PET Scan Reporting in Clinical Practice

6

Alberto Biggi

Abbreviations

5-PS	Five-Point Scale
AIMN	Associazione Italiana di Medicina Nucleare
BM	Bone Marrow
CT	Computed Tomography
DLBCL	Diffuse Large B-Cell Lymphoma
EANM	European Association of Nuclear Medicine
FDG	^{18}F-Fluoro-Deoxyglucose
HL	Hodgkin Lymphoma
HRS	Hodgkin and Reed-Sternberg Cells
PET	Positron Emission Tomography
SNM	Society of Nuclear Medicine
SUV	Standardized Uptake Value

6.1 Introduction

The medical report is "a written document by which the specialist states conform to the truth the results of diagnostic imaging, together with the clinical interpretation of the results themselves, in relation to the clinical and medical history" [1].

A. Biggi, MD
Nuclear Medicine Department, ASO Santa Croce e Carle, Cuneo, Italy
e-mail: biggi.a@ospedale.cuneo.it

The medical report is a structured as a formal vehicle for a written and understandable communication between the doctors and eventually between the doctors and the legal system. It represents the subjective interpretation of physical findings in images by the specialist (either nuclear medicine physician or radiologist), is based on the semiotics of a given imaging technique, and provides the answer to the clinical questions arisen by the treating physician. The content of each report will vary according to the exact circumstances concerning each case. While a degree of flexibility is necessary to encompass all the relevant points, a structured framework for the reporting document is strongly recommended. In general, the PET/CT report (a) describes the presence or absence of abnormal FDG accumulation in the PET images in combination with their size and intensity, (b) correlates these findings to other diagnostic tests and interprets them in that context, and (c) contextualizes imaging findings in the available clinical information in order to reply to specific question posed by the clinician.

The aim of this chapter is to suggest a minimum of dataset for PET reporting in lymphoma according to previously published guidelines or recommendations by EANM [2], SNM [3], AIMN [4], the expert session "How to report a baseline and end of treatment PET scan" held in Menton (France), September 18th, 2014 [5], the "Consensus of the International Conference on Malignant Lymphomas Imaging Working Group"

A. Gallamini (ed.), *PET Scan in Hodgkin Lymphoma*, DOI 10.1007/978-3-319-31797-7_6

[6, 7], and the author's personal experience. Finally, the framework for PET/CT reporting in lymphoma presented in this chapter has been drawn in accord with the general semiotics elements of nuclear medicine for clinical reporting.

6.2 Image Requirements for Reporting

Reporting is performed on reconstructed PET and CT images displayed on workstation screen. The software packages for current PET/CT systems enable visualization of PET, CT, and PET + CT fusion images in the axial, coronal, and sagittal planes as well as intensity projections in a 3D cine mode. PET images can be displayed with and without attenuation correction. On the attenuation-corrected images, quantitative information with respect to size and FDG uptake can be derived. Images must be evaluated using software and monitors approved for clinical use in nuclear medicine. Both uncorrected and attenuation-corrected images need to be assessed in order to identify any artifact caused by contrasts agent, metal implants, and/or patient motion. PET scans are best reported using a fixed display and color table scaled to the SUV to assist with consistency of reporting, for serial scans, and to reduce the effect of patient size.

6.3 How to Interpret PET/CT Images at Baseline and After Treatment

PET/CT has been used long since for pretreatment tumor burden assessment and staging purposes, as well as for treatment response assessment [8]. Tumor stage is just one of the prognostic indices increasingly used for pretreatment risk stratification and therapy selection. Recently a modification of the Ann Arbor classification for anatomic description of disease extension was proposed [7]. PET/CT is generally assessed using visual criteria; the SUV is currently used as a semiquantitative measure of the degree of FDG uptake, but it is not a determinant tool for scan interpretation. The detection limits of PET depend on the degree of contrast between the tumor and its immediate surroundings. PET is an intrinsically quantitative imaging technique and there are in principle no definite limits to the intensity of FDG uptake by the tissues. The latter, in turn, depends on histology (FDG avidity of the type of lymphoma), the burden of viable tumor cells, movement during acquisition (e.g., blurred signals in the case of pulmonary, hepatic, or splenic foci), and physiological uptake in the adjacent background. Although variable and depending on the clinical context, it has been demonstrated that the detection power of FDG-PET declines with the reduction of tumor diameter, being very low or absent for tumors with a diameter ≤6–8 mm, even in very FDG-avid tumors. The main criteria to report a PET/CT for staging purpose in lymphoma have been recently reviewed [9]. The typical finding of an abnormal scan is usually defined by a pathological focal FDG uptake in nodal and extranodal sites, including the spleen, liver, marrow/bone, or other organs. FDG accumulation should be visually compared to the background uptake in, e.g., mediastinum blood pool (MBPS) and the liver and reported as mild (≤ MBPS), moderate (> MBPS ≤ liver), or intense (> liver).

The hallmark of spleen involvement by lymphoma consists in a single or multiple areas of focal uptake with an activity higher than the liver with/without an enlarged spleen (longitudinal diameter > 13 cm) [10]. Both focal and diffuse uptakes with an activity higher than the liver are considered an harbinger of disease in non-Hodgkin lymphoma (NHL), while in Hodgkin lymphoma (HL), a histologic proof of organ involvement by disease has been reported only in presence a focal FDG uptake [10]. By converse, a diffuse uptake is frequently associated in HL with a diffuse bone marrow (BM) uptake and is more likely to represent inflammation due to chemokines produced by the Hodgkin and Reed-Sternberg cells (HRS) and no evidence of spleen invasion by lymphoma. On the other hand, the

association of splenomegaly and diffuse splenic uptake, with an intensity higher than the normal liver, may be suspicious of splenic involvement. There is not a given, definite pattern of FDG uptake which is deemed to portrait bone/bone marrow involvement (BMI) by lymphoma. While in HL and DLBCL in most cases, BMI is typically displayed by a focal FDG uptake with an intensity higher than the liver, in some cases diffuse uptake has been described in DLBCL [11–13]. By contrast, in follicular lymphoma (FL) bone marrow involvement is typically diffuse [14, 15]. Using PET/CT it is not possible and not strictly indispensable to distinguish with certainty BM from bone involvement, because in both cases the stage of the disease is the same. Moreover, the limits of space resolution and detection power of the currently available scanner equipment often preclude the distinction between cortical or spongy bone invasion by lymphoma. However, in general, the presence of areas of focal FDG uptake associated with abnormalities on CT, seen as osteolytic, sclerotic, or mixed lesions, support bone infiltration involvement, while the absence of abnormalities on CT supports BM infiltration only. Focal FDG uptake associated with abnormalities on CT may be also related to benign non-lymphomatous process including osteoporotic changes of vertebral body, spondylosis, osteoarthritis, fractures, osteomyelitis, osteoid osteoma, etc., often yielding false-positive results in PET and fused PET/CT images. Considering the CT criteria of these lesions will largely eliminate false-positive results regardless their uptake value. Thus, in combined PET/CT, CT images significantly improve PET specificity with better localization of bone involvement in case of focal BMI. On the other hand, PET can detect BM-based localization early and in the absence of morphologic changes on CT images, both in cases of focal and diffuse BMI by lymphoma, thereby improving CT sensitivity. The influence of the integration of PET and CT upon CT specificity is also notable in cases of treated healed bony lesions, which lack metabolic activity in spite of a suspicious morphologic appearance. In general an abnormal accumulation persisting longer than 3 months in a fracture site is likely due to either osteomyelitis or malignancy. A diffuse homogeneous uptake in BM is frequently associated with a diffuse increase of splenic uptake in HL and is more likely to represent inflammation due to chemokines. In NHL a diffusely increased BM uptake that is greater than that of the normal liver should be considered compatible with lymphoma unless the patient history discloses a recent cytokine administration. Lymphoma spread in other extranodal sites usually presents as a focal area of uptake with an activity usually higher than the liver uptake and is associated with an abnormal finding on the CT part of the PET/CT.

