

# The diagnostic role of 18-fluorodeoxyglucose–positron emission tomography/computed tomography in occult bacteremia searching underlying primary disease

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### Abstract

18-Fluoro-2-deoxy-D-glucose (FDG) is a structural analog of 2-deoxyglucose and accumulates in malignant tissues but also at sites of infection and inflammation. For this reason, FDG PET or PET/CT has great advantage in understanding of underlying pathology in assessment of FUO (Fever of unknown origin). However, till today, there are limited studies about the role of FDG PET or PET/CT in evaluation of FUO. Conventional diagnostic methods are still not adequate to reveal underlying reason in approximately 50% of patients with FUO especially in cases presenting with diagnostic challenges i.e. involvement of two or more organ systems with seemingly no correlation. We report a case of two years old Indian female child who presented with fever of one month duration, CT and MRI reported nonspecific findings. She underwent Whole body 18 FDG PET/CT for further evaluation, which revealed FDG avid rim lesion with central photopenic defect suspicious of pyogenic abscess in high parietal cortex along with bilateral lung nodules. This confirmed the diagnosis of a brain abscess secondary to pulmonary infection. We emphasize the utility of 18 FDG PET/CT as imaging modality, highlight the diagnostic difficulties using current serological and radiological measures, and propose managing FUO with 18 FDG PET/CT in cases empirically prior to more invasive measures.

### Key Words

18-FDG PET/CT, bacteremia, brain abscess, fever of unknown origin, magnetic resonance imaging

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### Introduction

The classical definition of FUO (Fever of unknown origin) as "a fever that is measured to be above 38.3°C on several occasions during a period longer than 3 weeks for which the etiology behind cannot be diagnosed at the end of at least 1 week hospital stay.<sup>[1]</sup>" The prevalence of FUO among pediatric patients is reported to be 2.9%.<sup>[2]</sup> In patients presenting with FUO, basic diagnostic methods are performed following detailed history and physical examination. As those methods can differ between the clinics, generally, the following are employed: routine biochemical blood tests, complete blood count, peripheral blood film, urinalysis, blood cultures and chest X-ray.<sup>[3]</sup> The rate of failure to reach a definitive

diagnosis in pediatric patients with FUO varies between 7%<sup>[4]</sup> and 53%.<sup>[5]</sup>

### Case Report

A 2-year-old Indian female child presented with irregular high-grade fever for 1 month accompanied by behavioral changes, namely aggressive fever and tendency to bite, for 7 days. Then, the patient developed difficulty in walking for 3 days. On evaluation, she was found to have normal milestone with no remarkable finding on physical examination. But, she continued to have high-grade fever and was subjected to further evaluation as a case of pyrexia of unknown origin. All other parameters, like complete blood count, peripheral blood film, urinalysis and blood cultures were within the normal range. Computed tomography (CT) brain showed mild cerebral atrophic changes, but milestones were normal. Magnetic resonance imaging (MRI) of the brain reported bilateral T2/FLAIR (fluid-attenuated inversion recovery) hyperintensity seen in periventricular and subcortical white matter. There was diffusion restriction seen in the bilateral frontal lobe white matter, peritrigonal white matter and genu of corpus callosum and mild corticocerebral atrophy [Figures 1 and 5]. Because the case was now trapped in a huge diagnostic dilemma, she was

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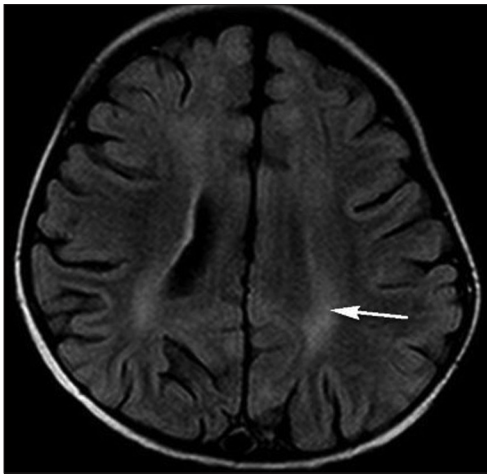


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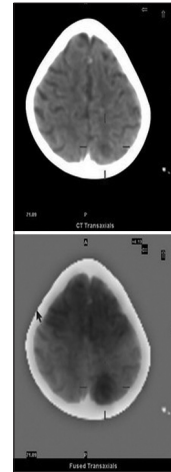
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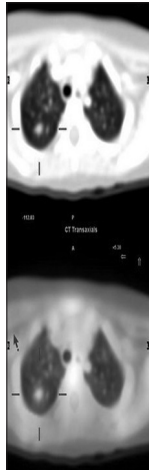
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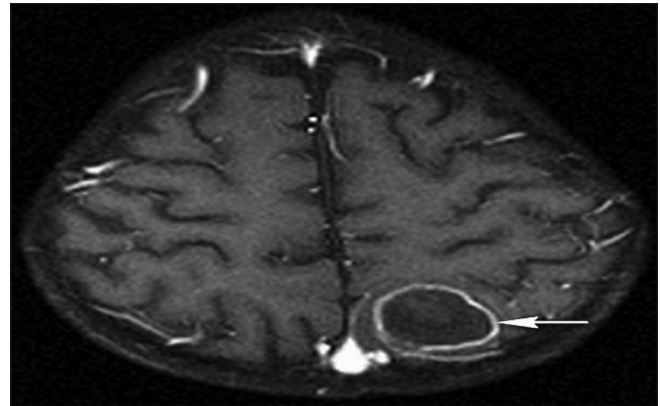
**Figure 1:** Pre-18-FDG PET/computed tomography magnetic resonance imaging scan showing bilateral non-enhancing T2/FLAIR hyperintensity in the periventricular and subcortical white matter with areas of diffusion restriction. The following differentials are to be considered: (1) encephalitis, (2) post-ischemic changes and (3) leukodystrophy



