

EHA-MSH Hematology Tutorial

Clinical Case – Session 6:
Imaging in Hodgkin Lymphoma

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| Disclosure

- The presenter has no conflicts of interest to disclose as related to companies or products mentioned in this presentation

| Learning objectives

Following participation in this activity, attendees will be able to:

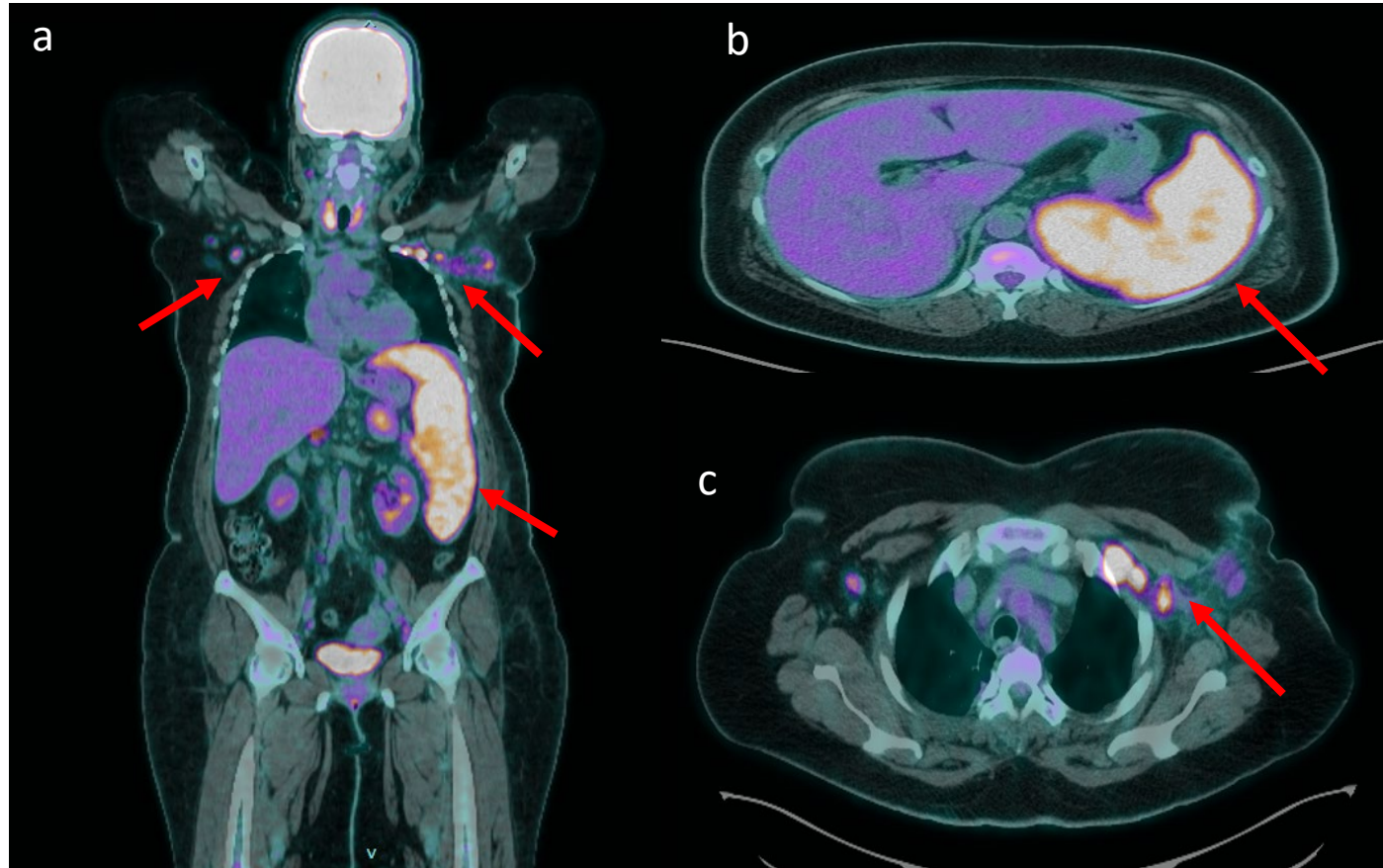
- Recognize the PET/CT scan as imaging modality of choice in staging, response assessment, and surveillance
- Understand the benefits of PET/CT scan in staging, prognosis, and management of Hodgkin lymphoma
- Collaborate with nuclear medicine specialists to interpret imaging findings
- Implement regular monitoring and surveillance protocols to detect disease progression and early relapse

| Clinical history

- 50-year-old female patient with no relevant medical history; ECOG PS of 1
- Patient presented in February 2022 with intermittent fever and left-axillary swelling progressively increasing in size
- Sought treatment at private center → excision biopsy performed
- HPE of left-axillary node:
 - Scattered atypical lymphoid cells; some cells binucleated, resembling Reed–Sternberg cells
 - Atypical cells were weakly and variably positive for CD30, PAX5, CD79a, MUM1, and OCT2

