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Published on: 01 Jul 2017 - Nuclear Medicine Communications (Nucl Med Commun)

Topics: Diffuse large B-cell lymphoma

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Usual and unusual pitfalls of 18F-FDG-PET/CT in lymphoma after treatment: a pictorial review

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Fluorine-18-fluorodeoxyglucose (18F-FDG) PET/computed tomography (CT) is now a standard of care in initial staging and treatment evaluation of lymphomas. It is also used in the interim evaluation in diffuse large B cell lymphoma and Hodgkin lymphoma. However, several pitfalls may occur during or after treatment, because of the nonspecificity of 18F-FDG for lymphoma disease and treatment as immunotherapy, thus possibly induces misinterpretation and wrong treatment decision. The aim of this pictorial review is to provide an illustrated tutorial of the most frequent pitfalls found on 18F-FDG-PET/CT during or after treatment.

Keywords: evaluation, false positive, lymphoma, PET, pitfalls

Introduction

Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/computed tomography (CT) is now a standard of care for initial staging in Hodgkin lymphoma (HL), diffuse large B cell lymphoma (DLBCL), and follicular lymphoma (FL) [1,2]. Its high diagnostic performance leads to an up-staging in about 20% of cases.

Furthermore, ^{18}F-FDG-PET/CT is recommended for both end-of-treatment and interim evaluation (after two or four cycles of chemotherapy in case of HL and DLBCL). For HL, ^{18}F-FDG-PET/CT shows very high negative and positive predictive values at the end-of-treatment and in the interim evaluation [3], but lower negative and positive predictive values in DLBCL [4]. In FL, ^{18}F-FDG-PET/CT evaluation is recommended only at the end-of-treatment [1,2], with low negative and positive predictive values for relapse [5].

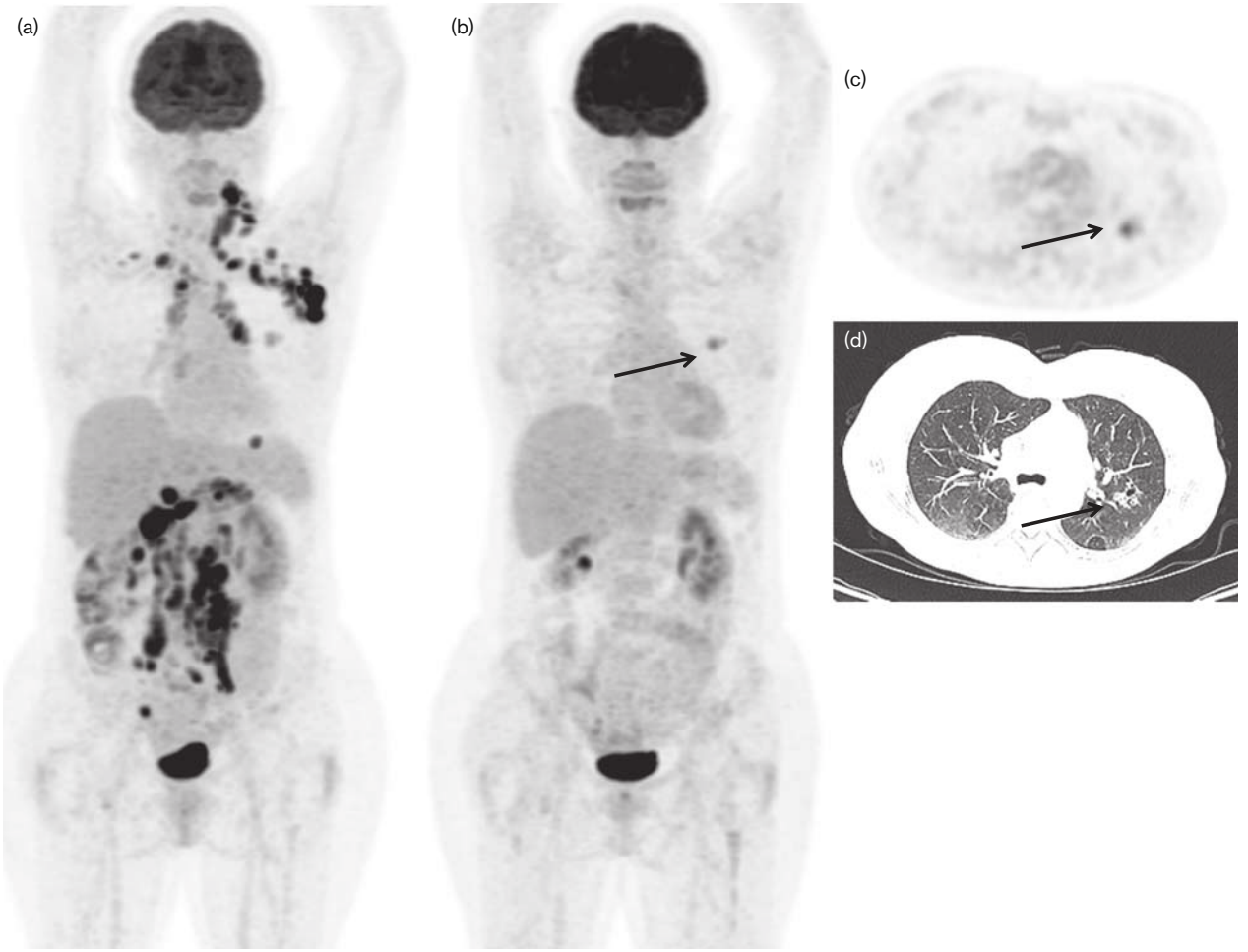
The interpretation criterion commonly used and recommended is the Deauville five-point scale [1,2]. According to international recommendations, Deauville 4 (uptake moderately increased compared with the liver at any site) and 5 (uptake markedly increased compared with the liver at any site) are considered positive, whereas Deauville 1 (no uptake above the background) and 2 (uptake $\leq$ mediastinum) are considered a complete metabolic response, and Deauville 3 (uptake $>$ mediastinum but $\leq$ liver) as a probable complete metabolic response. Few studies [6] have used semiquantification with delta-standardized uptake value (SUV) with good results, but this method should be more reproducible before being used in clinical practice [1,2].

Although ^{18}F-FDG-PET/CT is of great value in lymphoma evaluation, its specificity is limited, and many diseases can mimic a progression or a refractory disease [7], leading to a major impact on patient management. Recent studies have shown an excellent reproducibility between nuclear physicians, although lower between local and expert readers [8,9], highlighting the necessity to recognize pitfalls in ^{18}F-FDG-PET/CT lymphoma evaluation. The aim of this pictorial review is to describe the most frequent pitfalls usually found in PET evaluation lymphoma, which can be responsible for false-positive results and diagnostic errors with important consequences on patient management [10].

Current infection/inflammation

The most frequent pitfall at interim and the end of treatment is related to infectious disease, in particular, lung infection. These are easy to recognize, especially if no lung disease was described before treatment. On PET images, the ^{18}F-FDG pattern is mild and diffuse, and CT images usually show small peribronchic opacities with a tree-in-bud sign [11]. These results should not be related to a progressive disease and a CT control should be performed a few weeks after the end of antibiotic treatment. Conversely, in case of complete disease response with only one pulmonar nodule left, a second cancer should be suspected, especially in case of tobacco

Fig. 1



A 66-year-old man with T lymphoma. Initial ^{18}F-FDG-PET/CT (a) showed an intense uptake of supradiaphragmatic and infradiaphragmatic lesions with increased ^{18}F-FDG uptake of a subsolid lung nodule depicted on CT (define as pure ground-glass nodule or part-solid ground-glass nodule). After four cycles of chemotherapy, a new evaluation ^{18}F-FDG-PET/CT was performed (b), showing complete response of all lesions except the lung subsolid nodule uptake (c, d) with a SUV_{max} of 5.2 (arrows). A lung fibroscopy was performed and indicated infection, without neoplastic process certainly on an emphysematous bulla (another emphysematous bulla without infection is visible on the posterior chest wall). CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; SUV_{max}, maximum standardized uptake value.

