Significance of FDG-PET in Identification of Diseases of the Appendix – Based on Experience of Two Cases Falsely Positive for FDG Accumulation

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Key Words

FDG-PET · Diseases of the appendix · Falsely positive · Standard uptake values

Abstract

A discussion of the significance of F-fluorodeoxyglucose positron emission tomography (FDG-PET) in the identification of diseases of the appendix is presented based on two cases falsely positive for FDG accumulation. Both cases were palpable for a tumor in the lower right abdominal region and a prominently enlarged appendix was depicted by CT. Although the patients underwent ileocecal resection based on a strong suspicion of appendiceal cancer rather than appendicitis since abnormal accumulation exhibiting maximum standard uptake values (SUVs) of 7.27 and 17.11, respectively, was observed at the same site in FDG-PET examination and since there no malignant findings observed histologically, the patients were diagnosed with appendicitis. Although FDG specifically accumulates not only in malignant tumors, but also in diseases such as acute or chronic inflammation, abscesses and lymphadenitis, and identification based on SUVs has been reported to be used as a method of identification, the two cases reported here were both false-positive cases exhibiting high maximum SUVs. At the present time, although the significance of FDG-PET in the identification of diseases of the appendix is somewhat low and there are limitations on its application, various research is currently being conducted with the aim of improving diagnostic accuracy, and it is hoped that additional studies will be conducted in the future.

Introduction

F-fluorodeoxyglucose positron emission tomography (FDG-PET) has attracted attention in recent years and has been reported to be useful as a means of diagnosing malignant diseases and assessing therapeutic effects in various fields [1–3]. In this study, we performed FDG-PET examinations for the purpose of identifying and diagnosing diseases of the appendix, and as a result thereof, encountered two cases falsely positive for FDG accumulation that ultimately received excessive treatment selected on the basis of strong suspicion of malignant findings. The following provides a discussion of the significance of FDG-PET in the identification of diseases of the appendix based on our experience with these two cases.

Case 1

The first case was a 71-year-old male. This patient visited our hospital with the primary complaint of lower right abdominal pain that had begun one week earlier. The patient presented with a body temperature of 37.8°C and a tumor measuring several centimeters was palpable in the lower right abdominal region and accompanied by tenderness. Hematology and blood biochemistry data consisted of a WBC count of 8,800/mm³ and CRP of 14.92 mg/dl, while tumor markers consisted of CEA of 2.0 ng/ml and CA19-9 of 8 U/ml. CT revealed the appendix to be prominently enlarged. The appendix had become enlarged to 25 mm and the appendix walls exhibited hypertrophy (fig. 1a). The results of FDG-PET coincided with a tumor-like shadow observed in CT and abnormal accumulation of FDG was observed. The maximum standard uptake value (SUV) was elevated at 7.27 (fig. 1b, c). Surgical findings indicated the tip of the appendix to be oriented towards the dorsal side of the ileal mesenteric membrane, the tip was hard and enlarged as compared with the comparatively soft base and was determined to be tumor-like by palpation. Since appendiceal cancer could not be ruled out on the basis of surgical findings and since the SUV was elevated, the patient underwent ileocecal resection based on a strong suspicion of appendiceal cancer. Histologically, the appendix exhibited formation of ulcerations over a comparatively wide range accompanied by prominent eosinophil infiltration throughout all layers of the appendix wall, and inflammation was particularly prominent from the middle to the tip. No malignant findings were observed, and the patient was diagnosed with appendicitis associated with abscess in the surrounding fatty tissue.