Impression: Suggestive of classical Hodgkin lymphoma

| Staging



a: Coronal image of baseline PET/CT scan showed abnormal hypermetabolism involving multiple nodal sites and spleen.
b: Axial PET/CT image revealed hypermetabolic spleen.
c: Axial PET/CT image revealed hypermetabolic axillary nodes.

Staging CT-NTAP at private center

- Multiple lymphadenopathies of supra- and infradiaphragm with splenomegaly
- No focal splenic lesions

PET/CT scan

- FDG-avid lymphoma involving multiple nodal sites on both sites of the diaphragm and spleen
- Focal hypermetabolic left-rib lesion
- Diffuse hypermetabolic marrow

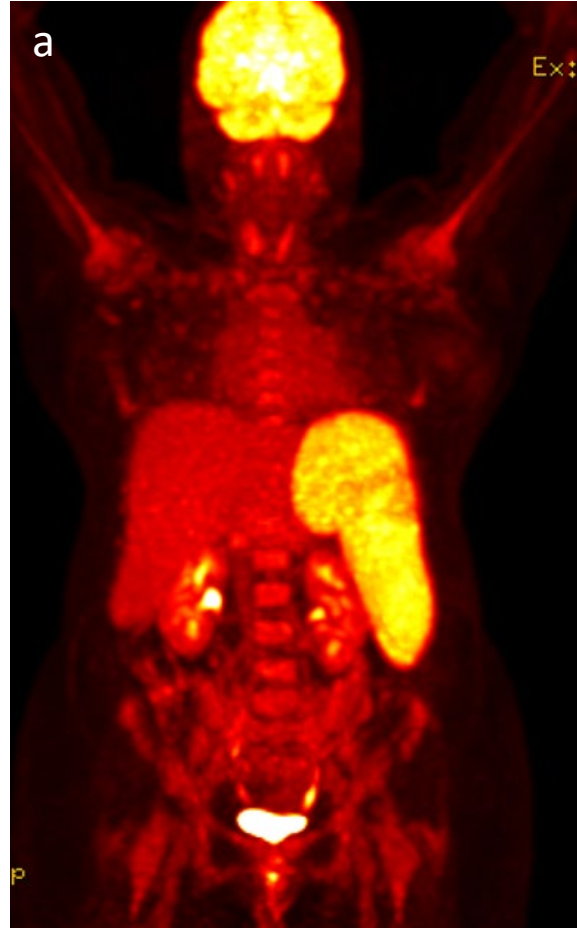
| Clinical history

- Bone marrow aspiration and trephine biopsy
→ no evidence of marrow infiltration

Impression: Classical Hodgkin lymphoma, stage 4, IPI score 4

Clinical history

- Received 2 cycles of BEACOPP in April/May of 2022
- Patient developed neutropenic sepsis → recovered with antibiotics and G-CSF
- Patient had COVID-19 pneumonia (category 1) after second cycle of BEACOPP



a: Interim PET/CT showed resolved axillary lymph-node metabolic activity with persistent hypermetabolic spleen.

Interim PET scan:

- Majority of nodes have reduced in size and metabolic activity (some resolved)
- Only peripancreatic node remains at Deauville score of 4
 - Smaller in size
- No new hypermetabolic nodes
- The spleen remains enlarged (stable in size) and hypermetabolic (SUV_{max} 7.4)
- Hypermetabolic lesion on left-seventh rib resolved