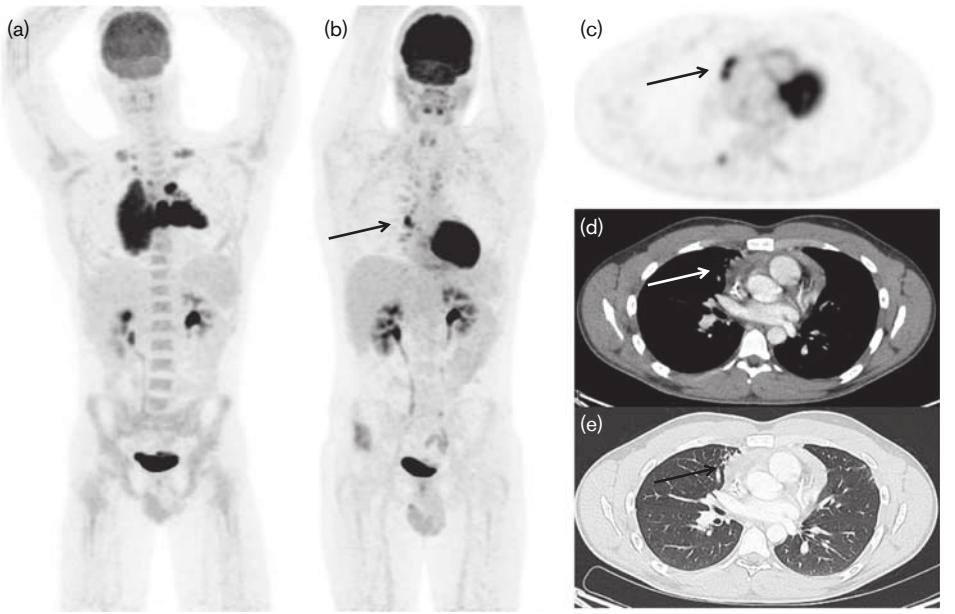
smoking (Fig. 1). Interstitial lung disease secondary to rituximab or bleomycine should also be well recognized, although CT scan is the method of choice for diagnosis [12].

A previous mediastinum bulky mass, according to our experience, can induce local infection with positive uptake in lung sub pleural parenchyma (Fig. 2). This type of false positive has already been reported and it is hypothesized that bulky mass leads to inflammatory changes in pleura and pulmonary parenchyma because of its anatomical contiguity [13]. In the same way, splenic involvement with a mass observed on CT at baseline could induce the inflammatory process observed on ^{18}F-FDG-PET/CT after treatment (Fig. 3). A biopsy should be performed in case of doubt before considering partial response.

Thymus hyperplasia

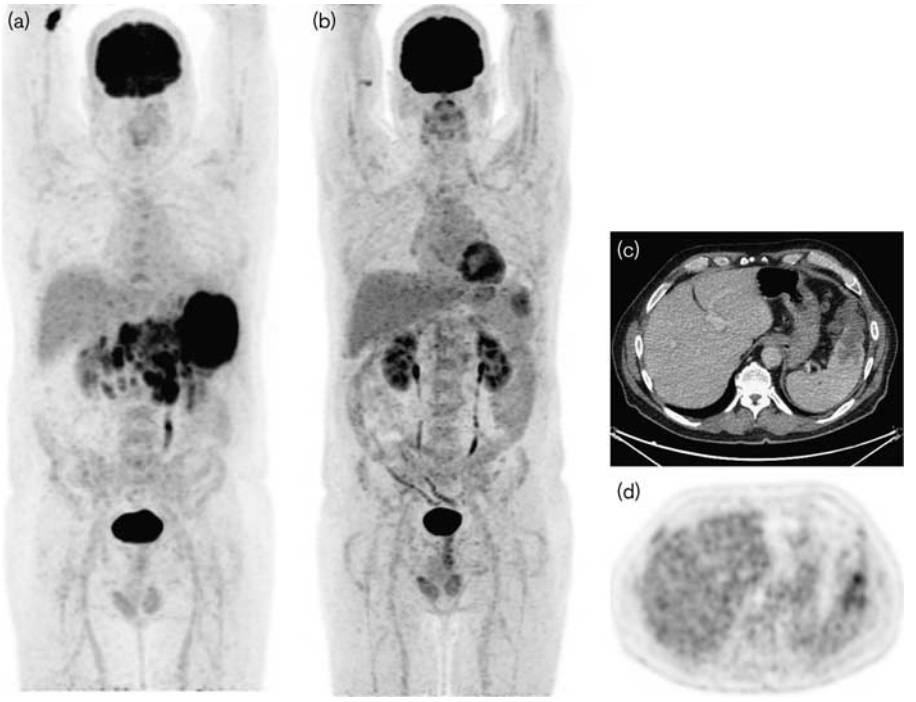
Another well-known pitfall in thoracic evaluation is thymus hyperplasia, also called rebound hyperplasia. The thymus gland is the largest during childhood and gradually disappears in young adults [14]. Thymus hyperplasia is frequently observed on follow-up until 6 months, and less frequently during the following 2 years [15]. This phenomenon is secondary to chemotherapy treatment that induces suppression of thymus activity [16,17], followed by regrowth and hyperplasia in about 5% of adults [18]. ^{18}F-FDG uptake is usually described in young adults after systemic therapy [19], but can persist after 40 years [20] or occur before therapy in case of hyperthyroidism or corticotherapy [15,21]. Most patients (60%) showed an inverted V pattern of thymic uptake, (Fig. 4) with additional unilateral mediastinal extension

