Gallium 68-Fibroblast Activation Protein Inhibitor: PET/CT improves Diagnosis of Neurocysticercosis.

Abstract.

F18-FDG (Fluorine18- fluoro-deoxyglucose) Positron emission tomography/computerized tomography scan (PET/CT Scan) scan shows intense physiologic uptake in the brain parenchyma. This prevents evaluation of small cerebral lesions. Ga-68-FAPI (Gallium68-Fibroblast activation protein inhibitor) does not localize in normal brain parenchyma. Hence, it can detect cerebral lesions which concentrate the tracer. We report a case of neurocysticercosis in a 32 years old female who presented with headache, nausea and one episode of seizure. MRI brain raised possibility of tuberculoma over neurocysticercosis. There was a hypometabolic area in the right temporal lobe as revealed by F-18-FDG PET/CT, with no FDG avid lesions or lymph nodes identified in the body. Ga68-FAPI PET/CT was performed which showed increased tracer uptake within the right temporal lobe lesion. A focal FAPI uptake was also noted in a tiny hypodense lesion in the left internal oblique muscle of abdomen, which showed signal characteristics of intramuscular cysticercosis on limited MRI study.

Key word: Cysticercosis, MR imaging,, in Cancer Imaging, Neurology

Introduction

Fluoro-deoxyglucose (F18-FDG) has been used in PET imaging for around 20 years in India. However, the value of F18-FDG PET/CT imaging in brain tumors is limited because of physiological uptake by brain causing poor target to background ratio between lesion and normal cerebral tissue.

Ga68-FAPI is a novel radiotracer for making diagnosis and planning the management of several malignancies as FAPI has high affinity and sensitivity for Fibroblast activation protein (FAP); a transmembrane serine protease seen in >90% of the epithelial tumors, also associated with tumor invasion and metastasis (1). Clinical value of Fibroblast activation protein inhibitor (FAPI) PET/CT in non-oncological conditions like liver cirrhosis, Crohn's disease, cardiovascular disease, IgG4 related disease and arthritis has been studied. However, its role in the assessment of infective and other inflammatory etiologies is still in the early phase (2).

Neurocysticercosis (NCC) is the commonest central nervous system (CNS) helminthic infestation in humans and one of the common acquired causes of epilepsy. Diagnosis is best by a multidisciplinary approach. On MRI, NCC has four stages: vesicular, colloid-vesicular, granular and calcified nodular stages. Vesicular stage shows a thinned wall cyst with minimal or no surrounding edema. Scolex within the lesion appears as hypointense focus on MRI giving "hole with a dot appearance". Colloid-vesicular and granular stages show lesion with marked surrounding edema and post-contrast ring enhancement of the lesion. Calcified nodular stage is non-active as in this final stage the parasite is dead; hence, lesion shrinks down to half or almost a quarter of initial size and calcifies with no peripheral edema. F18-FDG PET does not play a

significant role in the diagnosis of CNS infections. Ga68-FAPI PET has a prominent target to background ratio in brain lesions, and has an added advantage of detecting extra-cranial lesions as shown in the present case report.

Objective-To establish the role of Ga68-FAPI PET/CT in the diagnosis of Neurocysticercosis.

Clinical presentation, imaging findings and differential diagnosis

A 32-year-old female presented with complaints of headache, nausea and one episode of seizure. MRI brain with contrast was done (Figure 1), which showed few coalescing ring-enhancing lesions measuring 2.4 x 1.4 x 1.5 cm in the right temporal lobe. The lesions showed central hyperintensity with hypointense wall surrounded by significant perilesional edema on T2w images. Associated leptomeningeal enhancement was also noted along the sulcal spaces on post contrast FLAIR images. On MR spectroscopy, there was a mild elevation of choline with reduction in NAA and creatine. No lipid lactate peak was noted. Considering the morphology of the lesions, possibility of tuberculoma was raised over neurocysticercosis.