**Disease status:
partial response**

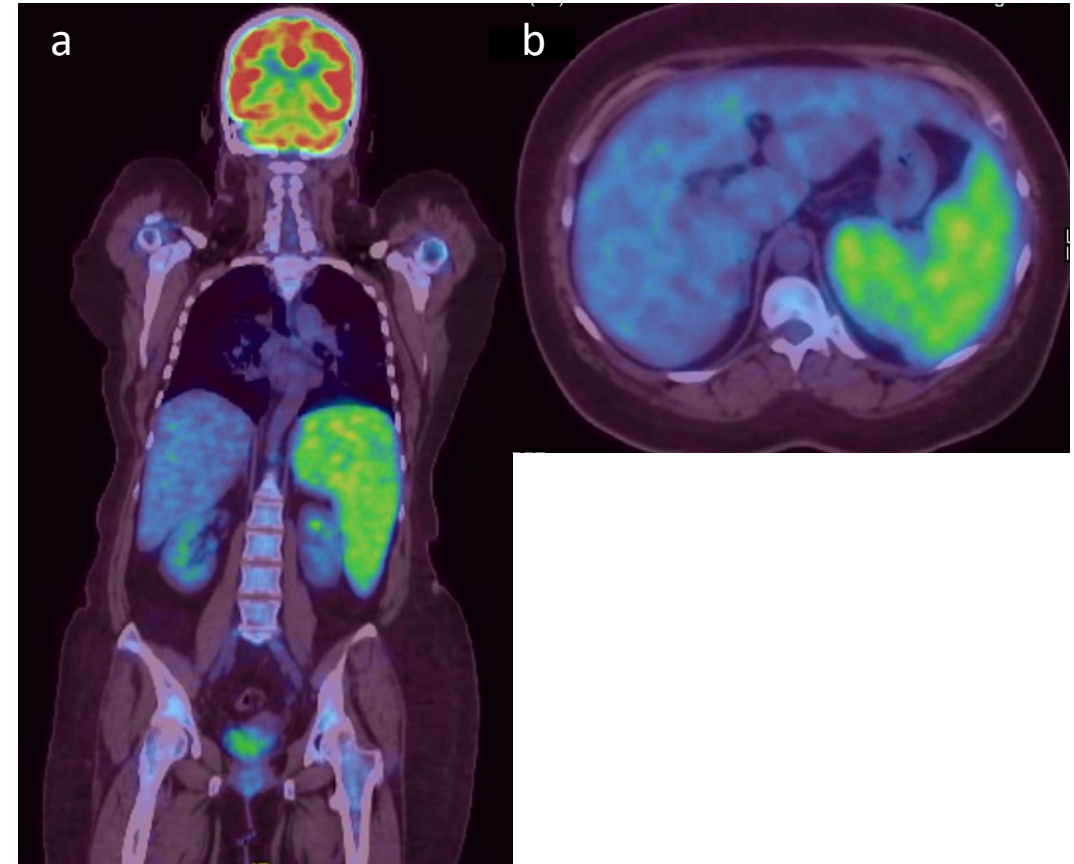
Patient continued with
2 further cycles of BEACOPP

Clinical history

- Total of 4 cycles of BEACOPP received
- PET/CT scan on August 3, 2022
- Splenomegaly is noted
 - Interval decrease in CC length (20.7 cm vs 22.4 cm)
- Stable diffuse FDG increase noted within the spleen
 - SUV_{max} 7.0 (Deauville score of 4) vs SUV_{max} 7.4 (Deauville score of 4)

Impression:

- No hypermetabolic nodal disease above or below the diaphragm
- Stable diffuse FDG increase noted within the enlarged spleen
- No hypermetabolic extranodal disease elsewhere



a, b: PET/CT scan showed diffuse enlarged hypermetabolic spleen.

| Clinical history

- Patient is clinically well
- Refractory Hodgkin lymphoma
- Persistent splenomegaly with PET-positivity and stable SUV
- Resolution of previous hypermetabolic nodes

What is a possible next step?

| Clinical history

Spleen biopsy report:

- Non-targeted spleen biopsy was done under ultrasound guidance
- A few small fragments of splenic tissue embedded in blood clot
- No Hodgkin cells or Reed–Sternberg cells were observed
 - Highlighted by CD30 and CD15
- No evidence of malignancy

Impression:

- Benign splenic tissue
- The biopsy specimen is scant; suggest a repeat biopsy if clinically indicated

