT are not routinely used for typical cutaneous lesions although if the typical cutaneous lesions have the presentation of paraneoplastic conditions as in our case, PET/CT definitely helps in early diagnosis, staging, early initiation of treatment, response evaluation, as well as changes in the treatment plan accordingly.

Aim

We present a case of primary musculocutaneous Hodgkin's lymphoma with a description of the clinical, pathological, radiological features and PET/CT findings and treatment history.

Description of the case

A 52-year-old man was presented to our hospital with complaints of swelling and discolored areas over the left leg and right arm associated with itchiness. Initially he started on treatment for varicose veins but his symptoms didn't improve. Along with that, he complained of unintentional weight loss without any history of night sweats or fever. The patient was then referred to the dermatology department for the discolored itchy lesions. Upon examination, there was fine scaling with erythema/discoloration over the body predominantly right arm and left leg with Gottron's papules on knuckles and heliotrope rash around the both eyes (Fig. 1).

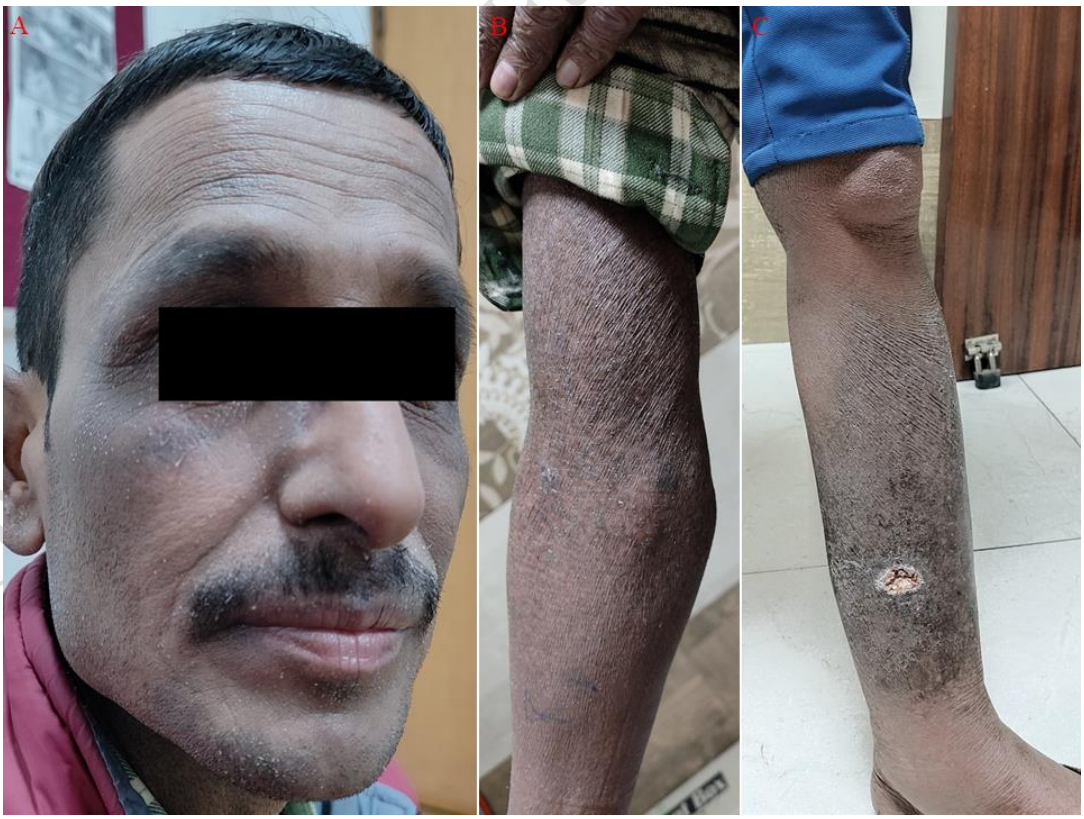

Fig. 1. A: Heliotrope rash on face, hyperpigmented scaly skin lesions of B: right arm C: and left leg