Fig. 2



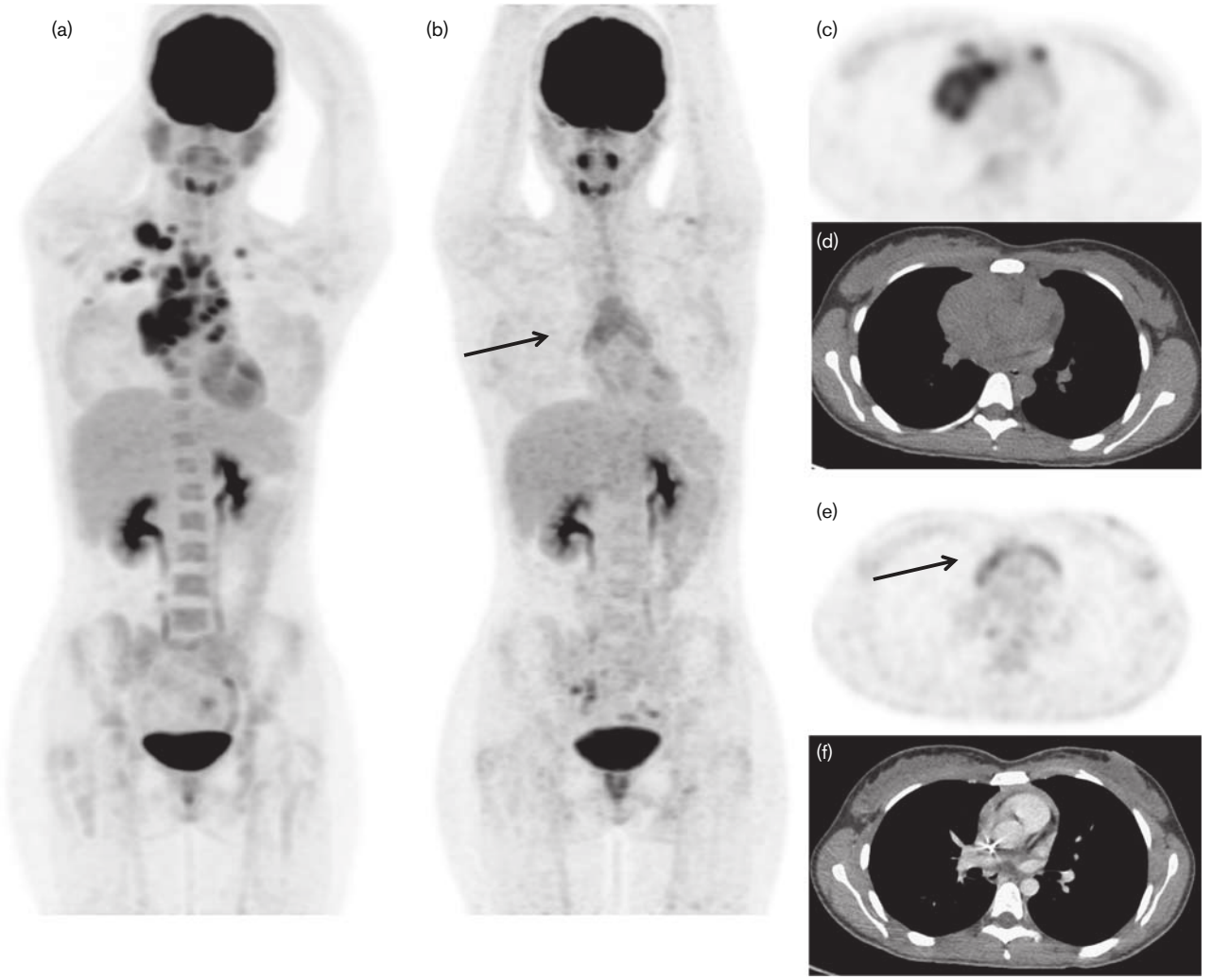
A 26-year-old man with HL. Initial PET/CT showed a bulky mediastinal mass (a). At the end of treatment, ^{18}F-FDG-PET/CT showed an intense paramediastinal uptake ($SUV_{max} = 13$) (arrows) with a right lung contact (and a small activation of brown adipose tissue) (b–e). Deauville five-point scale was at 5. A surgical biopsy was performed and indicated macrophage infiltration without Reed–Sternberg cells. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; SUV_{max}, maximum standardized uptake value.

Fig. 3



A 60-year-old man with DLBCL with infradiaphragmatic lymph nodes and massive spleen involvement (mass on ^{18}F-FDG-PET/CT) (a). After four cycles of chemotherapy, ^{18}F-FDG-PET/CT was considered positive, showing one persistent spleen uptake on the initial site, with a SUV_{max} of 6.07 and a Deauville score at 4 (b–d). A splenectomy was performed, showing on pathologic analysis a necrotic and inflammatory lesion without lymphoma infiltration. CT, computed tomography; DLBCL, diffuse large B cell lymphoma; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; SUV_{max}, maximum standardized uptake value.

Fig 4



A 22-year-old woman with HL. Initial PET/CT (a) showed pathologic uptake of supradiaphragmatic lymph nodes, including anterior mediastinal (c, d). ^{18}F-FDG-PET/CT 6 months after the end of treatment showed a characteristic pattern of V inverted on MIP because of thymus hyperplasia, with a SUV_{max} of 4.4 (arrows) (b–f). One-year follow-up confirmed this diagnosis. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

in 24% and focal midline uptake in 16% of studies (Fig. 5) [15]. The SUV_{max} is usually moderately intense (about 3,7), but can be above 4 in 44% of patients [15]. In case of mediastinal mass at initial staging, it is always challenging to distinguish residual disease from thymus hyperplasia. MRI with diffusion weight-imaging and biopsy should be performed in doubtful cases.

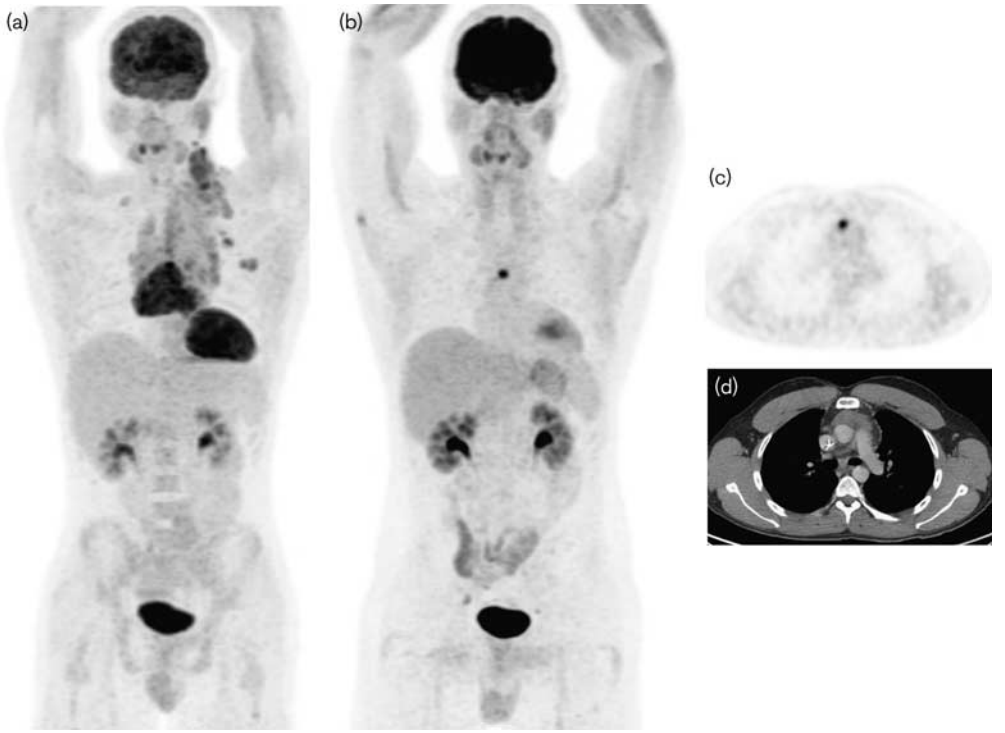
Granulomatosis

A frequent pitfall is the persistent hilar and mediastinal lymph nodes uptake, which can be related to various diseases. Sarcoidosis should be systematically evoked because of its frequency [22] and its well-known association with lymphoma [23]. Granulomatosis can also be induced by new treatment including immunotherapy (pembrolizumab, nivolumab; see below) [24,25]. The persistence of mediastinal lymph nodes on ^{18}F-FDG-PET/CT is not sufficient to affirm the relapse of lymphoma or refractory disease as Zinzani *et al.* [26] have shown that only 57% of positive lymph nodes found during the follow-up were true positive. In case of symmetric mediastinal–hilar lymph node uptake, a control of non-progression should be performed after a few months (Fig. 6). Conversely, in case of atypical uptake, a biopsy should be considered (with mediastinoscopy or endobronchial ultrasonography) before proposing another line of treatment.