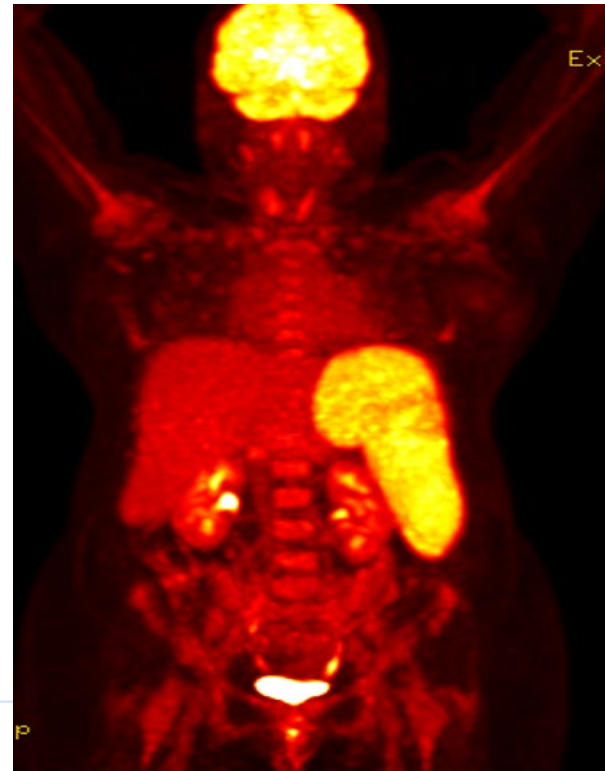
Clinical history

- Proceed with 2 cycles of salvage chemotherapy (with ICE and R-ICE)
- Patient applied for financial support for brentuximab due to financial constraints

Post salvage PET/CT scan:

- Enlarged peripancreatic node with fluctuating metabolic activity
 - Deauville score of 4 (previously Deauville score of 2)
- Bilateral subcentimeter external iliac nodes demonstrate fluctuating metabolic activity
 - Deauville score of 3 or 4 (previously Deauville score of 2)
- Further increase in size of the diffuse hypermetabolic spleen with slight reduction in metabolic activity (SUV_{max} 6)
- Indeterminate response, likely due to immune-related changes

After 2 cycles of BEACOPP



After 4 cycles of BEACOPP + 2 cycles of ICE



| Clinical history

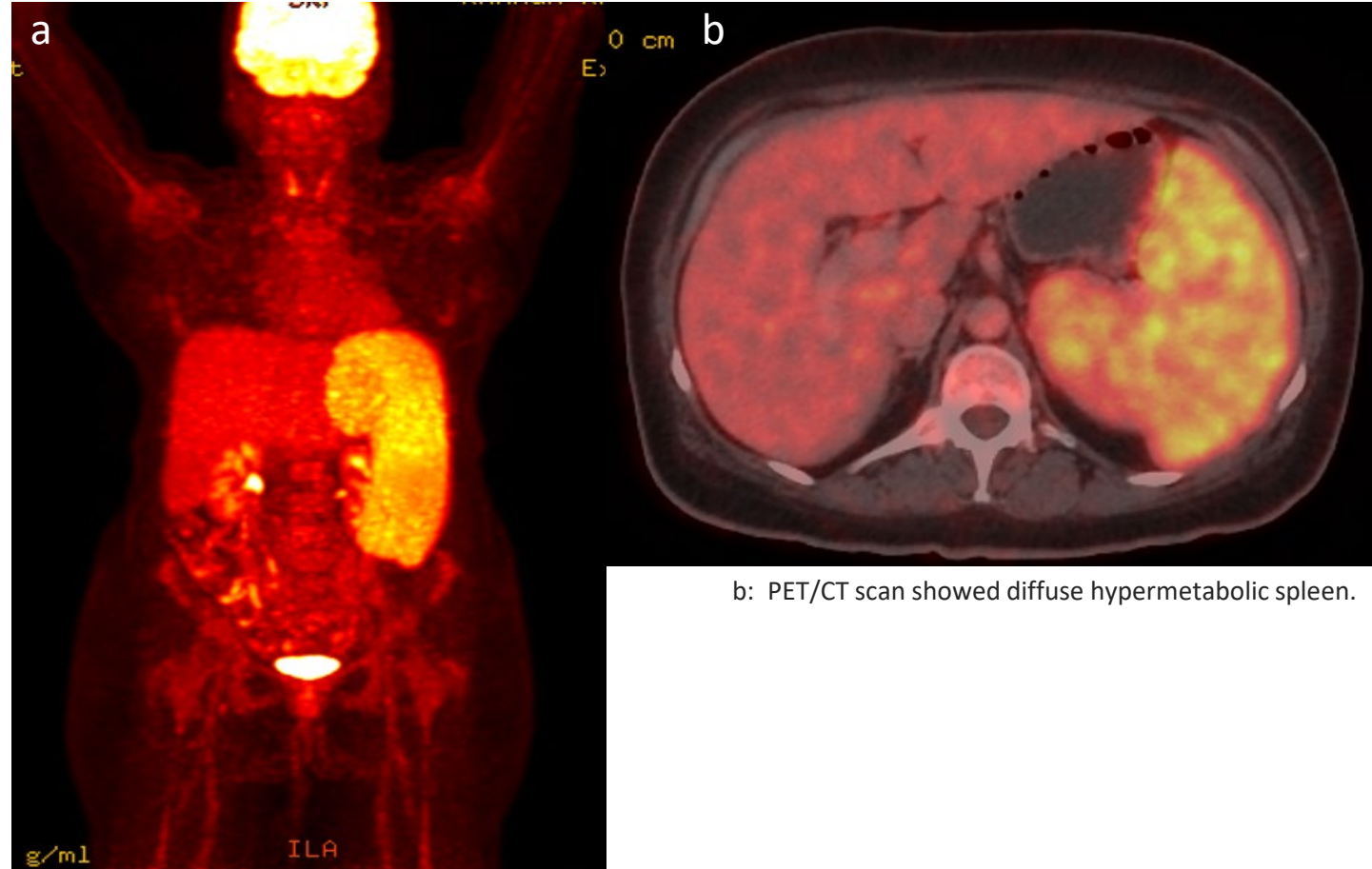
- Patient was given third-line DHAP
- Attempt was made to harvest stem cells → collection was not successful
- Financial support was approved for 1 vial of brentuximab only
- Therefore, patient received 2 further cycles of DHAP