Patient was referred for whole body F18-FDG PET/CT to look for the occult primary. 8.3 mCi-F18-FDG was administered intravenously in the overnight fasting state and scan was gained after 60 minutes on LSO detector based PET CT system. The scan showed hypometabolic area in the right temporal cortex corresponding to the lesion seen on MRI. (Figure 2) No FDG avid lesions or nodes were seen in the whole body. The lung also showed no nodules or features of tuberculosis.

As F18-FDG PET/CT was inconclusive; Ga68-FAPI PET/CT was performed on another day using 3.4 mCi-Ga68-FAPI. The PET/CT showed increased FAPI uptake by the lesion in the right temporal lobe with SUVmax of 2.9. Another lesion with focal FAPI uptake was detected in the left internal oblique muscle measuring 10 x 10 mm with SUVmax of 2.66 at the level of left iliac crest. (Figure 3) Limited MRI of the suspected area revealed tiny well-defined T2 hyperintense lesion with a hypointense focus within suggestive of scolex. Another well-defined T2 hyperintense lesion with scolex was also noted in the left gluteus medius muscle which was inconspicuous on FAPI scan (Figure 4). Hence, the diagnosis of NCC was made.

Treatment

Patient was started on Albendazole 15 mg/kg/day for 3 weeks was doing well at 3 months follow up.

Discussion

Neurocysticercosis is one of the major causes of acquired epilepsy in around 29% of the cases worldwide. Ingestion of raw or improperly cooked meat and improper cleaning of leafy vegetables containing eggs from the faeces of a tapeworm carrier can lead to the infection. The

parasite can involve any site in the body, most commonly central nervous system, eyes and muscles (3).

The major diagnostic criteria for NCC include histologic evidence of parasites, sub retinal cysticercus, demonstration of scolex within a cystic lesion on neuro imaging (4). Histology shows double crown of hooks, spiral canal and rostellum with its four suckers. In subarachnoid cysts, the scolex may not be seen but the typical three-layered membrane wall can be identified in racemose cysticerci. However, the scolex and membranes may not be present in the calcified or granular phase of the disease (5). In such cases, calcareous corpuscles may help to identify the nematodes (6). Fundoscopic examination helps in detection of sub retinal cysticerci. These lesions may or may not be associated with brain involvement. Anterior chamber cysticerci are not grouped as NCC (7). The diagnosis of NCC can be made on MRI in the majority of the cases. The lesions are usually at the junction of cortical-subcortical brain parenchyma, basal ganglia, infrequently in the brainstem- cerebellum- spinal cord. Subarachnoid cysts are at the cortical sulci in the convexity of the brain. Ventricular cysts are within the ventricles (8). The scolex are "hole with dot" and considered being pathognomonic. Diffusion weighted imaging (DWI) and fast imaging employing steady state acquisition (FIESTA) help in identifying scolex that are not seen in conventional imaging (9). However, rarely a cystic neoplastic lesion may mimic scolex because of remnants of neoplastic cells in its interior. It can be mistaken for a space-occupying lesion in some cases.

Most NCC are less than 20mm, clearly demarcated from brain parenchyma, may show ring enhancing pattern. More than one lesion with distinct patterns, including typical calcifications (solid, less than 10mm, evenly distributed in cerebrum) also suggests NCC. Multiple cysts without discernible scolex present in parenchyma or in subcortical sulci between cerebral convolutions may give "Swiss cheese" appearance (10). These features with seizures, absence of signs of raised intracranial pressure, absence of midline shift suggest NCC. (11) On CT, the calcifications in NCC resemble "starry night" appearance (12). Enzyme linked immunoelectrotransfer blot (EITB) assay using lentil lectin-purified glycoprotein extracts to detect antibodies for *Taenia Solium* has high specificity and sensitivity (13). However, a positive test result does not mean CNS involvement, since it implies systemic response. The test may be falsely negative in single intracranial cysticerci and calcified parasite in upto 50% cases (14).