Other nonspecific lymph nodes

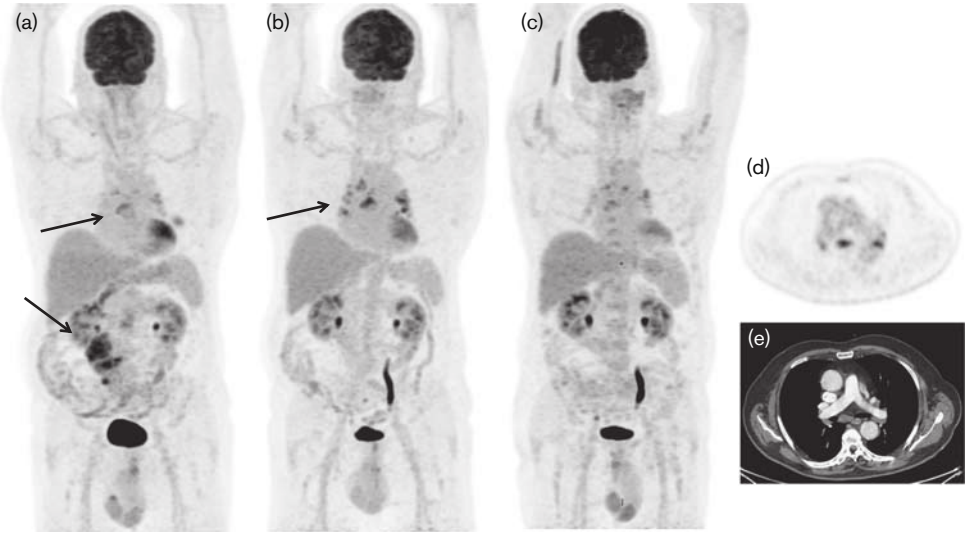
Similarly, cervical lymph nodes are often persistent at the end of treatment on ^{18}F-FDG-PET/CT imaging. A recent study [27] has shown the lack of specificity of

Fig. 5



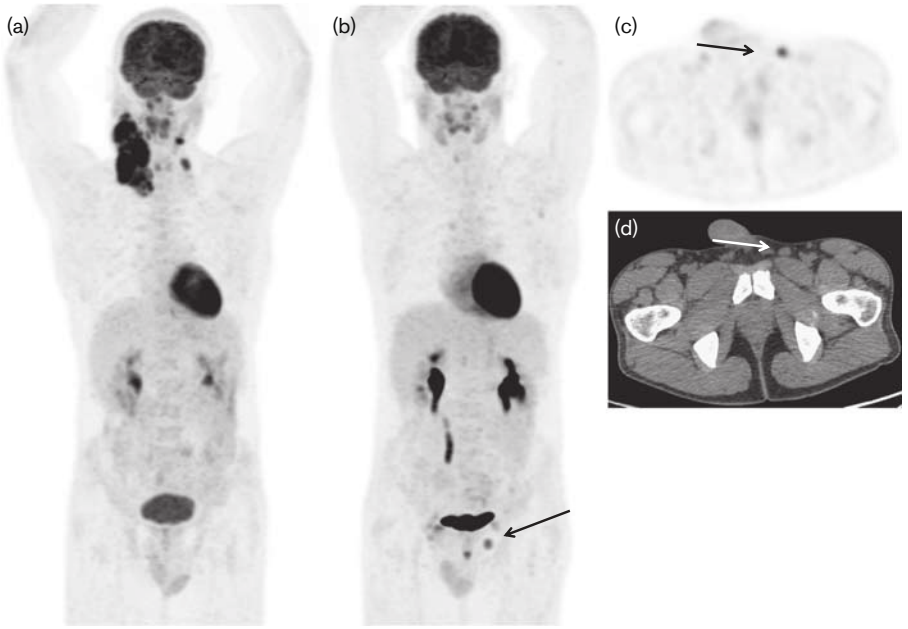
A 33-year-old man with HL. Initial ^{18}F-FDG-PET/CT (a) showed an intense uptake of a bulky mass and supradiaphragmatic lymph nodes. At the end of treatment, ^{18}F-FDG-PET/CT showed a moderate uptake of anterior mediastinum, which increased after 2 months ($SUV_{max} = 12.2$) (b–d), leading to surgical resection. No lymphoma was found. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 6



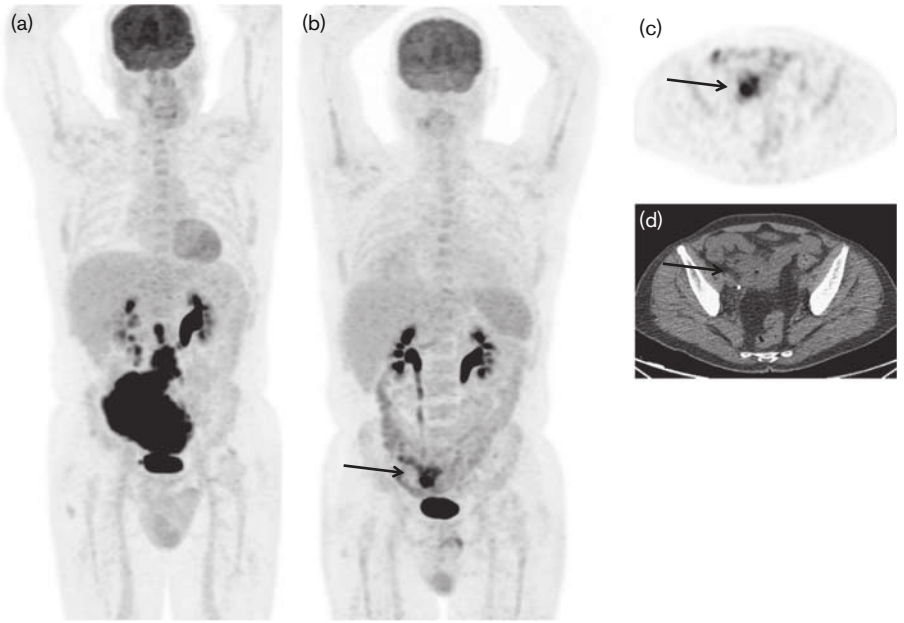
A 68-year-old woman with FL. Initial PET/CT (a) showed pathologic uptake of supradiaphragmatic and infradiaphragmatic lymph nodes (arrows on a). ^{18}F-FDG-PET/CT at the end of treatment (b) showed a complete response in the infradiaphragmatic area, but persistent and increased uptake of mediastinal lymph nodes (arrows on b) (d, e). Patient refused biopsy, but the 1-year ^{18}F-FDG-PET/CT follow-up did not show any progression of mediastinal uptake and no relapse of lymphoma disease (c). A mediastinal granulomatosis was evoked. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; FL, follicular lymphoma.

Fig. 7



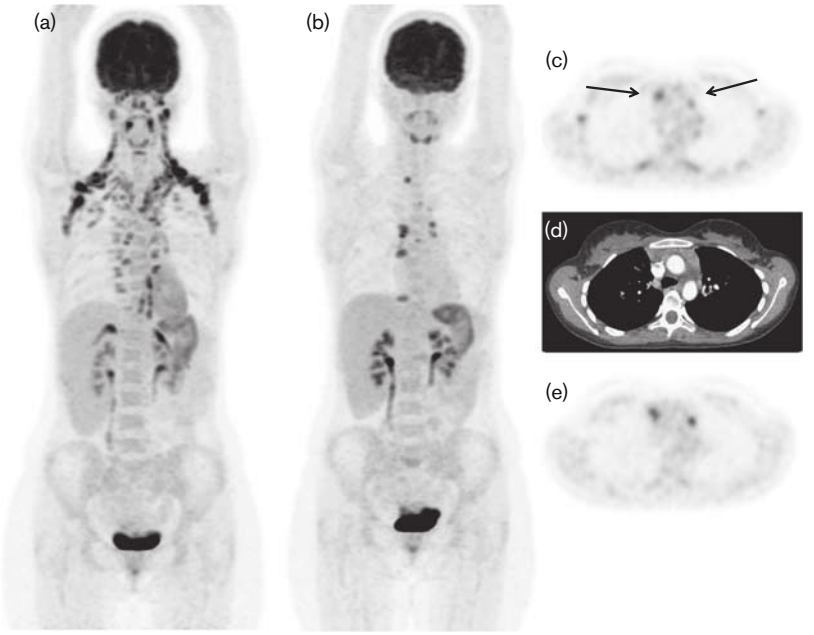
A 36-year-old man with a supradiaphragmatic HL (a). After three cycles of chemotherapy, ^{18}F-FDG-PET/CT showed an intense ^{18}F-FDG uptake of inguinal lymph nodes ($SUV_{max} = 9.9$) (b–d), which was not involved on initial staging (arrows). A biopsy was performed, showing the inflammatory process. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 8