PET/CT scan after 3 cycles of DHAP

1. All previously seen supra- and infradiaphragmatic nodes have reduced in size and metabolic activity (fluctuating); nodes are subcentimeter
→ Deauville score of 2 or 3
2. Slight reduction in size of the diffusely hypermetabolic spleen
→ further increased hypermetabolism (from SUV_{max} 6 to SUV_{max} 7.7)

Impression:

- In view of finding in point 2, recommend re-biopsy, considered as indeterminate response, no suspicious residual nodal involvement, to correlate clinically.



a: PET/CT scan showed diffuse hypermetabolic spleen with no suspicious nodal involvement.

b: PET/CT scan showed diffuse hypermetabolic spleen.

| Clinical history

- Failed three lines of chemotherapy; failed mobilization
- Discussed options for radiotherapy
- Patient is clinically well with no B symptoms

- Currently at ~ 1 year since diagnosis of Hodgkin lymphoma
- Eager to return to work
 - Patient is a single mother, sole breadwinner
- After discussion, decision is to watch and wait (with PET surveillance)

Clinical history

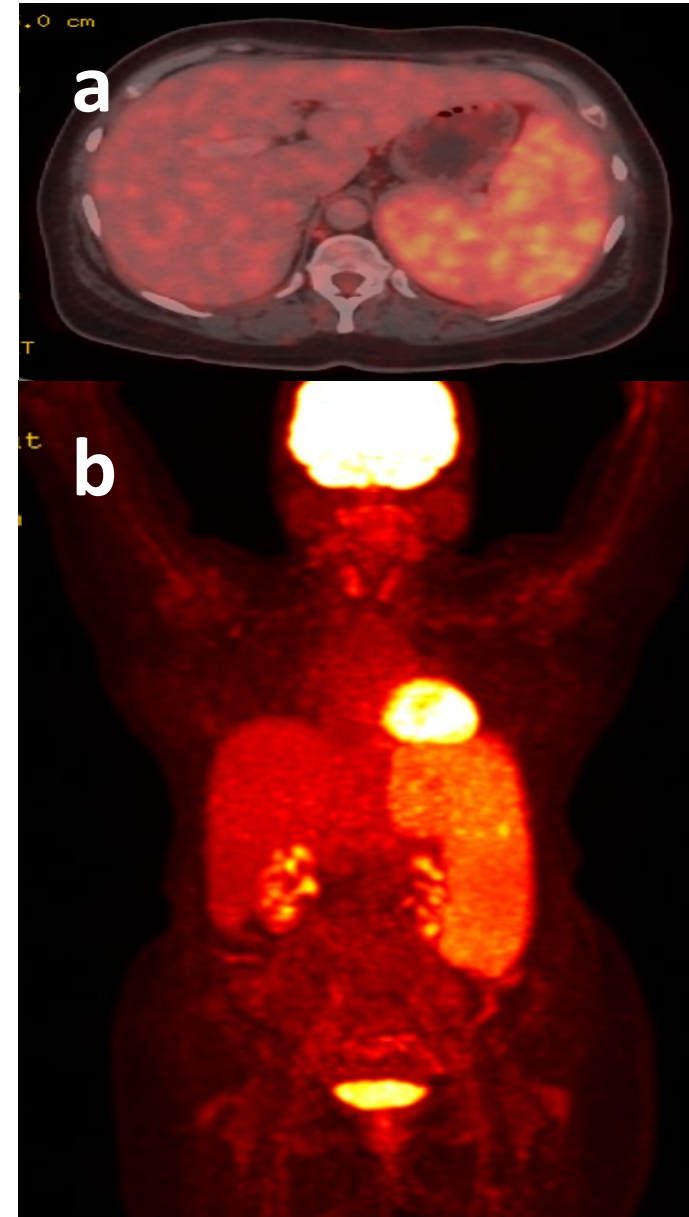
- Patient received 2 cycles of brentuximab 100 mg
 - Obtained through compassionate use from another patient