In our patient, the MRI showed mild pachymeningeal enhancement which was not basal, ring-enhancing lesions were seen with extensive area of edema and mild midline shift thus raising a suspicion of tuberculosis. A differential diagnosis of metastasis was made. Hence, F18-FDG PET was performed which ruled out occult primary in whole body scan. Brain showed a large area of hypometabolism in the right temporal cortex. Previous studies have showed low metabolism in NCC on FDG scan (15). Ga68-FAPI scan was done on the next day, which showed focal increased tracer uptake in brain corresponding to the ring-enhancing lesions seen on MRI. Additional foci of tracer uptake were noted in the left lower lateral abdominal wall. Regional MR showed focal hyperintense lesion on the left internal oblique with central hypo

intensity without surrounding edema. Features were characteristic of neurocysticercosis. Additional lesion with similar morphology was seen in the left gluteus medius which were inconspicuous in FAPI scan. Patient responded to anthelminthic therapy. Ga68-FAPI localizes in various neoplasms by their property of cancer associated fibroblast activity. Fibroblasts are also known to be associated with inflammatory and infectious conditions such as cholecystitis, pyelonephritis and tuberculosis. Ga68-FAPI has shown promising results in both oncological and inflammatory conditions (16). There is a report of its utility in intracranial syphilitic gumma (17). However, we could not find any reference to FAPI in NCC. Our case showed FAPI uptake by both the intracranial and extra-cranial cysticercosis. More studies with larger sample size are required to make use of this novel imaging technique.

Conclusion

In conclusion, MR imaging can show ring-enhancing lesions for both NCC and tuberculosis. Ga68 FAPI does not have any brain uptake, which makes it an excellent target for background localization in benign and malignant diseases, they aid in the identification of distant muscular lesions in NCC that can be subsequently targeted with MR to improve specificity.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

Data availability statement: The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Images

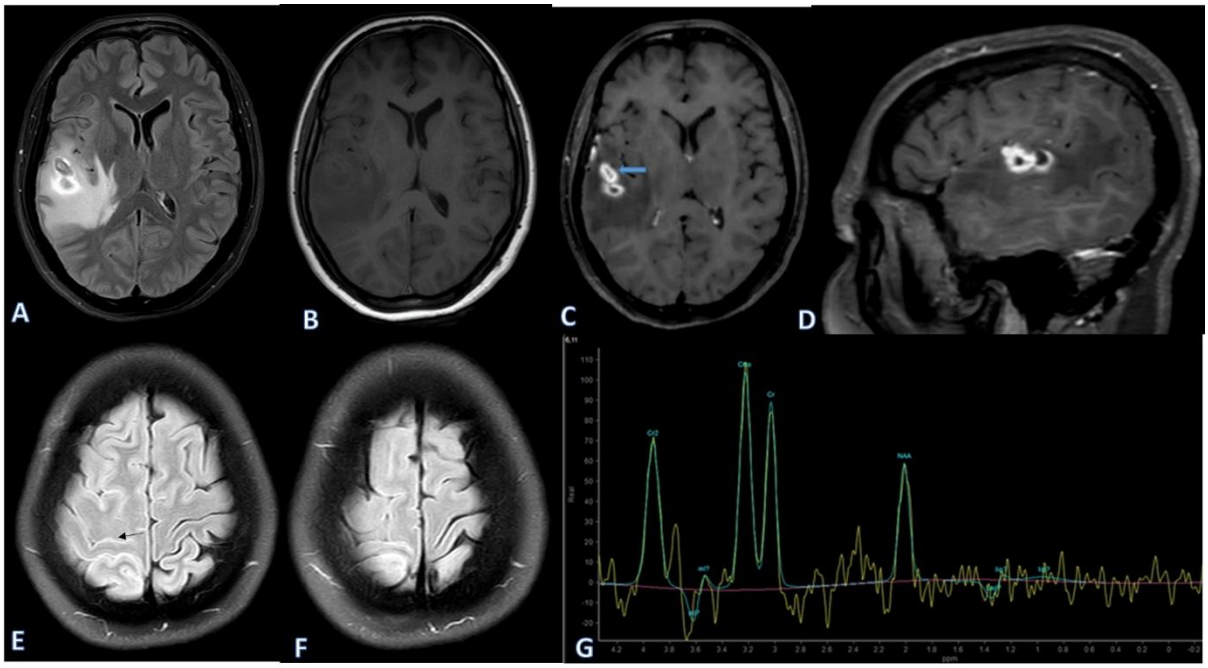

Figure 1- Brain MRI

(A) Non contrast T2 FLAIR shows coalescing lesions in right temporal lobe- central hyperintense signal with peripheral hypointense signal- oedema around the lesion- effacement of right lateral ventricle.