PET/CT is generally assessed using visual criteria after treatment also, and the 5-PS is recommended for reporting [6, 7]. Meanwhile, it is suggested, according to published data, that score 4 be applied to uptake > the maximum SUV in a large region of normal liver and score 5 to uptake 2X to 3X the maximum SUV in the liver. The 5-PS (so called Deauville score) criteria follow the continuum of uptake with the likelihood of malignancy increasing with the level of FDG uptake and were intended to be an objective reporting method, easy to understand, and to implement in different centers that would be reproducible when used by reporters in different countries. The 5-PS allow the outcome in patients with different levels of residual uptake to be analyzed; a high negative predictive value is desirable when de-escalation of therapy is proposed in patients with a good prognosis, while a high positive predictive value is desirable when intensification of therapy is proposed in patients with a poor prognosis. According to the 5-PS, the score of the patients is related to the activity of the most active lesion in the patient, i.e., to the activity of the "reference lesion" that is identified by scaling and eventually measuring its activity (SUVMax). A more detailed set of instructions was drawn up to deal with potential confounding variables in the interpretation of the interim and final PET [16].

6.4 What Is Normal and Abnormal in PET Images at Baseline and After Treatment?

The typical finding of an abnormal scan in lymphoma is usually defined by a focal pathological FDG uptake in nodal and extranodal sites. However soon after the introduction of FDG-PET for human studies, it became clear that FDG-PET imaging is not specific for cancer because nonphysiological variable uptake of FDG occurs in many tissues and in lesions characterized by a substantial presence of inflammatory cells. Therefore, as it is possible that benign and malignant lesions are present simultaneously in a single patient, it is not possible to know with certainty in a given imaging technique (either PET or CT) the pathology counterpart of the identified lesion. Accordingly, as taking a biopsy of all the sites of disease turns out unfeasible and unethical, it is difficult to clearly define what should be considered the "gold standard" reference for a given imaging technique for assessing its overall accuracy. In clinical practice, the need of a biopsy should be limited to those cases in which this information can change the stage of disease, at diagnosis, or the therapeutic choice during or at the end of treatment. A proper interpretation and accurate characterization of an abnormality detected in PET/CT could be given by complying with a narrow definition of "lesion" (area of focal uptake of tracer which corresponds to a CT imaging abnormalities, which is not explained by other causes than tumor) in the awareness of the conditions and the mechanisms yielding false-positive and false-negative results. Many articles in the current literature report about physiological and nonphysiological FDG accumulations observed in PET/CT and about pitfalls or artifacts observed at baseline and after treatment [17–20]. A physiological and variable FDG accumulation can be observed to a certain degree in most viable tissue like the brain, myocardium, breast, liver, spleen, stomach, intestine, kidneys, urine, skeletal muscle, lymphatic tissue, bone marrow, salivary glands, thymus, uterus, ovaries, and testicles. In whole-body PET/CT examinations, the brain shows a high FDG accumulation. For the detection of brain localization, FDG-PET is therefore only of limited value and thus FDG-PET is usually not used for the primary detection or exclusion of brain metastases.

A nonphysiological, variable and nonspecific FDG accumulation can be observed in brown fat, in myocardium, in granulation tissue (e.g., wound healing), in granulomatous disease (e.g., sarcoidosis), in infections and other inflammatory processes (pneumonia, esophagitis, gastritis, cholangitis, etc.), and in benign non-neoplastic disease (thyroid functioning nodules, adrenal nodules, salivary gland tumors, etc.). The distribution of brown fat includes the neck, axilla, upper mediastinum, and paravertebral region. Variable patterns of intestinal FDG uptake are present in the patients receiving anti-hyperglycemic drugs including metformin, with particularly diffuse, multifocal, or nodular variations with predominance in the large intestine, a lesser presence in the small intestine. The transient discontinuation of metformin therapy for 2 days just before a FDG-PET/CT scan markedly reduces the increased intestinal FDG uptake without causing a significant increase in the blood glucose level [21, 22]. Bone marrow is often suppressed during chemotherapy. To overcome chemotherapy-induced neutropenia, granulocytic colony-stimulating growth factors (G-CSF) are often administered to promote BM repopulation after treatment. Growth factors (G-CSF) rapidly increase BM FDG uptake, but the effects on FDG uptake do not last for more than 2 weeks after the final administration; during and after G-CSF treatment, a sustained increased FDG uptake is also often observed in the spleen, although less frequent and marked as that observed in the bone marrow. Elevated FDG avidity in the BM may also be seen in anemic patients. These findings must be distinguished

from malignancy [23, 24]. Thymic hyperplasia after chemotherapy is a common finding among children and adolescents and may also be seen in adults; thymic hyperplasia is allegedly accounted by an immunologic rebound phenomenon that is characterized by lymph follicles with large nuclear centers and infiltration of plasma cells after thymic aplasia. Although this phenomenon usually appears within 2–6 months after completion of chemotherapy and may persist for 12–24 months, in some cases a thymic rebound can develop as early as 1 week after therapy end [25, 26]. Bleomycin is an antibiotic agent with antitumor activity, commonly used as part of the cytostatic treatment in HL. Because of the lack of the bleomycin-inactivating enzyme, bleomycin hydrolase, in the lungs and the skin, bleomycin-induced toxic effect occurs predominantly in these organs. The central event in the development of bleomycin-induced pneumonitis is endothelial damage of the lung vasculature caused by bleomycin-induced cytokines and free radicals. This inflammatory process can result in an increase in pulmonary FDG uptake that may be seen within 2 months after the start of bleomycin treatment [27, 28]. Surgery is a form of tissue injury, and, as expected, it elicits an inflammatory response that can be visualized as an area of increased FDG activity. Postsurgical inflammation will be evident on FDG-PET/CT as FDG-avid soft tissue in the surgical bed; these changes usually resolve in a few weeks. The intensity of tracer uptake depends on the extent of surgery and how the wound was healed: for example, there are few visible signs on PET 10 days after mediastinoscopy but the inflammatory consequences of a sternotomy will remain visible for months. In patients who have undergone radiation therapy, normal tissues close to the boundaries of radiation fields are also, at least in part, exposed, and injury to these tissues often results in FDG-avid inflammation. As the effects of radiotherapy are somewhat longer lasting, end-of-treatment PET scan should be planned not earlier than 8–12 weeks after the end of treatment in order to reduce the post-radiation unspecific FDG uptake. This time frame fits well the clinical context of these patients, rarely experiencing a treatment failure within 3 months after the end of radiation treatment. Radiation pneumonitis is an inflammatory reaction within irradiated lung tissue in response to radiation injury and is characterized by the migration of leukocytes from the blood to irradiated lung tissue; radiation pneumonitis may appear as early as 2 weeks after irradiation and may persist for many months. On FDG-PET scans, radiation pneumonitis will result in elevated FDG avidity. The linear distribution of abnormalities seen on both CT and FDG-PET scans helps distinguish radiation pneumonitis from pulmonary infection or malignancy [29–31]. The interpretation of a FDG uptake by bone in a site previously involved by disease after treatment might be difficult because this phenomenon, especially in presence of a lytic lesions, may be related both to bone healing, which transiently increases FDG uptake, and to a residual disease. In general, in patients with residual disease, the degree of uptake is higher. These clinical observations suggest that an interval of at least 6 weeks should be allowed to minimize the risk of false-positive findings after treatment of bone lesions and of at least 3–6 months should elapse between surgery or traumatic bone lesions and PET scan.

6.5 Other Factors Interfering with PET Interpretation

There are no conclusive data on the optimum interval between chemotherapy and PET. The minimum interval between the last dose of chemotherapy and PET should be 10 days, and the latter should be planned as close as possible to the next treatment administration. This is because of any possible effects on tumor metabolism (such as macrophage impairment) and systemic effect (such as bone marrow

activation following bone marrow depression, which may or may not be caused by growth factor).

6.6 How to Write the Clinical Report

PET and CT findings should be integrated in a combined report rather than being reported separately. Typical report includes patient details/demographics, procedure description and imaging protocol, clinical information, clinical report interpretation/conclusion, and author/s.

1. *Patient details/demographics*

Mandatory These data may be country specific but in general they include name and family name, place and birthday of the patient, patient and study identifier, and date of examination.

2. *Procedure description and imaging protocol*

Mandatory The radiopharmaceutical administered and its activity (in MBq), the level of blood glucose before the examination and the diabetic status, the field of view and patient positioning (whole body, skull base, to mid-thigh), the CT protocol (low dose for attenuation correction and image fusion vs full-dose contrast-enhanced CT; the contrast agent should be specified), the actual interval between FDG administration, and the start of acquisition if outside the standard operating procedure (SOP) (SOP: 60 ± 10).

Recorded but not included in the report: Height and weight of the patients, site of injection, extravasation, quality control parameters of the radiopharmaceutical preparation, drug administration (benzodiazepines, beta-blockers, insulin, etc.); method of image reconstruction if outside the SOP (SOP: iterative reconstruction); motion or respiratory artifacts; camera details and quality control parameters; and CT dose.