PET CT scan on October 11, 2023

1. All previously seen subcentimeter supra- and infradiaphragmatic nodes have either resolved or remain similar in size, but demonstrate reduced metabolic activity → Deauville score of 2
2. Slight reduction in size and metabolic activity of the diffusely hypermetabolic spleen with no associated hypodense lesions seen on CT images → persistent hypermetabolism (SUV_{max} 5.2)

Impression:

- Unable to suggest site for biopsy as there is no obvious CT lesion, and the entire spleen demonstrates diffuse hypermetabolism with no focal uptake

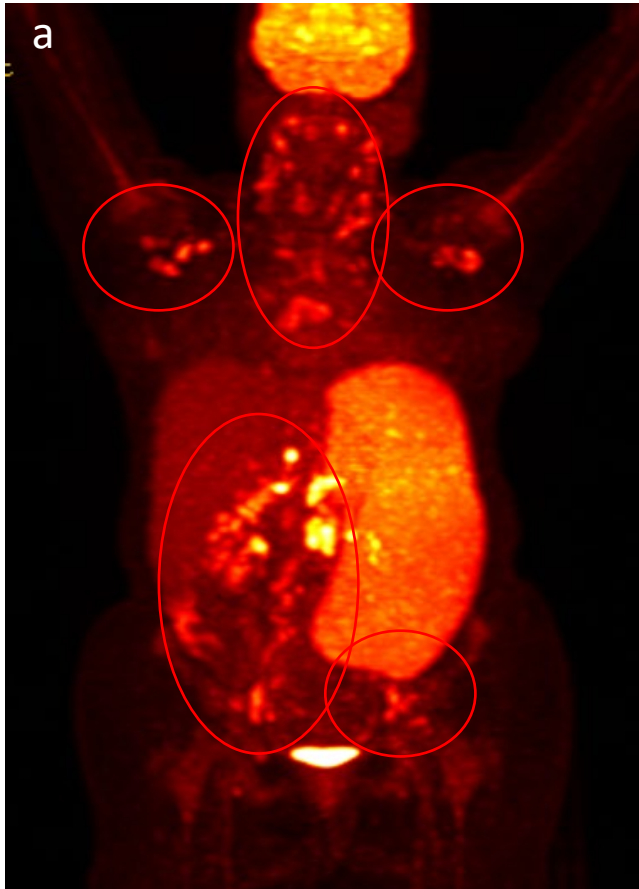


a: PET/CT showed hypermetabolic spleen.
b: PET/CT showed persistent hypermetabolic spleen.

| Clinical history

- In total, patient received 4 cycles of brentuximab; last was administered in December of 2023

PET/CT scan: February 29, 2024



a: PET/CT scan coronal view revealed emergence of new hypermetabolic nodes over supra- and infradiaphragm.