However, there was no complaint of any muscle weakness. Also, there were palpable lymph nodes in axillary and inguinal regions. For clinical evaluation contrast enhanced magnetic resonance imaging of the right arm and left leg were performed which revealed ill-defined heterogeneously enhancing soft tissue thickening with altered signals in subcutaneous tissue and muscles of flexor compartment of right arm and anterior, lateral and superficial posterior compartment of left leg. Multiple enlarged right axillary lymph nodes were also noted. The findings were suggestive of an inflammatory etiology likely dermatomyositis. The blood investigation shows raised LDH, and C reactive protein. ESR and antinuclear antibodies were positive (3+, speckled). Based on clinical suspicion, laboratory findings and radiological investigation, provisional diagnosis of erythrodermic dermatomyositis was made. The patient underwent FNAC from right axillary lymph node and skin and muscle biopsy from the left leg and right arm. The cytology findings from the lymph nodes were suggestive of Hodgkin's lymphoma and skin and muscle biopsy showed infiltration by Hodgkin's lymphoma likely mixed cellularity subtype. Immunohistochemistry was positive for CD 15 and CD 30 antigens. Then, the patient was referred to our department for a staging PET/CT, which revealed FDG avid multiple axillary, abdominal, pelvic and inguinal lymph nodes along with FDG avid mixed sclerotic lytic lesion in few dorsolumbar vertebrae and pelvis. FDG avid soft tissue thickenings were seen involving the cutaneous, subcutaneous tissue and muscle of upper arm, bilateral upper thigh & left lower leg. Patients had Deauville score 5. According to Lugano's classification, the patient was staged as IVb. The patient was then started on an ABVD regimen (adriamycin, bleomycin, vinblastine and dacarbazine).

After 3 cycles of ABVD chemotherapy, interim PET/CT was performed, which was suggestive of partial response to therapy with significant reduction of size, number and metabolic activity of lymph nodes, bony and right arm and left leg lesions (Deauville score 4). Completion chemotherapy PET/CT findings were suggestive of persistent hypermetabolism in right axillary, pelvic and inguinal lymph nodes, skeletal lesions and right arm and left leg cutaneous, subcutaneous and muscular lesions (Deauville score 4). There is appearance of similar type of cutaneous lesion in left arm. Then patient was switched to GDP regimen (gemcitabine, dexamethasone and cisplatin) and he underwent 4 cycles of chemotherapy. The PET/CT was performed after 3 months to look for response to the second line chemotherapy which revealed that there was increase in size and metabolic activity of axillary, pelvic and inguinal lymph nodes with diffuse hypermetabolism in the spleen along with persistent cutaneous and muscular lesions (Deauville score 4). Previously metabolically active bone lesions showed sclerosis with no FDG uptake. The PET/CT findings were suggestive of refractory disease (Fig. 2 and 3).