3. *Clinical indication*

Mandatory Indications for PET/CT examination, i.e., staging, early or interim restaging, and end of therapy restaging.

Recommended Relevant patient history.

4. *Description of findings in PET/CT and CT*

This is the main body of the report; it sets out the information you found when you read PET/CT. The meaning of this information may change in the different type of lymphoma and different time points of patient scanning before, during, and after treatment.

Mandatory *Description of relevant findings likely related to the disease*: PET/CT scans report (1) the anatomical location, the extent, and the intensity of pathological FDG accumulation in nodal and extranodal sites and (2) the relevant morphologic findings related to PET abnormalities on the CT images. The intensity of uptake in the different nodal area and in extranodal sites may be described as mild, moderate, or intense; a quantitative estimate of the intensity of FGD uptake (SUVMax) in the different nodal area can be provided especially if the pattern of uptake is suggestive of transformation (e.g., in follicular lymphoma and in chronic lymphocytic leukemia). Extranodal disease spread should be recorded according to the involved site (the lung, liver, bone/bone marrow, etc.). The dimension of the spleen should be given by measuring its largest diameter on CT scan (splenomegaly if >13 cm). The anatomical location, the activity (SUVMax), and the size of the most active lesion (reference metabolic lesion) and the dimension and location of the largest mass (transverse slice), even if the latter is not the reference metabolic lesion, where feasible, should be provided.

Description of incidental findings in PET/CT which are FDG-avid but unlikely disease-

related, such as focal colonic uptake, diffuse or nodular tracer uptake in thyroid, adrenal adenoma, salivary gland tumors, hilar and mediastinal node in sarcoidosis, etc.. These findings should be described both before and after treatment, with a warning on their nature not attributable to lymphoma (in posttreatment settings they may provide false-positive results).

Description of findings in CT that are relevant to patients care, even in the case they are PET negative. Comment on any potential life threatening or clinically critical finding, e.g., potential spinal cord compression, perforation, superior vena cava obstruction, pleural and pericardial effusion, aortic aneurysm, etc., should be added.

Recommended *Description of the incidental findings in CT* such as renal atrophy, gallstones, etc.

5. *Interpretation/conclusions*

The final interpretation of the findings is hereby reported and the conclusion should be sound to the clinical context in which a PET scan is required.

Mandatory at staging A synthetic comment on area/s of abnormal uptake in nodal and extranodal sites should be included. Whenever feasible, the most probable diagnosis should be given, resulting from a synthesis of the available clinical data and of the semiotics of the abnormal PET findings. When appropriate, a differential diagnosis should be given with an estimated probability of a diagnosis. The location, activity (SUVMax), and dimension of the most active lesion (reference metabolic lesion), the location and dimension of the largest lesion, and the extension of the disease (Ann Arbor or modified Ann Arbor Stage) should be reported. When appropriate, follow-up and additional diagnostic studies to confirm the clinical hypothesis should be recommended, e.g., site for biopsy or lymphoma with suspected transformation.

Report findings in CT that are relevant to patients' care.

Mandatory during and after therapy A synthetic comment on area/s of abnormal uptake, in nodal and extranodal sites, suspect to harbinger residual disease should be included. The location, activity (SUVMax), and dimension of the single most active lesion (reference metabolic lesion) and the location and dimension of the largest lesion should be reported.

The area/s of any new site/s of disease (due to lymphoma or nonspecific) should also be described. All the above information should be displayed by comparing the recorded persisting abnormality with that in the previous PET/CT scan and/or other previous imaging studies and clinical data that are relevant. Finally the Deauville score should be reported using the 5-point Deauville scale. According to the Lugano criteria for lymphoma response assessment, the abnormal (if any) finding recorded in the PET scan should be categorized in one of the following levels: complete metabolic response/partial metabolic response/stable metabolic disease/progressive metabolic disease. Recommendations for further imaging or investigation if relevant as well as a mention on CT findings that could be relevant for patient care should also be added. Representative case and an example of template for recording sites of involvement are reported in Figs. 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, 6.10, and 6.11

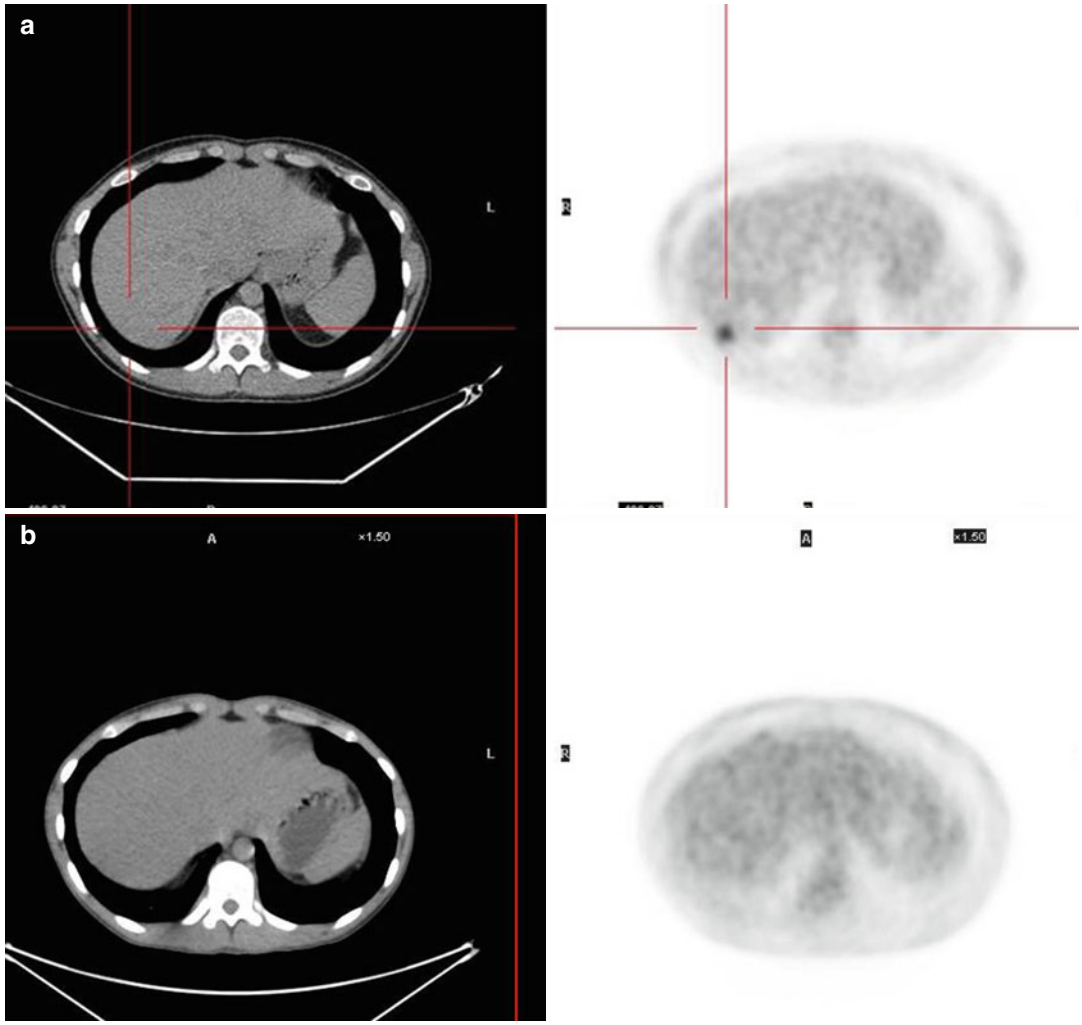

Fig. 6.1 Stage IV HL. Focal uptake in the liver at baseline (**a**) that disappears after treatment (**b**)