(B) Non contrast T1W image show central hypointense signal and peripheral hyperintense signal.

(C and D)- post contrast T1W image shows ring enhancement (blue solid arrow).

(E and F) post contrast T2 FLAIR shows lepto-meningeal enhancement in right fronto-temporal sulcal spaces (black arrow).

(G) MR spectroscopy shows raised choline with mild decrease in NAA and creatine. No lipid lactate peak.

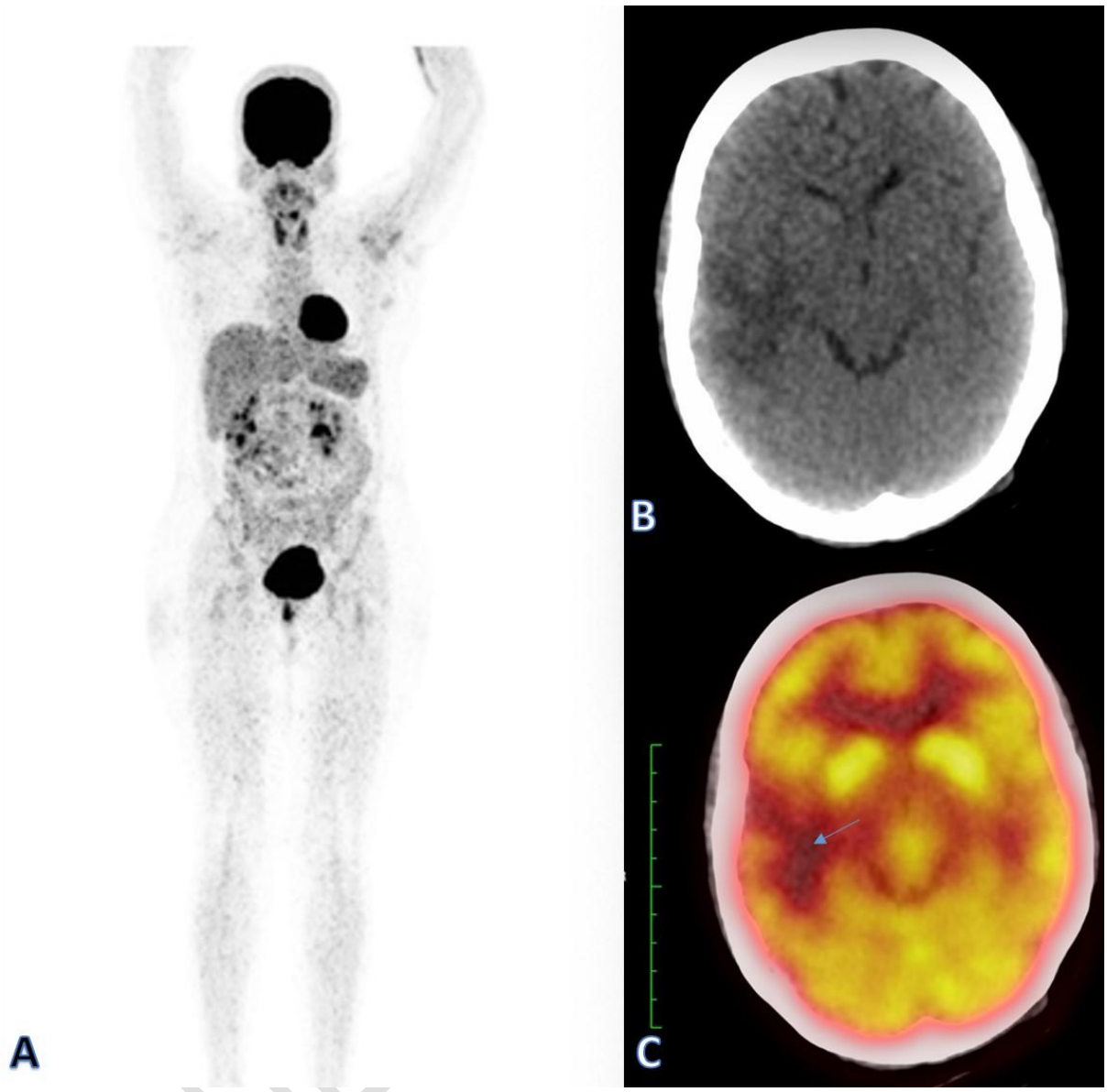