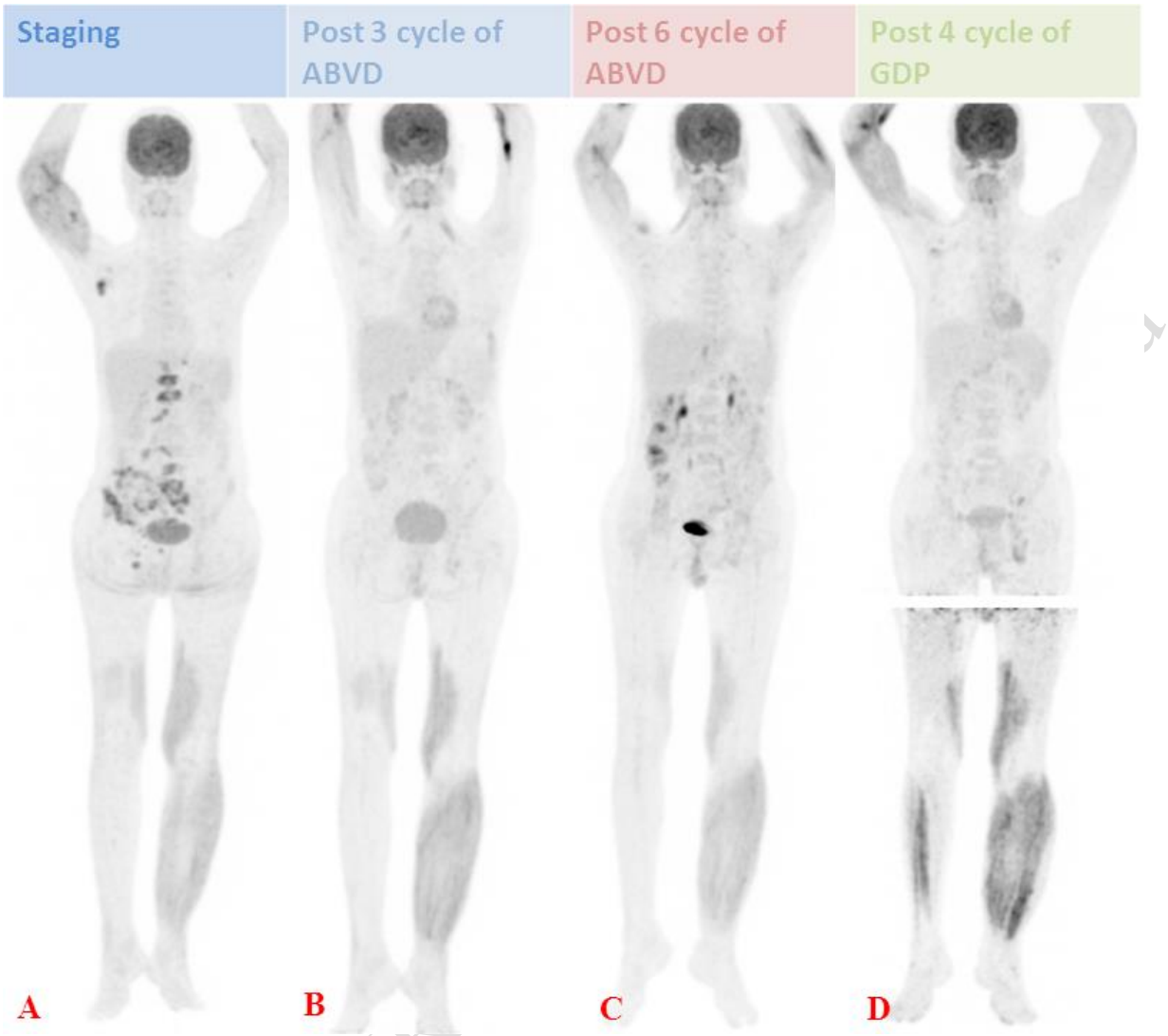

Fig. 2. Maximum intensity projection (MIP) image of ^{18}F FDG PET scan A: on staging PET demonstrate diffuse FDG uptake in right upper & bilateral lower extremities along with focal FDG uptake in right axillary, abdomino-pelvic and right inguinal region, B: interim PET demonstrate the partial response to treatment C: after 6 cycle of ABVD chemotherapy PET demonstrates appearance of new lesion in left upper extremity along with no significant change in previously seen extremity lesions after completion of chemotherapy D: post 4 cycle of GDP chemotherapy PET demonstrates decrease in metabolic activity of left upper extremity along with increased metabolic activity of previously seen extremity lesions and hypermetabolic spleen