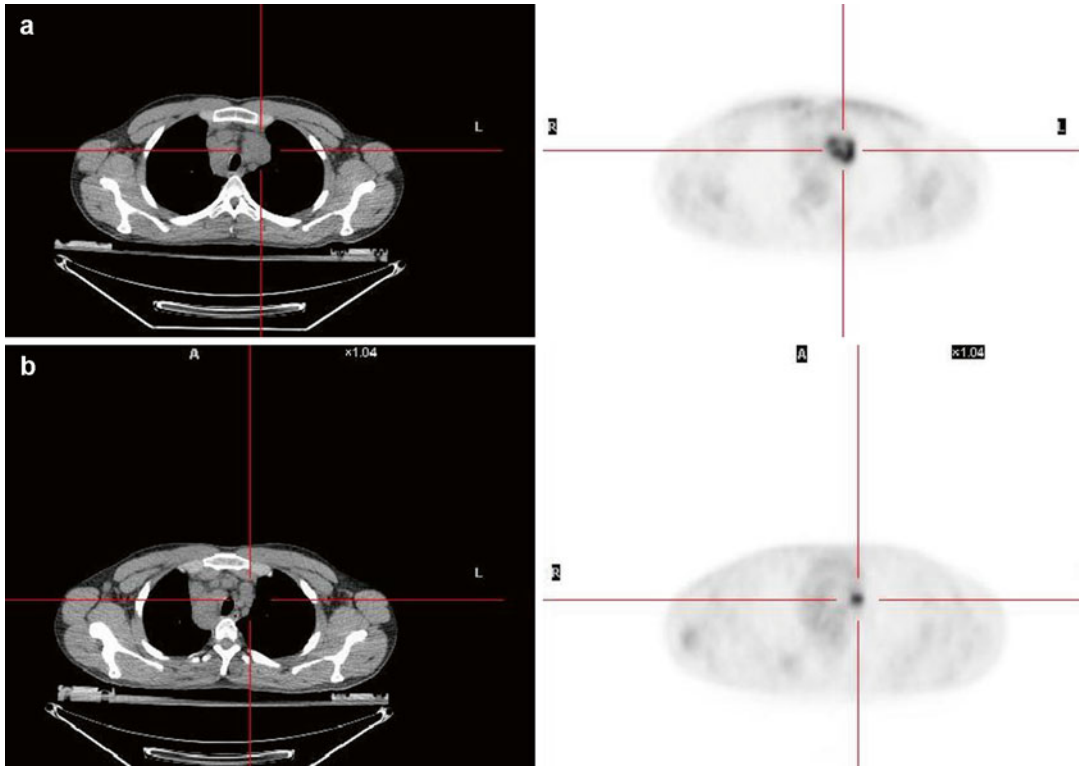

Fig. 6.2 Focal uptake in paratracheal left node at baseline (**a**) and after treatment (score 4) (**b**) in HL

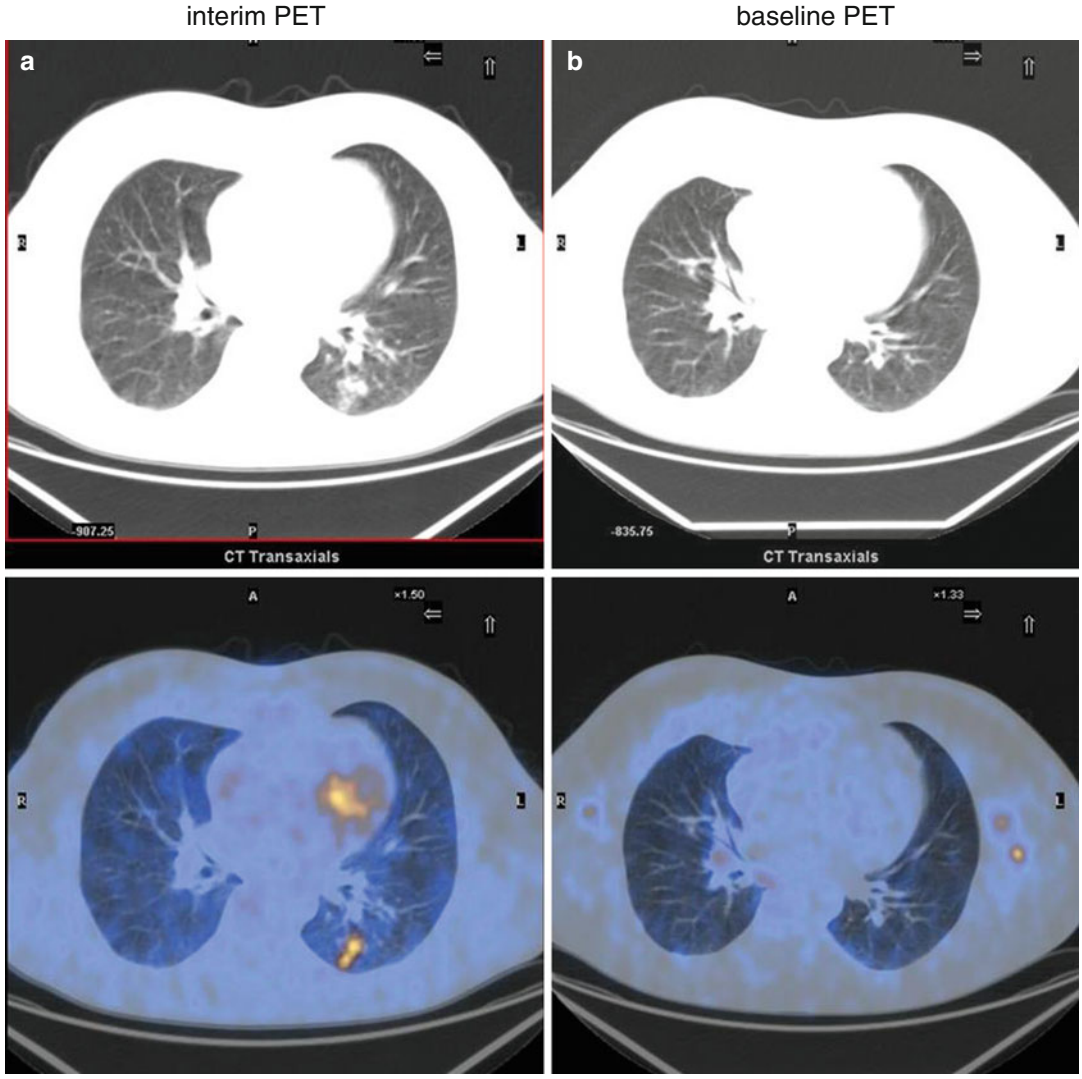

Fig. 6.3 Focal uptake in lung abnormalities in interim PET (**a**) after 2 ABVD not present in baseline PET due to pneumonia; nodes in left axilla present in baseline PET (**b**) were no more evident after treatment

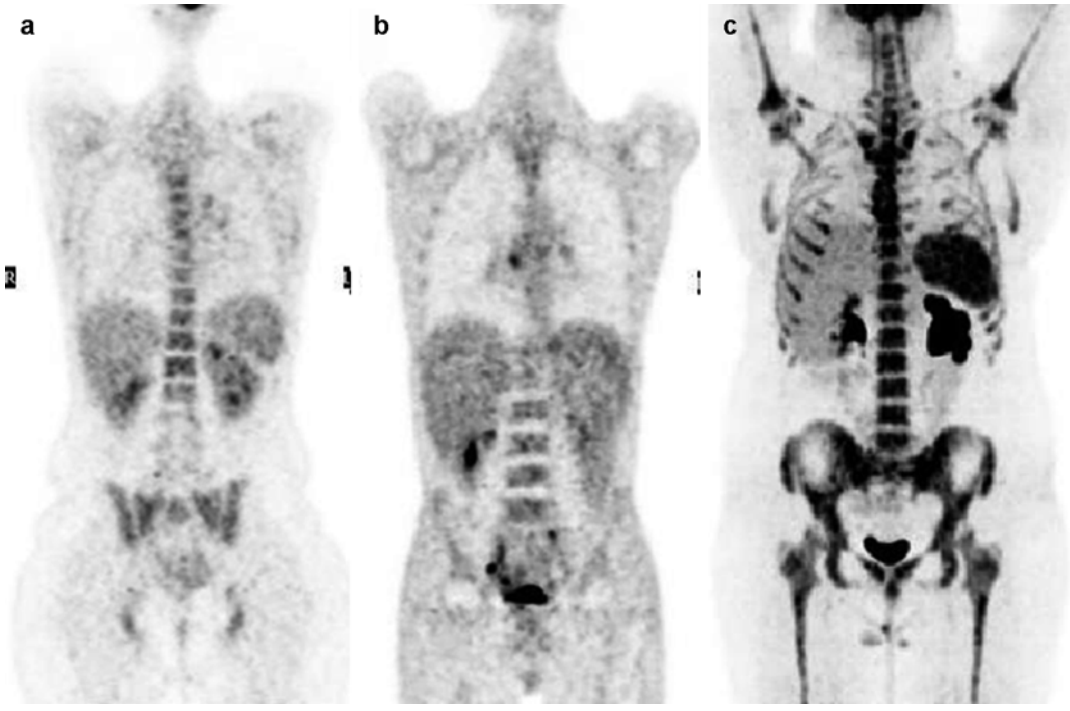

Fig. 6.4 Diffuse uptake in the bone marrow and spleen at baseline PET due to chemokines stimulation produced by the HRS cells in patients with HL (Case **a** and **b**); intense bone marrow and spleen uptake after 3 days of G-CSF treatment 8 days after the last BEACOPP treatment (Case **c**)