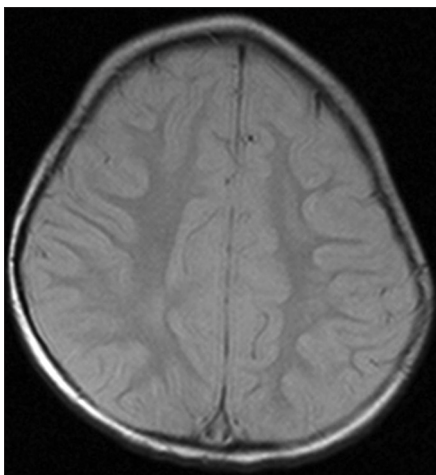
**Figure 2:** Abnormal rim of FDG uptake with central photopenic defect seen in left high parietal cortex (SUV max 4.4). There is generalized reduced FDG uptake in the bilateral parietal, temporal and occipital cortex. Preserved metabolism was seen in the bilateral frontal, basal ganglia and cerebellum



**Figure 3:** Abnormal focal sites of increased FDG uptake noted in multiple bilateral lungs nodules (SUV max 1.8)



**Figure 4:** Post-18-FDG PET/computed tomography magnetic resonance imaging scan showing ring-enhancing lesion seen at the left high parietal region measuring 2.6 cm x 2.5 cm in size



**Figure 5:** Pre 18-FDG PET/CT MRI scan showing bilateral non enhancing T2/ FLAIR hyperintensity in periventricular and subcortical white matter

referred for 18-FDG PET/CT, which revealed FDG avid rim lesion with central photopenic defect in left high parietal cortex suspicious of pyogenic abscess [Figure 2]. There was significant hypometabolism in the bilateral temporal and parietal cortex. Apart from this, multiple FDG avid bilateral lung nodules were seen, which were suspicious of infective etiology [Figure 3]. Then, MRI was done again, which reported ring-enhancing lesion seen at the left high parietal region [Figure 4]. Culture of bronchoalveolar lavage was positive for Klebsiella and aspirate from cerebral abscess was also positive for Klebsiella. The patient was treated accordingly, and she made steady progress, after which she was finally discharged with no residual sequel. This case provides an excellent example where FDG PET can resolve a diagnostic dilemma, and helped to make a definite diagnosis earlier and with more certainty than any other imaging/diagnostic modalities.

## Discussion

The diseases taking part in FUE etiology and their rates are as follows: infections (21-54%), non-infectious inflammatory causes

(13-24%), neoplasm (6-31%) and other causes (4-6.5%).<sup>[4]</sup> The other commonly encountered infectious diseases are endocarditis, typhoid fever, malaria, brucellosis, cytomegalovirus infection and AIDS in western countries.<sup>[4]</sup> In pediatric patients, infections take the first place among FUO etiologies with a rate of 56.7%, and mostly occur as localized infections. Because of the wide etiology spectrum of FUO, clinicians still experience difficulties in selecting and applying the diagnostic procedures in these cases. Because of the limitations of anatomical imaging, modalities such as ultrasonography, CT and MRI can only show certain parts of the body, they cannot provide information on pathological events in systemic disorders. Because of such limitations, invasive methods are resorted to in 30.8% of the cases, leading to increased morbidity and mortality.<sup>[3]</sup> Eventually, there is failure to reach a definitive diagnosis in patients with FUO in 7-53% of the cases.<sup>[5]</sup> 18-FDG PET/CT has proved to be an excellent non-invasive modality in diagnosing infective/inflammatory etiology. The high uptake of fluoro-18 FDG in inflammatory cells, granulation tissues and granulomas is due to overexpression of GLUT-1 and GLUT-3. FDG-PET is a valuable imaging method for its success in demonstrating both neoplasms and infection-inflammation foci. As in our case, the patient presented with fever as the chief complaint with normal blood parameters. MRI showed diffuse restriction in bilateral frontal lobe white matter, peritrigonal white matter and genu of corpus callosum, which may give the differential diagnosis of cerebral edema, encephalitis, post-ischemic changes, diffuse gliomatosis or multifocal leukodystrophy. This led to a diagnostic dilemma only, as the child's milestones were normal. FDG PET/CT *per se* was able to show, firstly, that the pathology was infective in origin and, secondly, also to delineate the brain, as other focus of infection. This led to the excellent diagnosis and successful treatment outcome.

## Conclusion

Although FDG PET/CT is a state-of-the-art procedure for the assessment of multiple malignancies, it is still not a routine

procedure in the workup of FUO due to high cost and limited availability. However, the experience with FDG-PET/CT should eliminate application of many unnecessary invasive and non-invasive diagnostic techniques for detection of the main disease underlying FUO etiology. Currently, data in the literature indicate that FDG-PET has an important role as a second-line procedure in the management of nearly 50% of the patients with FUO. Even though the results of previous FDG-PET studies are promising, still, prospective studies using PET/CT on larger populations of FUO are limited. It is well known that hybrid PET/CT improves the diagnostic impact of FDG PET in malignant diseases. For this reason, accurate diagnosis of primary diseases in the context of FUO is expected to increase.

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