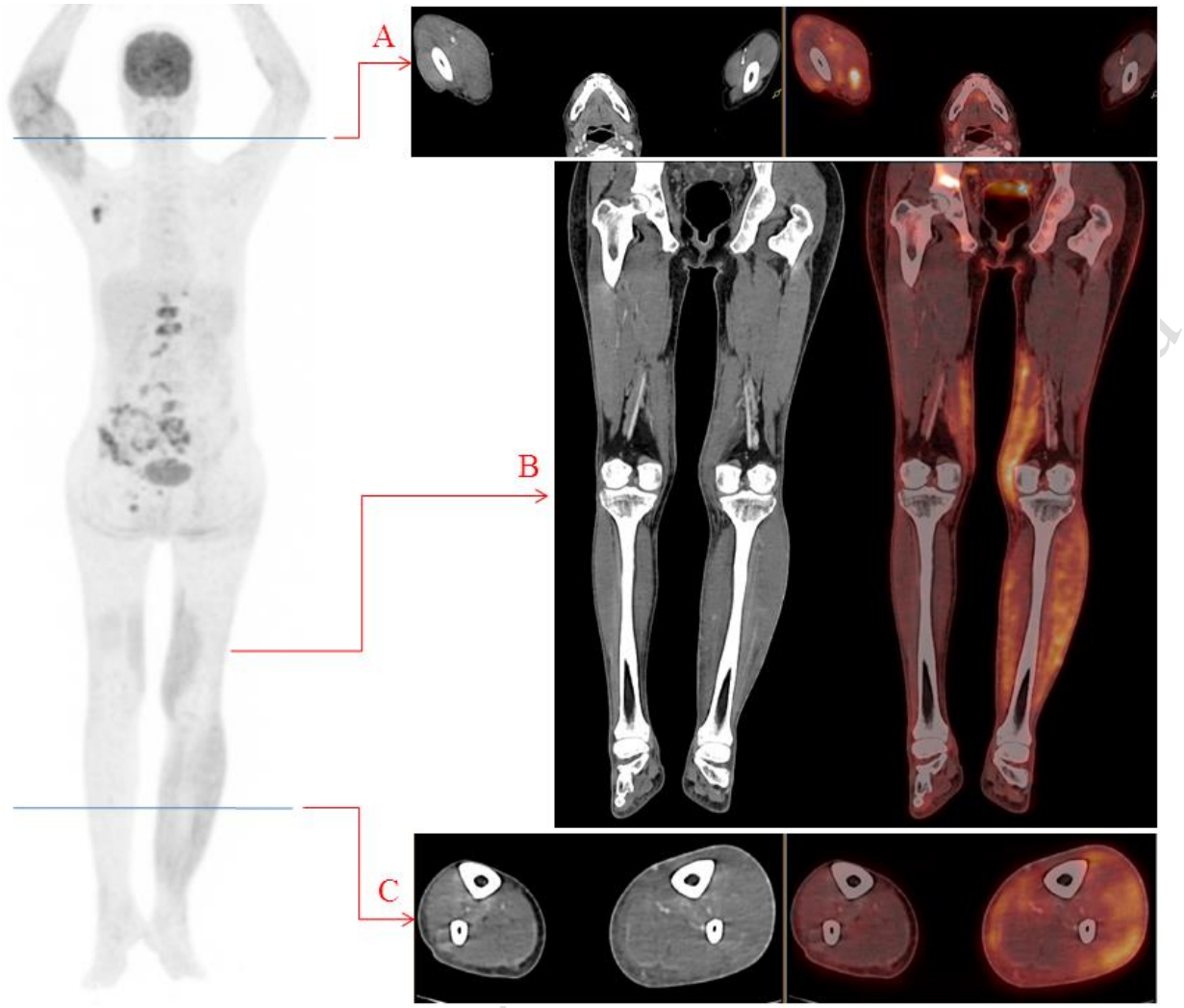

Fig. 3. Maximum intensity projection (MIP) image of staging ^{18}F FDG PET scan A: axial section at the level of mid arm of CT and corresponding PET/CT shows metabolically active musculocutaneous lesion with enlarged muscles of left extremity without CT attention changes in muscles B and C: coronal and axial sections of CT and corresponding PET/CT show metabolically active bilateral semitendinosus, left leg muscles and overlying skin lesions without CT changes in enlarged affected muscles

Discussion

Hodgkin's lymphoma previously known as Hodgkin's disease is a rare monoclonal lymphoid proliferative disease with a high chance of being cured.[6] It constitutes a significant proportion of malignancy with bimodal age distribution. The etiology and pathophysiology for disease remains unclear, however a few risk factors have been identified like familial predisposition, immunocompromised state, Epstein Barr virus or Human immunodeficiency virus infection etc.[7] The WHO has divided Hodgkin's lymphoma into two major groups: classical Hodgkin's lymphoma and nodular lymphocytic predominant. The classical Hodgkin's lymphoma is more common than the nodular lymphocytic predominant and it is further divided