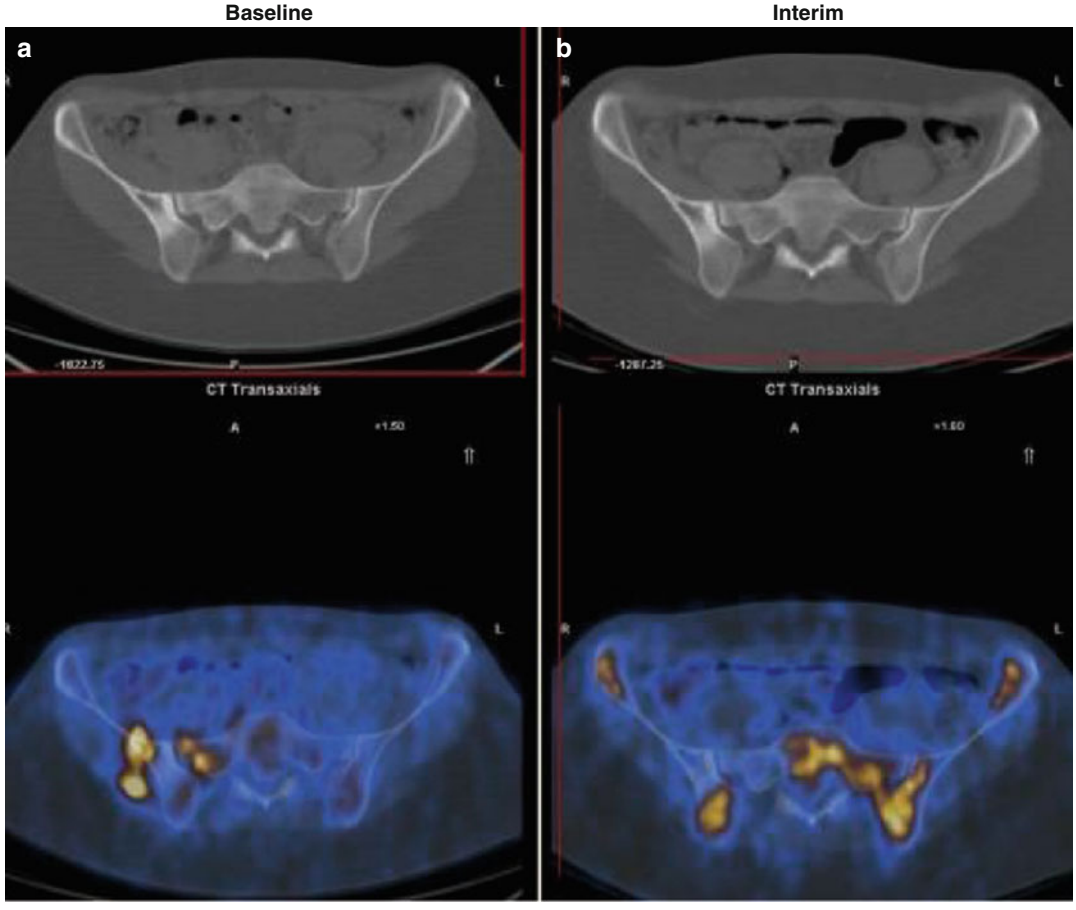

Fig. 6.5 Focal uptake in the right ileum, right sacrum and in the left side of L3 in baseline PET (**a**). After treatment with 2 ABVD (**b**), is evident an increased uptake in normal bone marrow due to chemotherapy effect associated with focal cold areas in bone site previously involved by disease

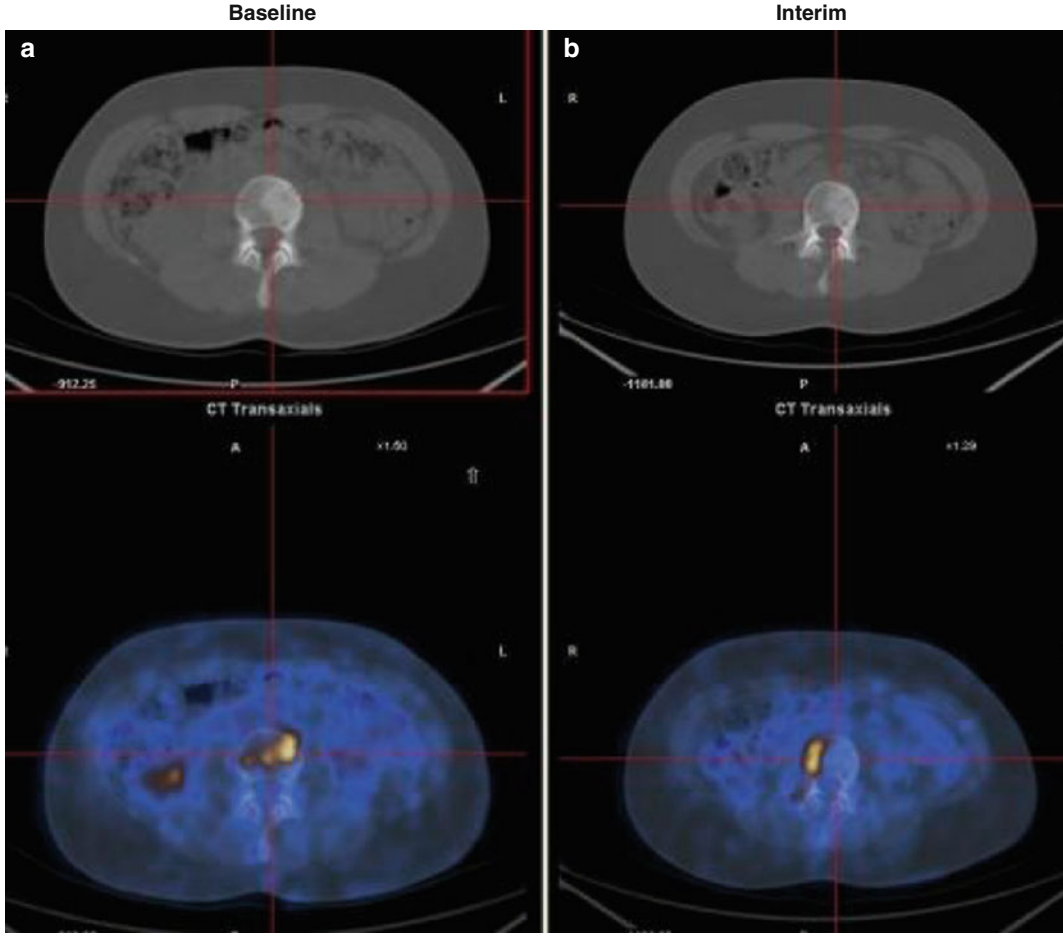

Fig. 6.5 (continued)