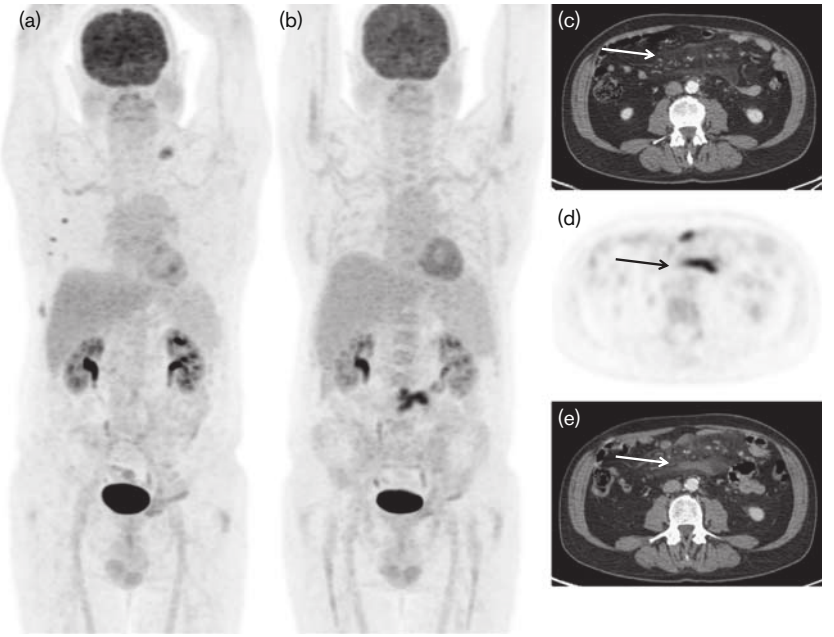
A 48-year-old man with DLBCL. Following the initial CT scan, ^{18}F-FDG-PET/CT was performed (a), showing intense uptake of a caecal lesion and retroperitoneal lymph nodes. An interim ^{18}F-FDG-PET/CT after two cycles of chemotherapy was still positive on the caecal lesion, requiring a second control by ^{18}F-FDG-PET/CT after four cycles (b), showing an increased uptake of the caecal lesion (arrows) ($SUV_{max} = 17.8$) (c, d), with a complete response of retroperitoneal lymph nodes. After two new cycles of chemotherapy, the decision to perform a surgical resection was made. Pathologic analyses showed no tumor but a cecum perforation with abscess. No relapse was encountered after 1 year. CT, computed tomography; DLBCL, diffuse large B cell lymphoma; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; SUV_{max}, maximum standardized uptake value.

Fig. 9



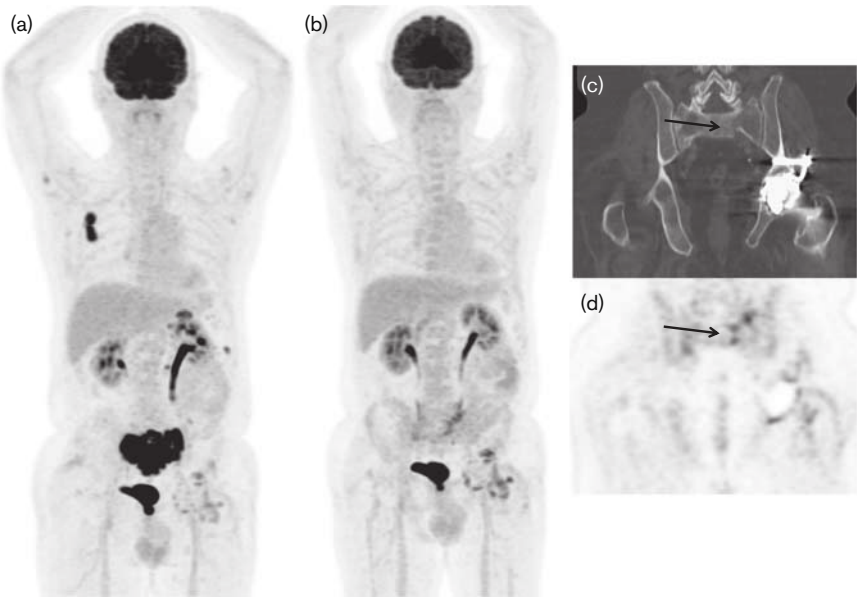
A 29-year-old woman with a HL. ^{18}F-FDG-PET/CT after four cycles of showed a diffuse uptake of brown activation tissue (a). Because of abnormal uptake in the mediastinum, not typical for brown activation tissue (arrows) (c, d), a new ^{18}F-FDG-PET/CT was performed 2 weeks later, after premedication with 20 mg of propranolol administered 45 min before injection of ^{18}F-FDG (b). ^{18}F-FDG-PET/CT data confirmed the partial metabolic response with the Deauville five-point scale at 5. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 10



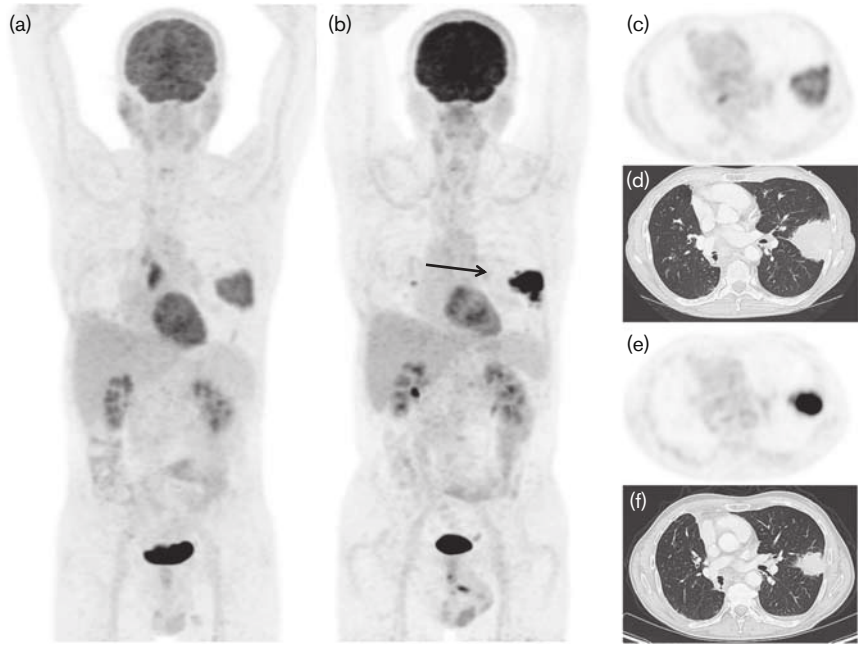
A 61-year-old man with a relapse of FL. The pretherapeutic ^{18}F-FDG-PET/CT (a) showed a supradiaphragmatic disease associated with panniculitis (c), without clear ^{18}F-FDG uptake. After three cycles of chemotherapy (b), all initial pathologic sites showed complete response. Conversely, an intense ^{18}F-FDG uptake appeared in mesenteric folds (arrows), without a mass clearly visible on CT (d, e). A biopsy was performed, in favor of fat necrosis. The ^{18}F-FDG-PET/CT performed one month later was considered negative. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; FL, follicular lymphoma.