Case 2

The second case was a 68-year-old male. The patient visited our hospital with the primary complaint of epigastric pain and lower right abdominal pain starting about one month earlier. The patient presented with a body temperature of 37.2°C, and a tumor measuring several centimeters was palpable and accompanied by mild tenderness in the lower right abdominal region. Hematology and blood biochemistry data consisted of a WBC count of 14,950/mm³ and CRP of 6.81 mg/dl, while tumor markers consisted of CEA of 3.3 ng/ml and CA19-9 of 20 U/ml. CT revealed the appendix to be enlarged in the manner of a tumor and accompanied by nonhomogeneous enhancement. The appendix had become prominently enlarged to 30 mm and was accompanied by hypertrophy of the appendix wall (fig. 2a). The results of FDG-PET coincided with the mass portion observed in CT and abnormal accumulation of FDG was observed. The maximum SUV was elevated at 17.11 (fig. 2b, c). Although surgical findings did not reveal well-defined abnormalities in the base of the appendix, a mass measuring about 3 cm was observed in the tip and was adhered to the retroperitoneal membrane and sigmoid colon. Since appendiceal cancer could not be ruled out on the basis of surgical findings and since the SUV was elevated, the patient underwent ileocecal resection and partial resection of the sigmoid colon based on a strong suspicion of appendiceal cancer. Histologically, the appendix was accompanied by formation of ulcerations, and since prominent infiltration of inflammatory cells and inflammatory foci comprised of macrophages were observed over a wide range through all layers, including surrounding fatty tissue, the patient was diagnosed with appendicitis.

Discussion

Appendiceal cancer is a comparatively rare disease occurring at a frequency lower than that of appendicitis. Collins reported that, in a study of 71,000 cases of resected appendix specimens, primary appendiceal cancer was observed in only 57 cases, demonstrating an incidence of 0.08% [4]. In addition, appendiceal cancer is not associated with characteristic symptoms or signs, and since symptoms accompanied by occlusive complication of the appendix are similar to acute appendicitis, this is one of the factors contributing to difficulty in discriminating between these two diseases. Actually there are a significant number of cases in whom appendectomy was performed based on a diagnosis of acute appendicitis only to find, based on the results of postoperative histopathological analysis, that the disease was actually appendiceal cancer.

CT scans are considered to be useful in diagnosing diseases of the appendix such as acute appendicitis and appendiceal cancer [5]. Examples of CT findings associated with acute appendicitis include appendix enlargement to a diameter of 6 mm or more, presence of appendiceal stones, increased density of periappendiceal fatty tissue, formation of abscesses and ascites [6]. In addition, an enhanced or missing appendix wall is important in enhanced CT. On the other hand, examples of CT findings associated with appendiceal cancer vary according to the respective type. Appendiceal cancer is classified into two types, consisting of mucinous cystadenocarcinoma and nonmucinous (colonic type) adenocarcinoma. Mucinous cystadenocarcinoma is depicted as a cystic mass on CT, and is strongly suspected if accompanied by nodes accompanied by enhancement in the tumor wall. In contrast, although reported examples of CT findings associated with nonmucinous (colonic type) adenocarcinoma include appendix enlargement to 15 mm or more, wall thickening, focal or diffuse soft tissue mass and periappendiceal fat stranding [7], imaging findings are presented that resemble those of abscess-associated appendicitis, thus making it difficult to conclude that these findings are specific. The two cases examined here also presented with these imaging findings, and although appendiceal cancer could not be ruled out on the basis of CT, both cases were eventually determined to have appendicitis.

FDG-PET examinations were performed on these two cases for the purpose of identification and diagnosis. FDG-PET has been reported in recent years to be effective for diagnosing the presence of tumors, identifying the range of invasion and evaluating the degree of malignancy of various neoplastic diseases [1–3]. FDG-PET is an examination method that uses ^{18}F FDG, a glucose-like substance labeled with ^{18}F (fluorine-18), to depict and visualize increased absorption and metabolism of glucose in tumor cells [3]. Since malignant cells exhibiting extremely accelerated proliferation exhibit greater glucose metabolism activity than normal cells, this can be noninvasively captured in images in the form of increased accumulation of FDG. However, since FDG does not specifically accumulate in malignant tumors only, but rather also reacts to leukocytes and macrophages exhibiting active increases in glucose absorption and metabolism, it also accumulates in diseases such as acute or chronic inflammation, abscesses and lymphadenitis corresponding to the degree of inflammation, thereby resulting in the potential for the occurrence of false positives [8, 9].

