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Abdominal Positron Emission Tomography Combined With Magnetic Resonance Imaging in Chronic Granulomatous Disease

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INTRODUCTION

Chronic granulomatous disease (CGD) is a primary immunodeficiency and most patients are diagnosed in early childhood (1). Due to mutations in genes encoding the nicotinamide adenine dinucleotide phosphate enzyme complex, the production of reactive oxygen species in phagocytic cells is reduced or extinct, impairing the intracellular killing of invading pathogens (2) and leading to unregulated hyperinflammation (3). Hyperinflammation occurring in the gastrointestinal tract prompts clinical and radiological findings similar to those in Crohn disease and ulcerative colitis (4). Radiological images from CGD patients are consistent with findings typically encountered in patients with Crohn disease or ulcerative colitis. Computed tomography (CT) shows bowel wall thickening, narrowing of small and large bowel segments, and engorged vasa recta (4, 5). Furthermore, a prospective diagnostic study of patients with known CGD showed that [18F]-fluorodeoxyglucose positron emission tomography ([18F]-FDG PET) may augment the identification of active lesions compared to stand-alone CT (6) with a higher sensitivity of PET in detecting granulomatous gastritis and colitis, which in their study influenced the decision to perform an endoscopy. Still, CT scanning entails the use of ionizing radiation, which is of particular concern in children and adolescents. In CGD, magnetic resonance imaging (MRI) can visualize mucosal thickening of the colon, abscess formation, and fistulization (7). During the past decade, hybrid PET/MRI scanners have become available in a clinical setting. In this light, it is increasingly relevant for clinicians and radiologists alike to be familiar with the radiologic appearance of CGD as a differential diagnosis in patients with chronic colitis. In this article, we present the case of a boy with symptoms of chronic colitis and describe the utility of hybrid PET/MRI imaging in the diagnostic approach.

CASE REPORT

An 11-year-old boy presented with abdominal pain, fever, and nonbloody diarrhea. C-reactive protein was 365 mg/L and the leukocyte count was 26.2×10^9/L. A central, mesenteric abdominal abscess was identified on CT and drained under ultrasound guidance. Bacterial cultures showed growth of *Aggregatibacter aphrophilus* and the patient was treated with relevant antibiotics. At discharge, the patient was apyrexial, C-reactive protein was 31 mg/L, and the leukocyte count had normalized.

At follow-up after 2 months, he had persistent abdominal pain and had developed bloody diarrhea. Physical examination revealed a nontender abdominal mass in the umbilical region. Fecal calprotectin was elevated to 4347 µg/g (normal value < 50 µg/g). The differential diagnoses based on the clinical presentation and physical examination were Crohn disease, ulcerative colitis, infectious enterocolitis, and recurrence of the abscess.

We performed a hybrid [18F]-FDG PET/MRI (GE Signa 3T PET/MRI; GE Healthcare, Boston, MA) for diagnostic evaluation of inflammatory bowel diseases. FDG activity of 4 MBq/kg was injected after an overnight fast. After a subsequent rest period of 1 hour, an [18F]-FDG PET/MRI was performed using 2-bed positions with 27% overlap each with 5 minutes acquisition time. Within each bed position, axial diffusion-weighted imaging sequence with b values of 50 and 900, respectively, was acquired. PET images were reconstructed using a Bayesian Penalized Regularized algorithm in a 256 × 256 matrix using a Dixon based attenuation correction. Additional MRI sequences included coronal fast imaging employing steady-state acquisition and a navigator-gated T2 single-shot fast spin-echo. Coronal and axial T1 liver acquisition with volume acceleration sequences were performed before and after injection of gadolinium contrast. Images are presented in Figure 1.

The scan showed pathological FDG uptake in a mesenteric mass resembling a lymph node conglomerate adjacent to the duodenum (Figure 1, blue arrow). In the distal colon, there was bowel wall thickening and pathological FDG uptake (Figure 1, red arrow). A subsequent colonoscopy revealed an inflamed mucosa and multiple ulcers extending from the transverse colon to the rectum. Fecal samples were positive for *Clostridium difficile*, which was treated with intravenous metronidazole and vancomycin. Due to continued symptoms despite antibiotic treatment, the FDG avid central mass was surgically removed and histologic analysis established that is consisted of lymphoid tissue with the formation of multiple noncaseating granulomas with central neutrophil accumulation. The adjacent small intestinal tissue was normal. Test for tuberculosis was negative.

A dihydrorhodamine test showed an extinct oxidative response in the neutrophil granulocytes consistent with CGD. The diagnosis was confirmed by genetic analysis, where a novel missense mutation was detected in the *Cytochrome B-245 Beta Chain* gene located on the X-chromosome.

Treatment for ongoing infection was initiated and the patient was listed for a bone marrow transplant. At the most recent follow-up after 2 years, the patient received prophylactic antibiotics and antifungals and was in good state of health while he was listed for a bone marrow transplantation.