Fig. 11



A 78-year-old man with DLBCL. Initial PET/CT showed a large sacral lesion ($SUV_{max} = 26.9$) with supradiaphragmatic lymph nodes (a). After three cycles of chemotherapy, interim ^{18}F-FDG-PET/CT showed a clear response (b), except a persistent focus of the right sacrum ($SUV_{max} = 7$) (arrows on d) (c, d). On CT images, there was a fracture line corresponding to the focal uptake (arrows on d). Treatment was continued and no relapse has been reported after 6 months. CT, computed tomography; DLBCL, diffuse large B cell lymphoma; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; FL, follicular lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 12



A 66-year-old man with lung MALT lymphoma. Initial ^{18}F-FDG-PET/CT (a) showed a moderate uptake of a pathologic lesion located in the left lung ($SUV_{max} = 6.4$) (c, d) associated with a subcarenar lymph node ($SUV_{max} = 8.4$). After six cycles of chemotherapy, a new evaluation ^{18}F-FDG-PET/CT was performed (b) and showed a decrease in the size of the lung lesion on CT (f), whereas an increase of uptake was observed on ^{18}F-FDG-PET (arrow on b) (e). SUV_{max} reached 29.4. A new biopsy confirmed a transformation in B cell lymphoma. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; MALT, mucosa-associated lymphoid tissue; SUV_{max}, maximum standardized uptake value.

positive cervical lymph nodes in the follow-up as only 9% of them were positive for lymphoma at the end of treatment. Furthermore, cervical lymph node hyperplasia are frequent in teenagers and children [28].

In the same way, axillary lymph nodes can be a source of false-positive results. A usual case is tracer extravasation [29,30]: the lymph node is usually not enlarged and shows an adipose tissue component. In clinical practice, axillary lymph node uptake after treatment should be considered as pathologic only if associated with another abnormal uptake, increasing the rate of true positivity from 20.8 to 79.6%, [31]. In case of bilateral ^{18}F-FDG uptake, axillary hyperplasia should also be considered [32]. Finally, a second cancer can occur, in particular, breast cancer for women [31].

According to our experience, inguinal lymph nodes uptake is also responsible for a high rate of false positives [33]. A single inguinal lymph node uptake should not be subjected to biopsy, especially if there was no initial involvement in the same location (Fig. 7), and a follow-up after a few months can be performed. In doubtful cases, an ultrasonography with cytologic analysis should be performed.

Nonspecific digestive uptake

There is physiological ^{18}F-FDG uptake in the stomach, duodenum, small, and large intestine because of peristalsis, mucosal structures, or lymphocytic cell concentration. Thus, ^{18}F-FDG-PET/CT assessment of digestive involvement could be less specific at initial staging. At interim or end-of-treatment evaluation, reduced specificity is often related to ulcerative or mucosal lesions (Fig. 8) [34,35].

Brown adipose tissue activation

Brown fat tissue is a well-known potential source of misinterpretation. Its involvement in cold-induced and diet-induced thermogenesis [36] leads to tissue activation, which can induce intense ^{18}F-FDG uptake in the supraclavicular area, mediastinum (anterior and posterior), and in the perirenal area [37]. These uptakes should not be considered an incomplete response on ^{18}F-FDG-PET/CT evaluation. Conversely, an intense and diffuse uptake of brown adipose tissue should not mask an incomplete response (Fig. 9). In doubtful cases, repeating ^{18}F-FDG-PET/CT after appropriate premedication by propranolol or diazepam is necessary [38–40].

Fat necrosis

Another source of false-positive results is fat mesentery necrosis, described in few case reports [41–43], and only one study [44] is available on this topic. According to our experience, fat necrosis should be considered in case of ^{18}F-FDG uptake corresponding to low-density tissue on CT images and is usually described in fat mesenteric folds. Furthermore, mesenteric lymph nodes are frequently described on the PET/CT baseline evaluation, which can be related to panniculitis, especially if the other sites of initial disease completely responded (Fig. 10). However, confirmation by biopsy is required as ^{18}F-FDG-PET/CT cannot distinguish fat necrosis from lymphoma.

Bone response

^{18}F-FDG-PET/CT can be sufficient in baseline evaluation to assess bone marrow involvement in DBLCL and HL only in case of focal uptake [1,2]. However, focal bone uptake can be related to small fractures during bone regeneration after chemotherapy. These fractures are usually ^{18}F-FDG avid if recent [45] and can be difficult to distinguish from residual disease, especially in case of initial bone involvement in the same area (Fig. 11). In case of doubt, a control by ^{18}F-FDG-PET/CT should be proposed.

Lymphoma transformation

^{18}F-FDG-PET/CT can be used for the end-treatment evaluation of indolent lymphoma including FL. In case of incomplete response and increased lesion uptake (SUV_{max}), lymphoma transformation should be systematically evoked. Indeed, histological transformation can occur up to 20% of patients at the end of treatment [46]. According to Bodet-Milin *et al.* [47], transformation of indolent lymphoma should be considered if SUV_{max} is above 14, with a positive predictive value and a negative predictive value of 93.9 and 95.3%, respectively. In this case, a new biopsy should be performed focused on the suspicious lesion (Fig. 12).

This transformation usually occurs on the initial pathologic site. However, discordant evolution with new site involvement and a complete response on initial sites have been described [48]. According to our experience, lymphoma transformation is the main situation of discordant evolution. To our knowledge, discordant evolution with a complete response on initial sites and a proved progression on a new site are almost non-existent for HL and rare for DLBCL and FL, except in the central nervous system (Fig. 13) [49], but because of the high risk of false positivity and the impact on treatment management, a biopsy should always be performed.

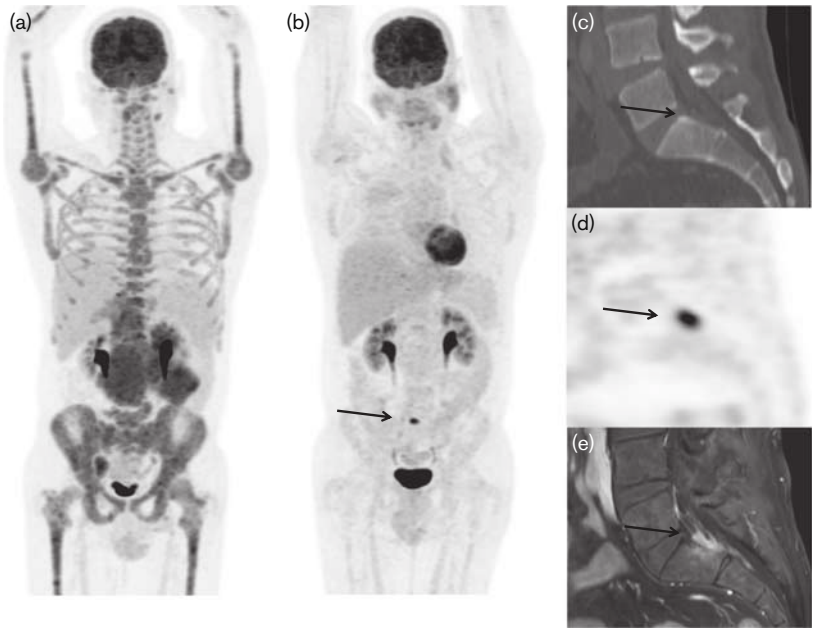
Second malignancy

^{18}F-FDG-PET/CT has excellent diagnosis performance for lymphoma, but is also used in others malignancies that can be detected at initial staging [50] and at the end of treatment (Fig. 14). In particular, lung cancer [51] and colon cancer [52] should be considered especially after 50 years of age.