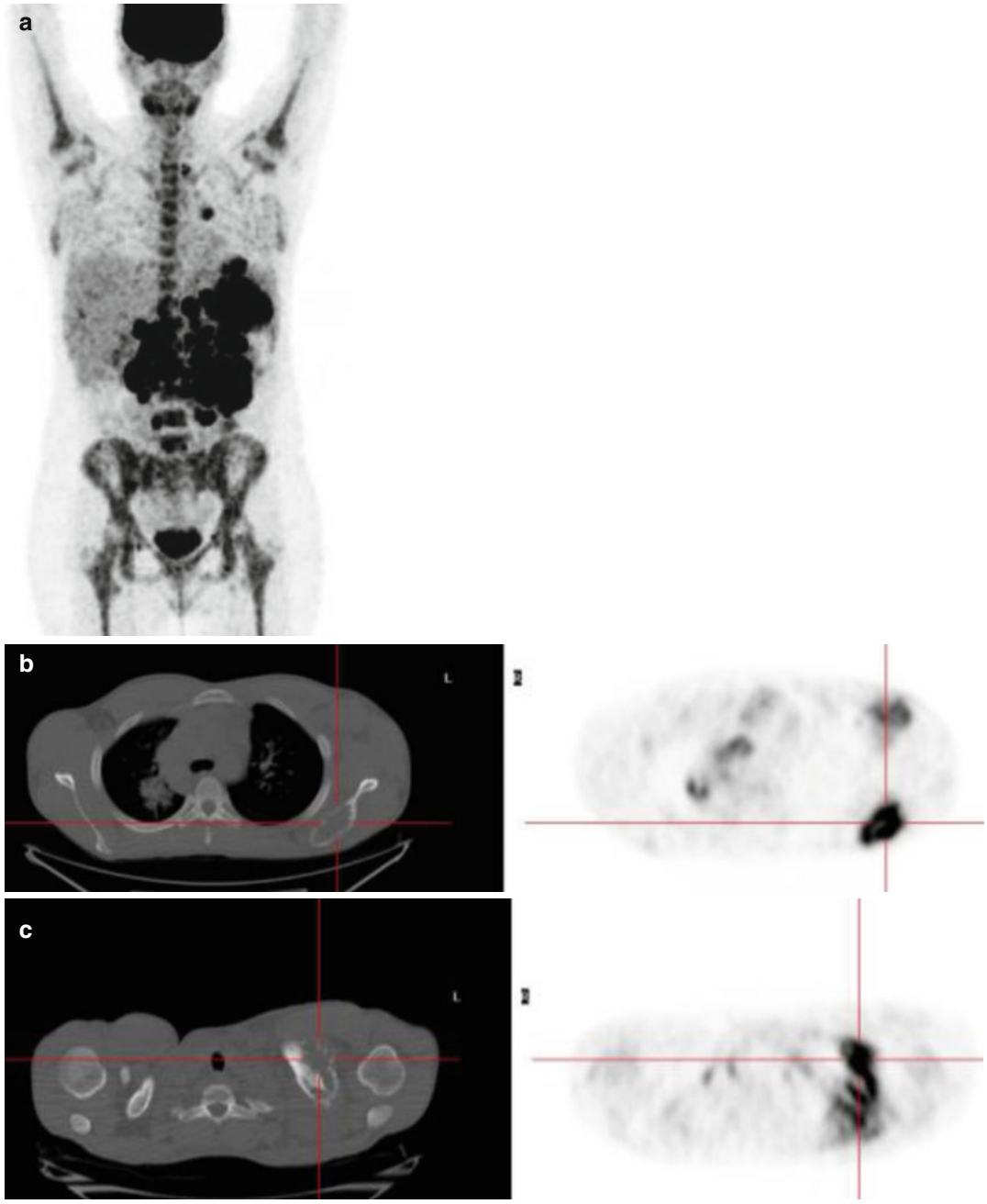

Fig. 6.6 (**a**) Stage IV HL; diffuse bone marrow and spleen uptake due to chemokine stimulation (**a**) associated with lytic lesion in the left scapula (**b**) and in the left clavicula (**c**). (**b**) Interim PET after 2 ABVD; diffuse bone marrow and spleen uptake due to chemotherapy (**d**); diffuse residual uptake in the left scapula due to the healing process of the osteolytic lesion (score 3) (**e**) and focal uptake in the left clavicle due to residual disease (score 4) (**f**)

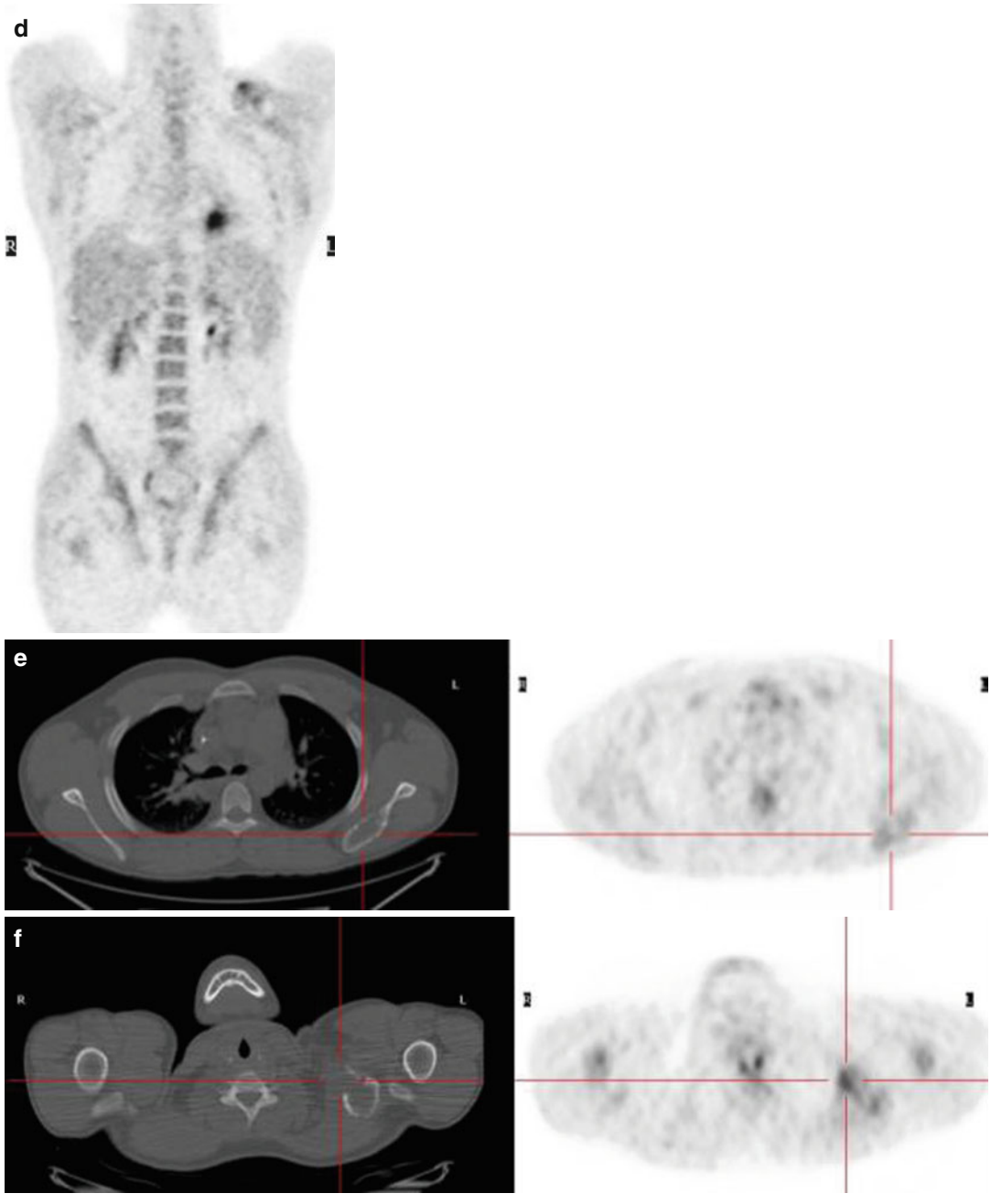

Fig. 6.6 (continued)

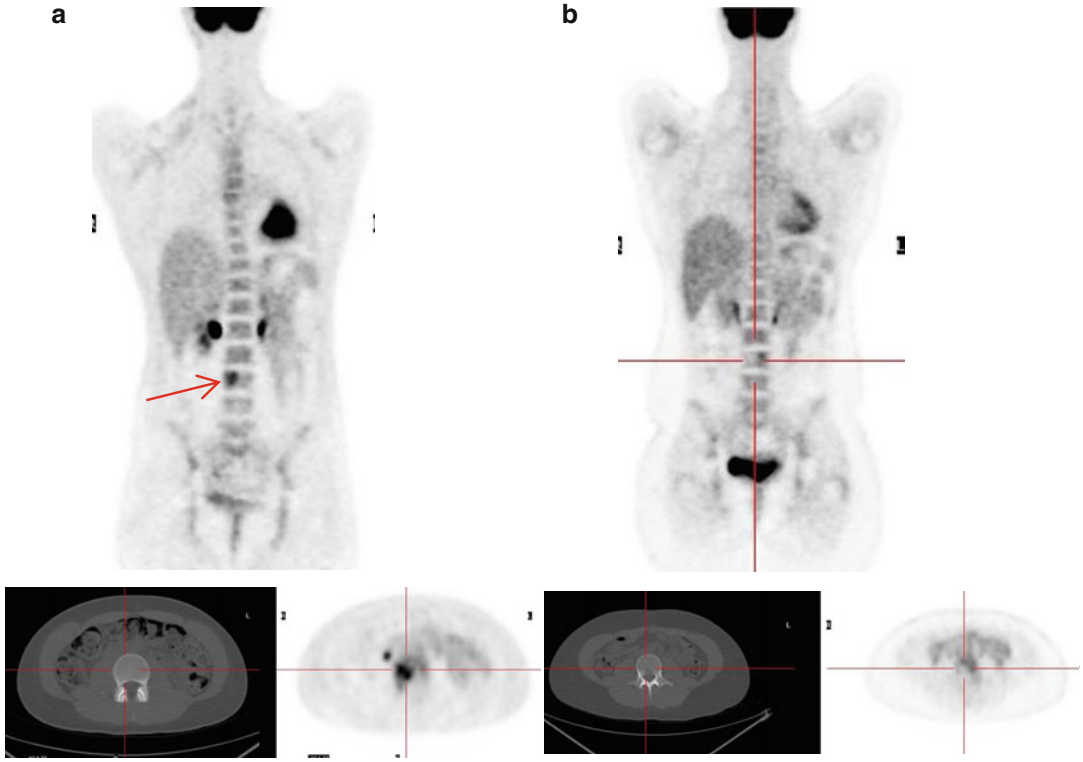

Fig. 6.7 Focal uptake in right side of L3 without abnormalities in CT due to bone marrow involvement at Baseline (*red arrow*: focal bone marrow uptake) (**a**); after treatment focal reduction of uptake due to bone marrow ablation (*mirror effect*) (**b**)