Figure 2. 18F-FDG PET/CT images showing the hypo-metabolic area (blue arrow) corresponding to the location of the lesion. No FDG avid lesions or lymph nodes were noted in rest of the study.

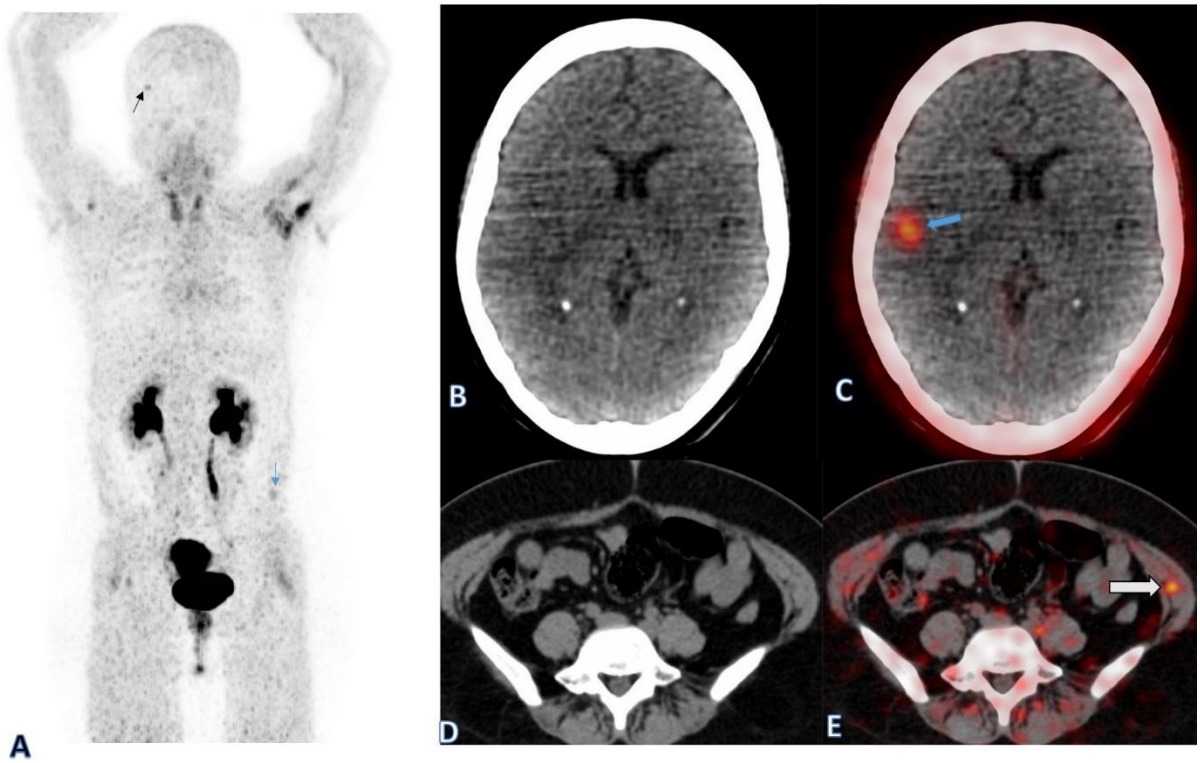

Figure 3. (A) MIP image of FAPI scan showed increased uptake in region of brain (black arrow) and (B and C) FAPI avid lesion in right temporal lobe (blue arow); (D and E) focal tracer uptake corresponds to the hypodense lesion in left internal oblique muscle at the level of iliac crest. (white arrow).