Postsurgical uptake

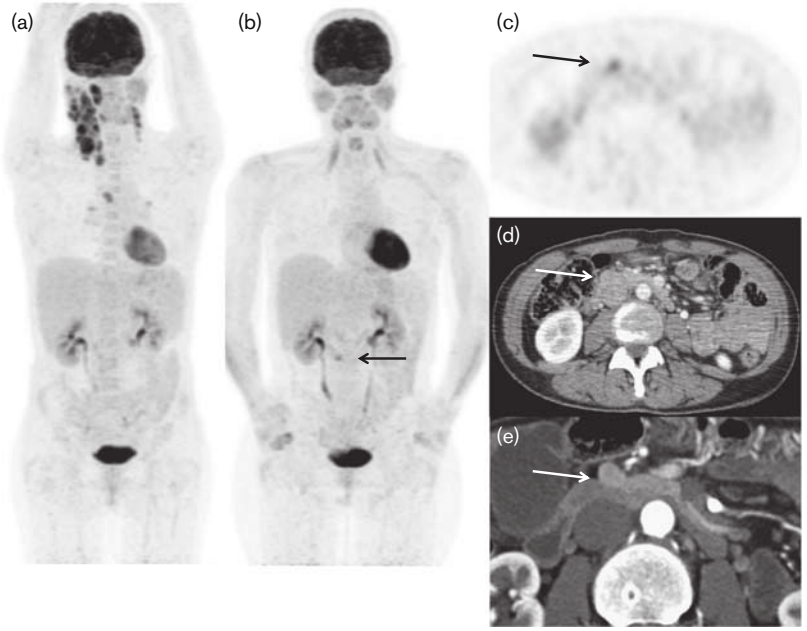
Increased ^{18}F-FDG uptake is systematically observed after surgical intervention, especially in the next 3 months after surgery. Thus ^{18}F-FDG-PET/CT is not

Fig. 13



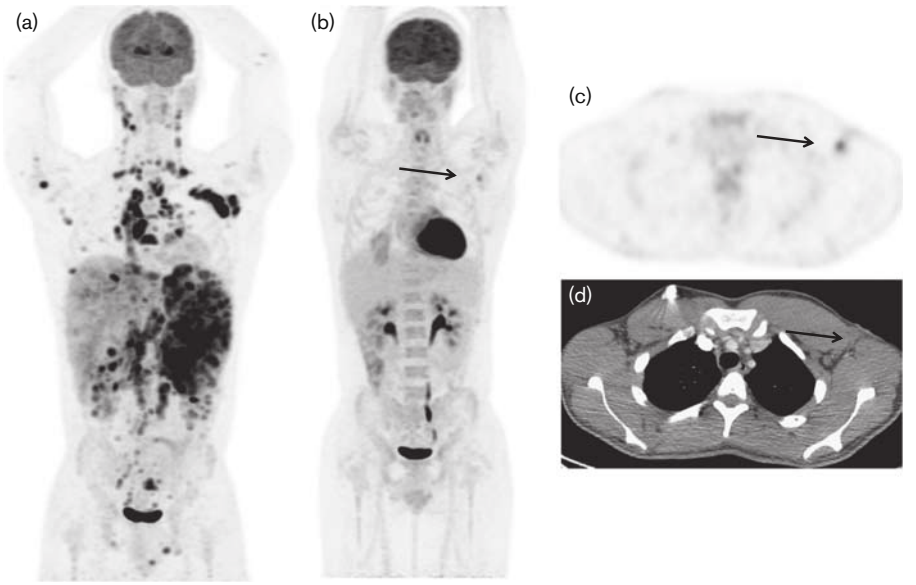
A 48-year-old man with FL. Initial ^{18}F-FDG-PET/CT (a) showed an intense uptake of supradiaphragmatic and infradiaphragmatic lesions with bulky mesenteric and a diffuse medullar uptake with positive bone marrow biopsy. At the end of treatment, an ^{18}F-FDG-PET/CT was performed (b) and showed a complete metabolic response. However, a focal and intense uptake of cauda equina appeared ($SUV_{max} = 12.75$) without correspondence on CT (arrows) (c, d). A complementary MRI (e) was performed and showed a nodule contrast-enhanced of cauda equina, with bone adjacent edema of S1. The biopsy performed 3 months later on contiguous bone lysis confirmed the relapse of lymphoma, probably related to initial dural involvement. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; FL, follicular lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 14



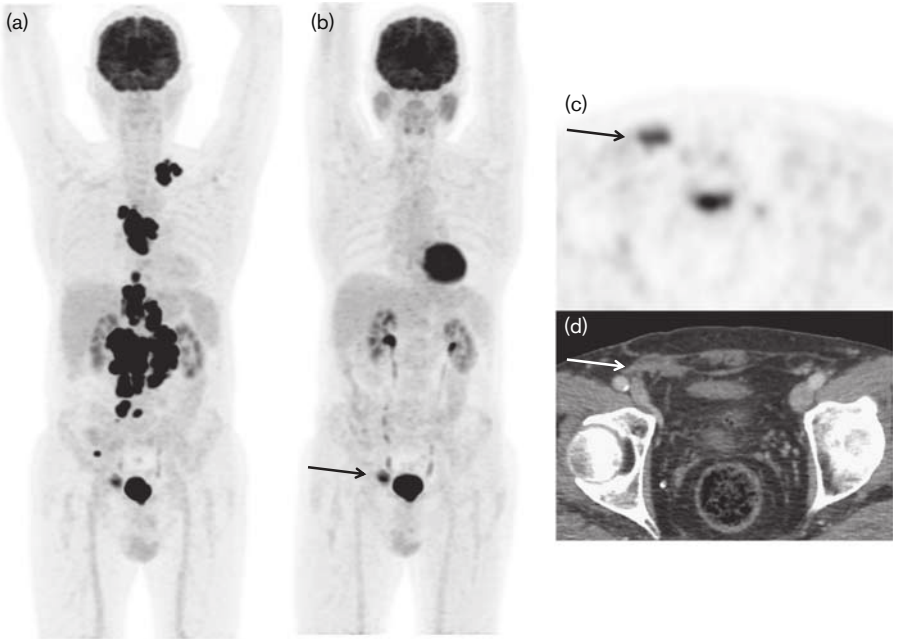
A 50-year-old woman with HL. Initial ^{18}F-FDG-PET/CT (a) showed intense and suspicious uptake of supradiaphragmatic and infradiaphragmatic lymph nodes. At the end of treatment, few peripancreatic lymph nodes persisted. After 1 and 5 years of follow-up, and because of the significant evolution on ^{18}F-FDG-PET/CT (b–d), a diagnosis of neuroendocrine tumor was suggested (arrows on b–d), confirmed by angio-CT (arrow on e) (e) and cephalic duodenopancreatectomy. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 15