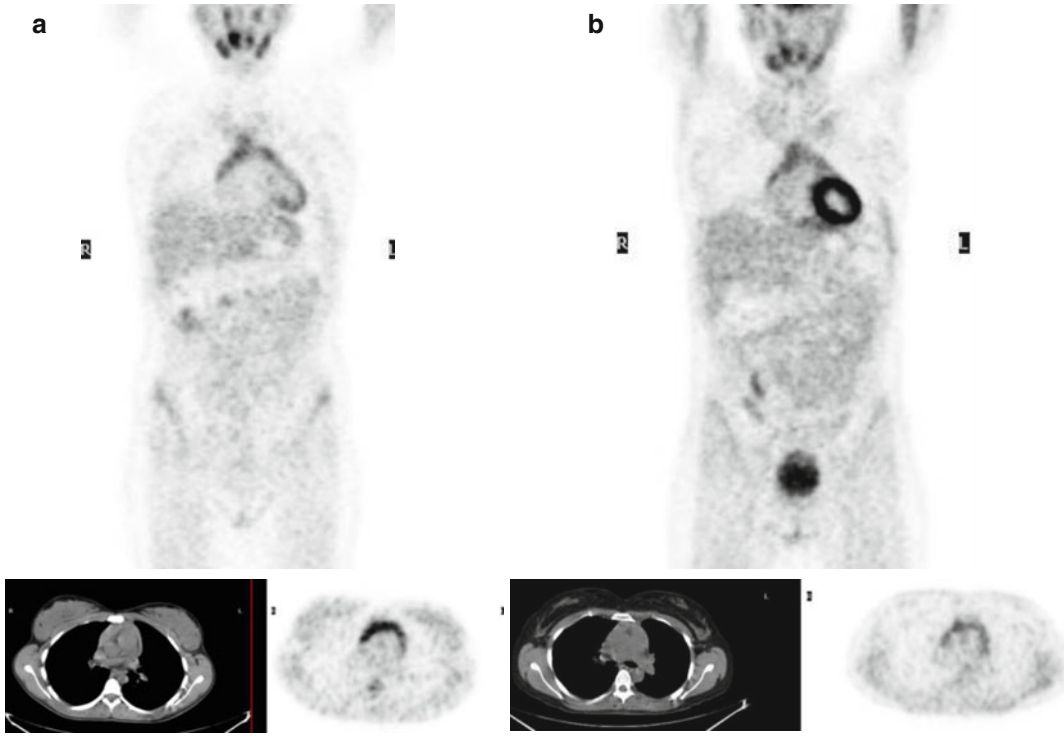

Fig. 6.8 Diffuse uptake in the anterior mediastinum due to thymic iperplasia 6 months (**a**) and 10 months (**b**) after the end of treatment for HL

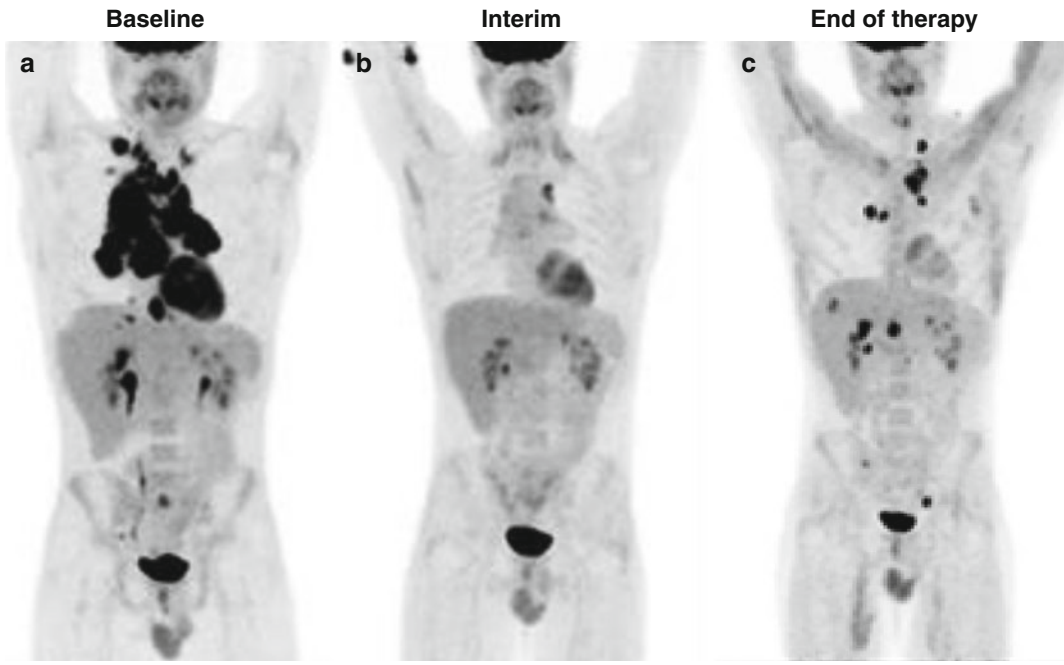

Fig. 6.9 (**a**) Stage IV HL; (**b**) PMR (score 4 upper mediastinal node) after 2 ABVD; (**c**) PMD at end of therapy after BEACOPP (new liver and bone lesion)

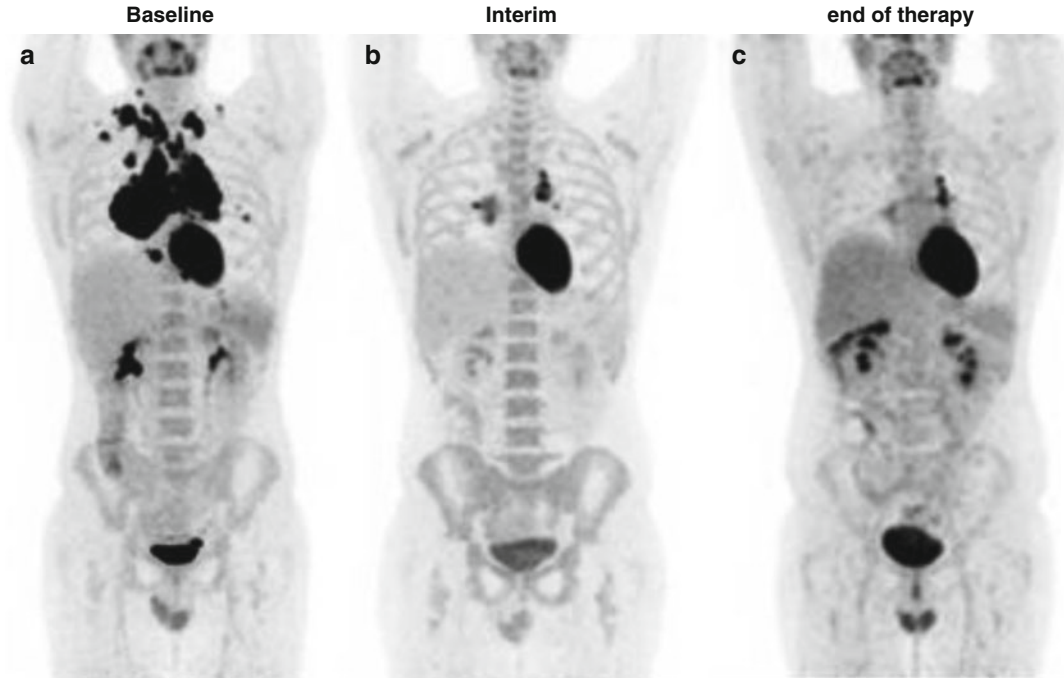

Fig. 6.10 (**a**) Stage IV HL (lung) HL; (**b**) residual disease in the pulmonary hilum (Score 4) (PMR); (**c**) Residual disease in the left pulmonary hilum after BEACOPP (Score 4) (PMR)

Site	Percentage
Nodal	
Cervical	55.8 (L); 47.4 (R)
Axillary	28.8 (L); 28.0 (R)
Infraclavicular	6.4 (L); 4.2 (R)
Hilar	23.0
Mediastinal	38.8
Periaortic	37.8
Pelvic	31.4 (L); 31.6 (R)
Inguinal	33.6 (L); 28.6 (R)
Extranodal	
Spleen	17.8
Bone marrow or bone	20.0
Lung	5.4
Liver	10.0
Bowel or gastric	5.4
Other nodal sites*	8.0

*Muscle, subcutaneous tissue, breast, and uterus.