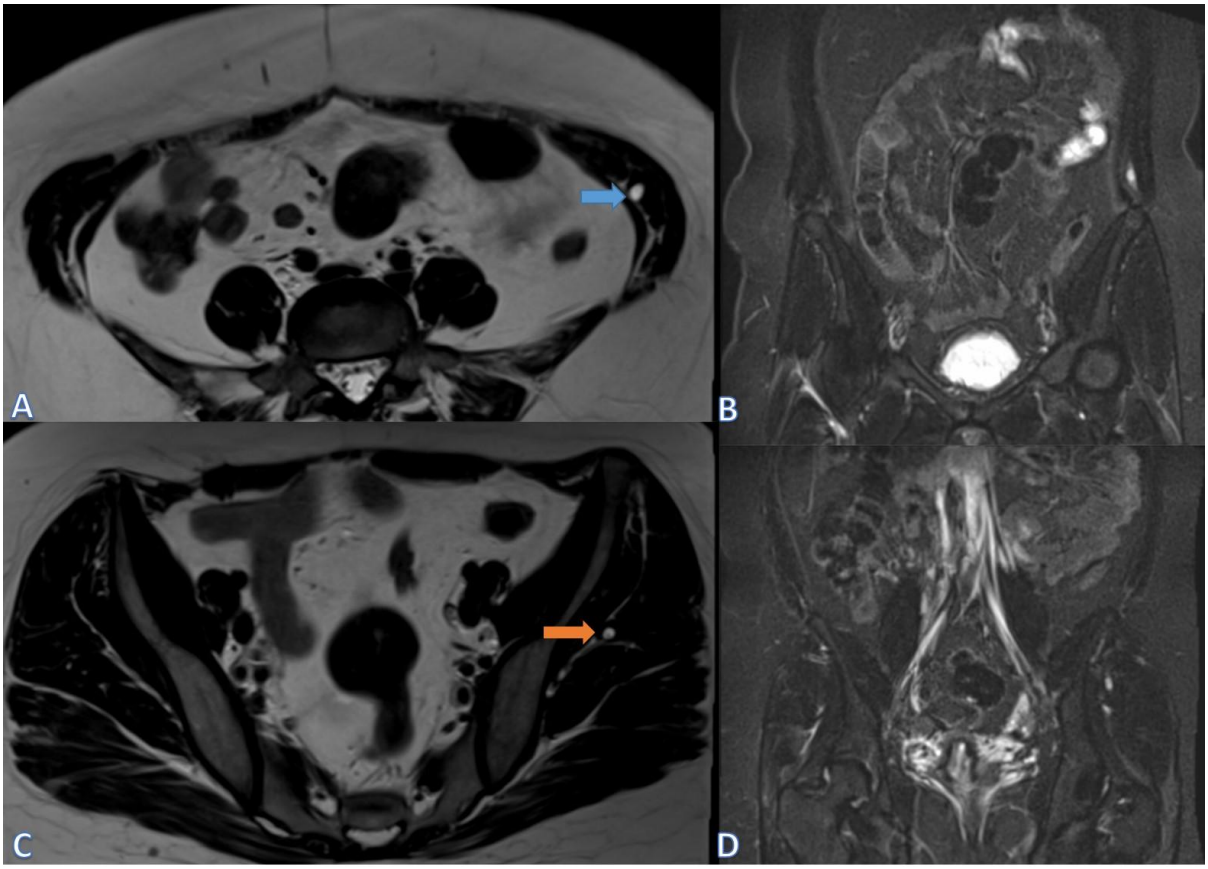

Figure 4. (A) Axial T2w (B) Coronal T2W small showing tiny hyperintense intramuscular lesion in left internal oblique (blue solid arrow); (C) Axial T2w (D) coronal T2W image showing tiny hyperintense intramuscular lesion left gluteus medius muscles (orange solid arrow). A hypointense focus is noted within the lesion, representing a scolex.

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