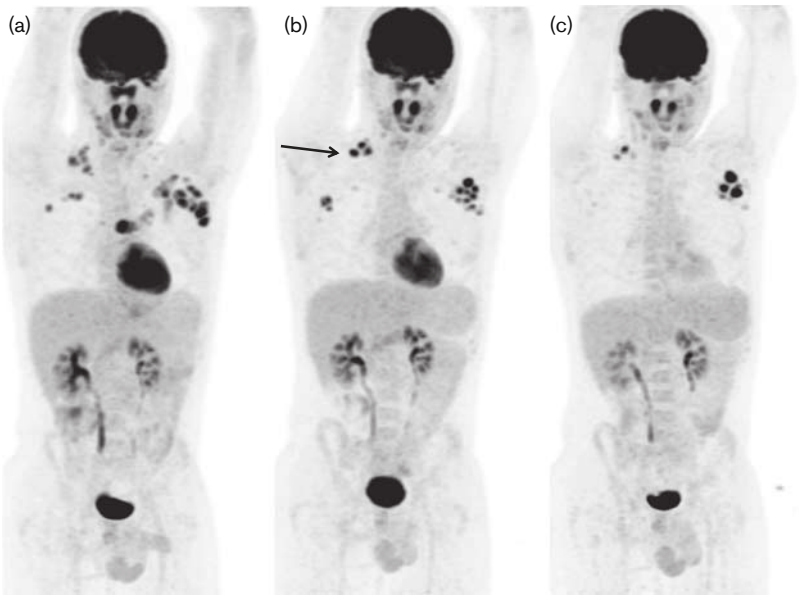
A 27-year-old man with nodular lymphocyte predominant HL. Initial ^{18}F-FDG-PET/CT (a) showed an intense uptake of supradiaphragmatic and infradiaphragmatic lesions with splenic, liver, and renal involvement. At the end of treatment, an ^{18}F-FDG-PET/CT was performed (b), showing a lung infection and persistent uptake in the axillary area ($SUV_{max} = 5$), without the corresponding nodule on CT (arrows) (c, d). Because of the initial biopsy performed in the same site, a postsurgery uptake was considered. A control 6 months after the end of treatment showed no lymphoma cells, but inflammatory scarring tissue, and confirmed the diagnosis. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 16



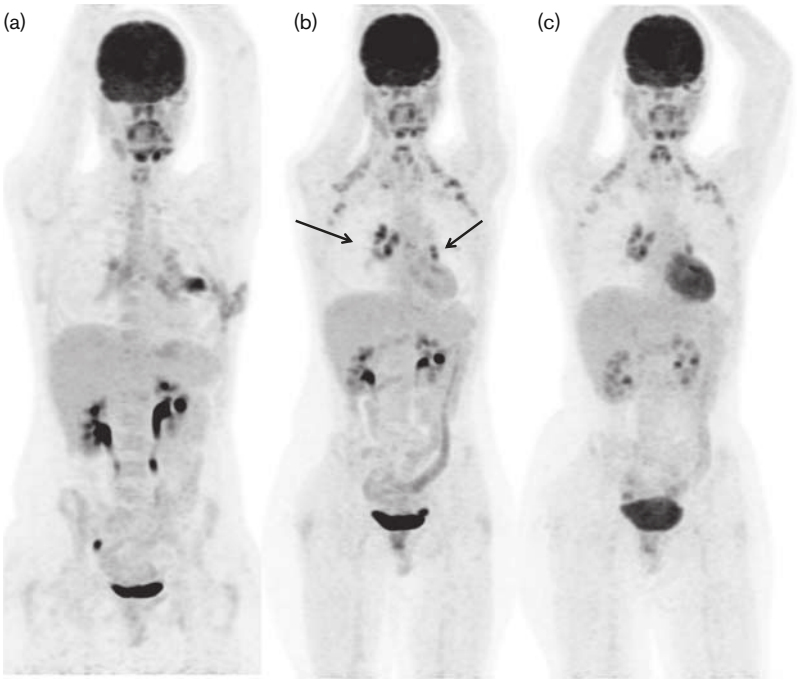
A 71-year-old man with DLBCL. Initial ^{18}F-FDG-PET/CT (a) showed an intense uptake of a supradiaphragmatic and infradiaphragmatic lymph nodes. An interim ^{18}F-FDG-PET/CT after four cycles (b) of chemotherapy showed a complete response, except in the right inguinal area ($SUV_{max} = 12$) (arrows) (c, d). CT images findings evoked a previous inguinal hernia surgery. Patient had a history of right inguinal hernia repair that was performed 4 years ago. CT, computed tomography; DLBCL, diffuse large B cell lymphoma; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; SUV_{max}, maximum standardized uptake value.

Fig. 17



A 22-year-old patient with a relapse of HL after allogeneic stem cell transplantation. ^{18}F-FDG-PET/CT before treatment with nivolumab (a) showed an intense uptake of supradiaphragmatic lesions. After seven cycles of chemotherapy with nivolumab (b), few lesions (arrow) increased of ^{18}F-FDG uptake in right cervical nodes and right axillary lymph nodes (for right cervical nodes: SUV_{max} 13.4 vs. 7.4 before treatment) without an increase in lesion size (immune response type 3). ^{18}F-FDG-PET/CT performed 3 months later (c) showed an excellent partial response of these lesions, without significant metabolic or morphologic changes, and confirmed treatment efficacy. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

Fig. 18



A 30-year-old woman with HL. Initial ^{18}F-FDG-PET/CT (a) showed an intense focus uptake into the lung because of a relapse, proven by biopsy. After eight cycles of chemotherapy with pembrolizumab (b), few new lesions were observed in the mediastinohilar area (arrows) (b). A granulomatosis induced by immunotherapy was suspected, especially because of the fact that the initial lung lesion disappeared. ^{18}F-FDG-PET/CT performed 6 months later (c) showed global stability and confirmed a false-positive result because of immunotherapy. CT, computed tomography; ^{18}F-FDG, fluorine-18-fluorodeoxyglucose; HL, Hodgkin lymphoma; SUV_{max}, maximum standardized uptake value.

recommended in lymphoma evaluation during the 6 weeks following surgery [40]. Furthermore, ^{18}F-FDG uptake can last for months (Fig. 15), especially if a surgical device has been implanted. For example, inguinal hernia repair with implantation of a mesh prosthesis leads to persistent uptake during many years because of foreign body reaction (Fig. 16) [53,54].

Immunotherapy

During the last few years, immunotherapy (rituximab, brentuximab, ibrutinib, pembrolizumab, etc.) has shown efficacy, especially for HL [55,56] and DLBCL [57]. However, this new therapy is responsible for false-positive results because of lymphocyte infiltration [58]. Thus, new criteria are available (Lyrics criteria) [59], which define three distinct types of indeterminate response: type 1, defined as increase of initial lesion of at least 50% in the first 12 weeks of treatment, for which a control in the next 12 weeks or a biopsy is strongly recommended; type 2, defined as increase of initial lesions or apparition of new lesions at any time during treatment for which a biopsy is strongly recommended; and type 3, defined as increase in ^{18}F-FDG uptake without a concomitant increase in lesion size fulfilling the criteria for progression disease. In some cases, patients can fulfill criteria for different types of indeterminate response (Fig. 17).

These therapies are also responsible for false-positive results related to treatment, such as granulomatosis, arthritis, hepatitis, pancreatitis, hypophisitis, and colitis [60]. All these side effects can be detected on ^{18}F-FDG-PET/CT and should not be confused with lymphoma (Fig. 18).

Conclusion

As we know, ^{18}F-FDG-PET/CT is now a standard of care to assess response to treatment. Most of the time, it is easy to identify complete response. However, we should bear in mind potential pitfalls that can lead to wrong response evaluation, in particular, lymph nodes uptake and thymus hyperplasia. Secondary malignancy is, according to our experience, a frequent source of pitfalls and should be considered systematically in case of unusual positive ^{18}F-FDG-PET on follow-up evaluation. A complementary CT or MRI scan should also be performed in case of doubt. Furthermore, it is crucial to keep in mind that a complete response on the initial site with the appearance of a new lesion in a new location is rare for HL and DLBCL, but more frequently in FL, especially in case of lymphoma transformation. Finally, a biopsy should be performed to prove residual disease, especially in the case of treatment by immunotherapy.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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