Fig. 6.11 Example of template for reporting nodal and extranodal sites. In parenthesis the percentage of patients with lymphomatous involvement at specific nodal and extranodal sites [32]

References

1. Linee Guida per la Dematerializzazione della Documentazione Clinica in Diagnostica per Immagini, 4/4/2012, Conferenza permanente per i rapporti tra lo Stato, le Regioni e le provincie autonome di Trento e di Bolzano. www.statoregioni.it/dettaglio Doc.asp?idprov=10549&iddoc.
2. Boellard R, O'Doherty MJ, Weber WA, et al. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging. 2010;37(1):181–200. doi:10.1007/s00259-009-1297-4.
3. Delbeke D, Coleman RE, Guiberteau MJ, et al. Procedure guidelines for tumour PET imaging with ^{18}F-FDG PET/CT 1.0*. J Nucl Med. 2006;47:885–95.
4. Giordano A, Fanti S. Raccomandazioni Procedurali AIMN – Imaging Oncologico con 18F-FDG/PET – Vrs. 03/2012. www.aimn.it/pubblicazioni/LG/RP_AIMN_18F-oncologia.pdf.
5. 5th International workshop on PET in lymphoma. Palais de l'Europe. Menton, 19–20 Sept 2014. Organizing Committee M. Meignan, A. Gallamini, C. Haioun, S. Barrington, E. Itti, S. Luminari, E. Zucca. www.lymphomapet.com.
6. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the international conference on Malignant Lymphomas Imaging Working Group. doi:10.1200/JCO.2013.53.5229.
7. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. doi:10.1200/JCO.2013.54.8800.
8. Cheson BD, Pfstner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol. 2007;25:579–86.
9. Biggi A, Guerra L, Hofman MS. Current status of FDG-PET/CT in staging of adults lymphoma. Clin Transl Imaging. 2015. doi:10.1007/s40336-015-0127-x.
10. Rosemberg SA, Dorfman RF, Kaplan HS. The value of sequential bone marrow biopsy and laparotomy and splenectomy in a series of 127 consecutive untreated patients. Br J Cancer Suppl. 1975;2:221–7.
11. Khan AB, Barrington S, Mikhaeel NG, et al. PET-CT staging of DLBCL accurately identifies and provides new insight into the clinical significance of bone marrow involvement. Blood. 2013;122:61–7. doi:10.1182/blood2012-12-473389.
12. Adams HJA, Kwee TC, Fijnheer R, et al. Bone marrow 18-F-fluoro-2-deoxy-Dglucose positron emission tomography/computed tomography cannot replace bone marrow biopsy in diffuse large B-cell lymphoma. Am J Hematol. 2014;89:726–31.
13. Adams HJ, de Klerk JM, Fijnheer R, et al. Bone marrow biopsy in diffuse large B-cell lymphoma: useful or redundant test? Acta Oncol. 2015;54(1):67–72. doi:10.3109/0284186X.2014.958531.
14. Le Dortz L, De Guibert S, Bayat S, et al. Diagnostic and prognostic impact of 18F-FDG PET/CT in follicular lymphoma. Eur J Nucl Med Mol Imaging. 2010;37(12):2307–14. doi:10.1007/s00259-010-1539-5.
15. Wohrer S, Jaeger U, Kletter K, et al. 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) visualizes follicular lymphoma irrespective of grading. Ann Oncol Off J Eur Soc Med Oncol ESMO. 2006;17(5):780–4. doi:10.1093/annonc/mdl014.
16. Biggi A, Gallamini A, Chauvie S, et al. International validation study for interim PET in ABVD-treated, advanced-stage Hodgkin lymphoma: interpretation criteria and concordance rate among reviewers. J Nucl Med.2013;54:683–90.doi:10.2967/jnumed.112.110890.
17. Bhargava P, Zhuang H, Kumar R, et al. Iatrogenic artifacts on whole-body F-18 FDG PET imaging. Clin Nucl Med. 2004;29(7):429–39.
18. Ulaner G, Lyall A. Identifying and distinguishing treatment effects and complications from malignancy at FDG PET/CT. Radiographics. 2013;33:1817–34.
19. Sarji A. Physiological uptake in FDG PET simulating disease. doi:10.2349/biij.2.4.e59. Available on line http://www.biij.org/2006/4/e59.
20. Mohei M, Abouzied MD, Elpida S, et al. 18F-FDG imaging: pitfalls and artifacts. J Nucl Med Technol. 2005;33:145–55.
21. Gontier E, Fourme E, Wartski M, et al. High and typical 18F-FDG bowel uptake in patients treated with metformin. Eur J Nucl Med Mol Imaging. 2008;35:95–9.
22. Oh JR, Song HC, Chong A, Ha JM, Jeong SY, Min JJ, Bom HS. Impact of medication discontinuation on increased intestinal FDG accumulation in diabetic patients treated with metformin. AJR Am J Roentgenol. 2010;195:1404–10.

23. Sugawara Y, Fisher SJ, Zasadny KR, et al. Preclinical and clinical studies of bone marrow uptake of fluorine-1-fluorodeoxyglucose with or without granulocyte colony-stimulating factor during chemotherapy. J Clin Oncol. 1998;16(1):173–80.
24. Sugawara Y, Zasadny KR, Kison PV, et al. Splenic fluorodeoxyglucose uptake increased by granulocyte colony-stimulating factor therapy: PET imaging results. J Nucl Med. 1999;40(9):1456–62.
25. Jerushalmi J, Frenkel A, Bar-Shalom R, et al. Physiologic thymic uptake of 18F-FDG in children and young adults: a PET/CT evaluation of incidence, patterns, and relationship to treatment. J Nucl Med. 2009;50(6):849–53.
26. Goethals I, Hoste P, De Vriendt C, et al. Time-dependent changes in 18F-FDG activity in the thymus and bone marrow following combination chemotherapy in paediatric patients with lymphoma. Eur J Nucl Med Mol Imaging. 2010;37(3):462–7.
27. Kirsch J, Arrossi AV, Yoon JK, et al. FDG positron emission tomography/computerized tomography features of bleomycin-induced pneumonitis. J Thorac Imaging. 2006;21(3):228–30.
28. Buchler T, Bomanji J, Lee SM. FDG-PET in bleomycin-induced pneumonitis following ABVD chemotherapy for Hodgkin's disease: a useful tool for monitoring pulmonary toxicity and disease activity. Haematologica. 2007;92(11):e120–1.
29. de Prost N, Tucci MR, Melo MF. Assessment of lung inflammation with 18F-FDG PET during acute lung injury. AJR Am J Roentgenol. 2010;195(2):292–300.
30. Faria S, Lisbona R, Stem J, et al. Is post-treatment FDG-PET/CT useful in differentiating tumor from fibrosis after curative radiation therapy (RT) alone for lung cancer? Int J Radiat Oncol Biol Phys. 2007;69(3 Suppl):S519–20.
31. Guerrero T, Johnson V, Hart J, et al. Radiation pneumonitis: local dose versus [18F]-fluorodeoxyglucose uptake response in irradiated lung. Int J Radiat Oncol Biol Phys. 2007;68(4):1030–5.
32. Hofman MS, Smeeton NC, Rankin SC, et al. Observer variation in interpreting 18F-FDG PET/CT findings for lymphoma staging. J Nucl Med. 2009;50:1594–7.