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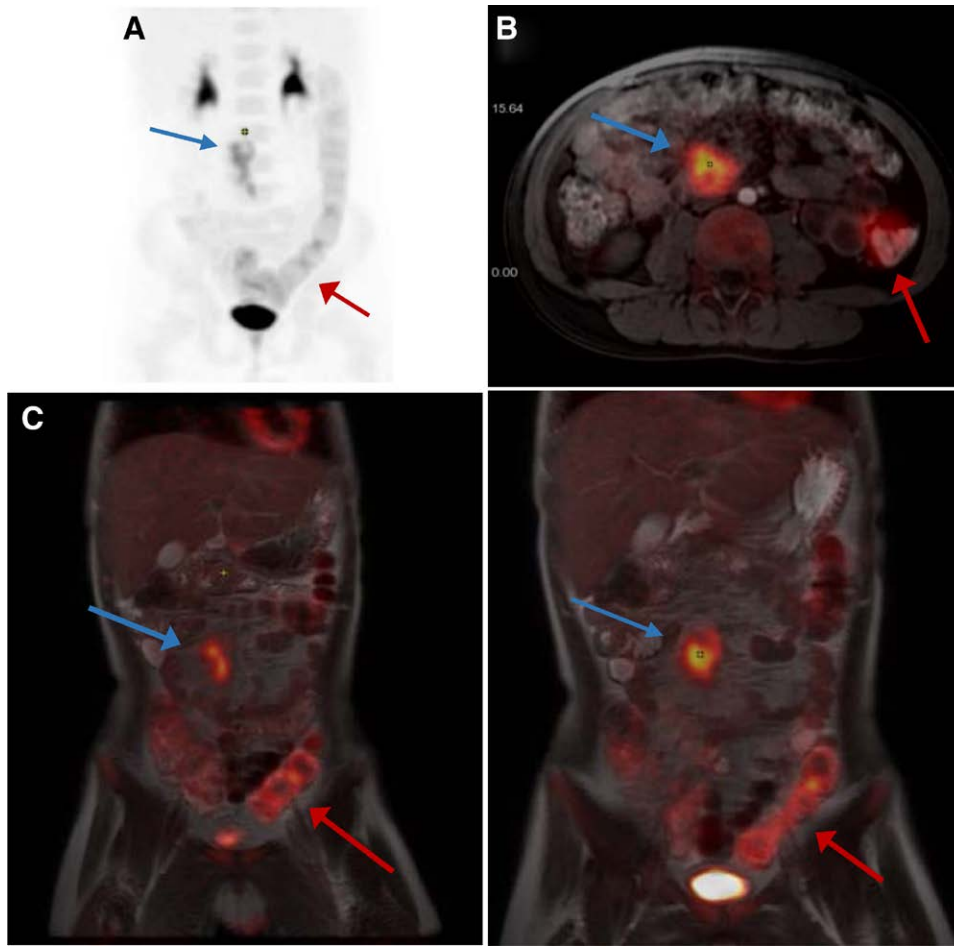

FIGURE 1. [18F]-FDG PET/MR images with pathological FDG uptake in an abdominal granuloma (blue arrow) and a thickened colonic bowel wall (red arrow) (FDG uptake in bladder, heart, and kidney are physiological). [18F]-FDG PET/MR = [18F]-fluorodeoxyglucose positron emission tomography/magnetic resonance.

DISCUSSION

PET/MRI is a novel diagnostic tool, which combines the excellent detection of inflammation and tumor processes of PET with the anatomical localization of MRI and with a minimum of radiation exposure. In this report, PET/MRI was utilized in the differential diagnosis of colitis. CGD is a rare disease found to affect 1 in 250,000 in a Danish cohort (8). The clinical presentation is characterized by bacterial or fungal infections, most often causing pneumonia, suppurative adenitis, osteomyelitis, and skin infections. Formation of abscesses may occur in various locations with a predilection for skin, liver, and lungs. The most common infectious agents are *Aspergillus* species, *Staphylococcus* species, and *Burkholderia cepacia* (1). The patient, in this case, had a mesenteric abscess in close relation to the duodenum caused by *A. aphrophilus* (formerly *Haemophilus aphrophilus*), which is a Gram-negative bacterium commonly found in the oral flora. *A. aphrophilus* causes cerebral abscesses and is a part of the HACEK group, which includes *Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species, known to cause infective endocarditis (9). It is not a common infective agent in CGD and in our case, the bacteria were assumed to have passed through the gastrointestinal tract and formed an abscess near the duodenum.

Noninfectious manifestations of CGD include granulomas and inflammatory processes. In our case, the PET/MRI scan showed signs of a lymph node conglomerate rather than abscess formation in the mesentery, which led to surgical intervention. When radiologic imaging reveals granulomatous lesions along with intestinal inflammation, CGD may be considered as a differential diagnosis.

In CGD patients, PET is valuable in detecting active infectious lesions (6). Our case exemplifies the usefulness of PET/MRI in this rare disease and illustrates the utility of PET/MRI in the evaluation of infection and inflammation in a child with symptoms of chronic colitis resembling inflammatory bowel disease, in particular Crohn disease. The diagnosis of CGD should be considered even in older children with granulomas and intestinal inflammation.

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