Identification based on SUVs is used as a method for discriminating between malignant tumors and diseases other than tumors such as inflammatory diseases. SUV looks at the ratio of the degree of accumulation of FDG in a focus based on a value of 1 for the radioactive concentration of FDG uniformly distributed in the body, and since this enables evaluations to be made objectively, is considered to be useful in assessing

diagnosis, prognosis and therapeutic effects [10]. SUV is expressed as the ratio of tissue ^{18}F concentration (MBq/ml) to ^{18}F dose (MBq/body weight in g), is typically considered to be higher for malignant tumors than benign tumors, and a significant difference value of 2.0 or 2.1 to 3 has been reported to be used as a cut-off value [10, 11]. However, in the two cases reported here, despite SUVs being 3.0 or more, and that in case 2 being extremely high at 17.11, there were no malignant findings and both cases were determined to have appendicitis. Thus, on the basis of our experience with these two cases, we were unable to find any usefulness in FDG-ET for identifying and diagnosing appendiceal cancer and appendicitis. In addition, although inflammatory findings were observed in both cases on the basis of hematology and blood biochemistry data, since a mass was palpable, findings associated with peritonitis were mild, and CT findings indicated prominent enlargement of the appendix, appendiceal cancer could not be completely ruled out prior to surgery, and discrimination between appendiceal cancer and appendicitis was even difficult on the basis of surgical findings. When selecting the procedure, a method consisting of a two-stage procedure comprised of appendectomy and followed by ileocecal resection after waiting for postsurgical pathology results, and a method involving confirmation by intrasurgical rapid pathological diagnosis can be considered. However, since accumulation of FDG was observed in FDG-PET and maximum SUVs were elevated in both case 1 (7.27) and case 2 (17.11), appendiceal cancer was conversely strongly suspected and ileocecal resection was selected for the procedure, ultimately resulting in excessive treatment.

At present, imaging in a delayed layer, which is slower than ordinary layers, has attracted attention as a means of overcoming these problems associated with FDG-PET and improving diagnostic accuracy. This utilizes the fact that FDG reaches a peak by 1 h after administration in benign lesions, but demonstrates an increasing trend in accumulation even at 1 h after administration in malignant lesions, although subject to differences in the degree, thereby suggesting the potential for the usefulness of the delayed phase in breast and lung cancer as well [12, 13]. In addition, studies to reduce the likelihood of false positives have been conducted using multitracer studies and labeled amino acid PET scans instead of FDG scans [8], and in a comparison between FDG and 3-deoxy-3- ^{18}F -fluorothymidine (FLT) in rats, the tumor specificity of FLT was reported to be higher than that of FDG [14]. And ^{18}F -fluoroethyl-L-tyrosine has been reported to have greater ability in discriminating between tumors and inflammation and to have higher specificity for tumor diagnosis than FDG [15]. In the field of PET examinations, research is continuously being conducted to improve diagnostic accuracy, and it is believed that the day will come when it will be possible to use PET to discriminate between appendicitis and appendiceal cancer. It is therefore hoped that studies to that purpose will be conducted in the future.

Fig. 1. **a** CT revealed the appendix to be prominently enlarged. The appendix had become enlarged to 25 mm and the appendix walls exhibited hypertrophy (arrow). **b, c** The results of FDG-PET coincided with a tumor-like shadow observed in CT and abnormal accumulation of FDG was observed. The maximum SUV was elevated at 7.27 (arrows) (**b** coronal image; **c** axial image).

Fig. 2. **a** CT revealed the appendix to be enlarged in the manner of a tumor and accompanied by nonhomogeneous enhancement. The appendix had become prominently enlarged to 30 mm and was accompanied by hypertrophy of the appendix wall (arrow). **b, c** The results of FDG-PET coincided with the mass portion observed in CT and abnormal accumulation of FDG was observed. The maximum SUV was elevated at 17.11 (arrows) (**b** coronal image; **c** axial image).

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