Lymphoid: MBP SUVmax 1.5

Numerous new hypermetabolic nodes have emerged at the:

- bilateral level II, III, and IV cervical nodes (SUVmax 3.0 - 5.7, SAD 0.4 - 0.8 cm) - Deauville 4
- bilateral supraclavicular nodes (SUVmax 2.9 - 4.5, SAD 0.3 - 0.5 cm) - Deauville 4
- bilateral level I & II axillary nodes (SUVmax 2.7 - 5.4, largest SAD at the level I right axillary with 1.2 cm) - Deauville 4
- bilateral upper paratracheal, bilateral lower paratracheal, prevascular, aortopulmonary, subaortic, and subcarinal nodes (SUVmax 3.5 - 4.6, largest SAD at right upper paratracheal with 1.0 cm) - Deauville 4
- paraaortic (elongated and matted), paracaval, aortocaval, bilateral (common, internal, and external) nodes (SUVmax 3.7 - 11.1, largest at the paraaortic region, measuring 2.8 x 1.3 cm) - Deauville 5
- bilateral inguinal and bilateral femoral nodes (SUVmax 2.1 - 3.5, SAD 0.5 - 0.7 cm) - Deauville 4

The palatine tonsils are hypermetabolic bilaterally (SUVmax 5.7, left>right) with no obvious CT lesion. The nasopharynx and hypopharynx have normal morphology with physiological metabolism.

The enlarged spleen, displaying diffuse hypermetabolic activity, has significant increase in size (CC = 29.2 cm, previously CC = 24.7 cm, compared to 25.5cm) and exhibits increasing metabolic activity with an SUVmax of 7.0, in contrast to the previous SUVmax of 5.2 (compared to SUVmax 7.7). No discernible lesions are evident on the CT images.

→ Findings are suggestive of disease progression

Summary of serial PET/CT scans

	Date	PET findings
Staging ←	April 4, 2022	Multiple nodal sites on both sites of the diaphragm and spleen Focal hypermetabolic left rib lesion
BEACOPP × 2 ←	June 14, 2022	Spleen remains enlarged (stable in size) and hypermetabolic (SUV _{max} 7.4) At least partial response
BEACOPP × 2 ←	August 3, 2022	Splenomegaly with interval decrease in CC length Stable diffuse FDG with SUV _{max} 7.0 (Deauville score of 4)
ICE × 2 ←	November 1, 2022	Increase in size of the diffuse hypermetabolic spleen with slight reduction in metabolic activity (SUV _{max} 6)
DHAP × 3 ←	June 1, 2023	Slight reduction in size of the diffusely hypermetabolic spleen (SUV _{max} 7.7)
Brentuximab × 2 ←	October 11, 2023	Slight reduction in size and metabolic activity of the diffusely hypermetabolic spleen with no associated hypodense lesion seen on CT images → persistent hypermetabolism (SUV _{max} 5.2)
Brentuximab × 2 ←	February 29, 2024	New hypermetabolic nodes at supra- and infradiaphragm with increased SUV _{max} 7.0 of diffuse hypermetabolic spleen

| Discussion points

- FDG-PET/CT is the main imaging modality for staging and monitoring response to treatment
- PET-driven therapeutic strategy
- Early evaluation of treatment response
- Optimized disease control and toxicity

| Discussion points: Current challenges

- Lack of access to PET/CT services
- Financial burden
- False-positive and false-negative results
 - Inflammation, infection, technical artifacts
- Direct comparison between images produced by different scanners may not be possible
- Volumetric PET parameters
 - SUV_{max} is sensitive to image noise and motion; its value is dependent on image quality
 - Total metabolic tumor volume (TMTV), total lesion glycolysis (TLG)
- Immunotherapy evaluation
 - Challenging imaging-response evaluation, delayed response, pseudo-progression of the immune-related response¹

| Discussion points

- Interim FDG-PET/CT → predict response to brentuximab vedotin in relapsed and refractory Hodgkin lymphoma¹
 - FDG-PET/CT studies performed early after a median of 3 cycles of chemotherapy
 - One-year PFS was 100% in patients with negative interim FDG-PET/CT
 - Patients with positive interim FDG-PET/CT had one-year PFS of 38%
- Treatment modalities available for this patient:
 - Clinical trial (CAR-T cell therapy²)
 - Chemotherapy: Gemcitabine-based
 - Immunotherapy: Immune checkpoint inhibitors (pembrolizumab/nivolumab)

| References

- Cheson BD, et al. Refinement of the Lugano Classification lymphoma response criteria in the era of immunomodulatory therapy. *Blood*. 2016; 128: 2489-2496
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- Katsin M, et al. CAR-T cell therapy for classical Hodgkin lymphoma. *Hemasphere*. 2023; 7: e971



Thank you