into 4 subgroups: nodular sclerosis, mixed cellularity, lymphocyte rich and lymphocyte depleted.[8] The disease is clinically characterized by the lymph node infiltration usually in the cervical, mediastinal and axillary regions with contiguous lymph node group involvement and may have extra nodal involvement.[9] The involvement of other organs is usually limited to spleen, liver, bone or lungs; skin involvement is rare.[10] Cutaneous lymphoma has non-specific findings like pruritus, urticaria, papules, nodules, infiltrative plaques, hyperpigmentation, ichthyosis, ulcerative lesion or combined as erythroderma.[11,12] The three methods for the involvement of skin in Hodgkin's lymphoma have been proposed i.e. hematogenous dissemination, direct extension from the disease involved lymph nodes, and retrograde lymphatogenous spread from involved proximal lymph nodes. According to previously published case reports, the most common route is supposed to be retrograde lymphatogenous spread from the involved lymph nodes as in most of the cases the involved skin areas were drained by the involved lymph nodes.[13] However, in our case, there is involvement of muscle, subcutaneous and cutaneous tissue which can be either retrograde lymphatogenous spread or direct hematogenous spread. The involvement of skin and muscle classifies patient under stage IV (Ann Arbor staging system) and there is no specific therapeutic regimen for cutaneous involvement.

Lymphomatous involvement of muscles occurs in approximately 1.4% of cases, with 0.3% occurring in Hodgkin lymphoma and 1.1% in non-Hodgkin lymphoma.[3] Primary cutaneous Hodgkin's lymphoma is extremely rare entity with good prognosis.[5] Here we are dealing with the refractory musculocutaneous Hodgkin's lymphoma. Skeletal muscle lymphoma may be primary or secondary to invasion of the adjacent disease. Skeletal muscle lymphoma usually presents with painful enlargement of affected muscle representing as a diagnostic challenge to differentiate from various manifestation like deep vein thrombosis and various other benign and alignment neoplasms of muscles and bone.[3] In our patient, there were muscular lesions with cutaneous manifestations and these made definitive diagnosis complicated and delayed. The patient was treated with six cycles of ABVD and followed by three cycles of the GDP regime. The patient showed partial remission after three cycles of chemotherapy after that refractory.

PET/CT is helpful in early diagnosis and initiation of optimal treatment in such fairly rare cases. In our case, there was a delay in diagnosis and start of the treatment. The actual disease burden is much more than clinical presentation. As on CT, skeletal muscle lymphomas are either iso/ hypodense and these lesions are metabolically active on FDG PET/CT i.e. occult disease involvement or identifying extracutaneous disease. As we know, the stage of the disease is the most important predictor of the prognosis in primary cutaneous lymphoma and PET/CT provides the actual stage of the disease which guides the clinician for optimal individualized patient centered treatment plan selection. PET/CT provides not only the actual global disease burden in primary cutaneous/ musculocutaneous lymphoma but it also provides the quantitation of overall disease burden.[14] Quantitative data helps in response evaluation, restaging, surveillance and prognostication.

Conclusion

Primary muscle/musculocutaneous lymphoma is extremely rare. Patients of musculocutaneous lymphoma usually presented with pain, muscle enlargement with or without regional lymphadenopathy along with cutaneous lesions. On CT, masses are usually isodense to muscle. FDG PET/CT play a vital role in detection of muscle/ cutaneous involvement that is occult on CT. FDG/CT is also helpful in diagnosis, staging, therapeutic response evaluation with significant impact on therapeutic decisions, restaging, surveillance and prognostication.

Declarations

Funding

No funding was obtained for this study.

Author contributions

Conceptualization, M.M.S. and L.K.; Methodology, M.M.S.; Validation, L.K., M.M.S., S.D. and P.B.T.; Formal Analysis, S.D.; Investigation, P.B.T.; Data Curation, M.M.S.; Writing – Original Draft Preparation, L.K. and M.M.S.; Writing – Review & Editing, M.M.S.; Visualization, P.B.T.; Supervision, M.M.S. and S.D.

Conflicts of interest

There are no conflicts of interest.

Data availability

The dataset used and/or analysed during the current study available from the corresponding author on the reasonable request.

Ethics approval

Written consent to participate.

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