Case report

Gallium 68-Fibroblast Activation Protein Inhibitor - PET/CT IN THE DIAGNOSIS OF NEUROCYSTICERCOSIS.

Comment [U1]: Change the title to: Gallium 68-Fibroblast Activation Protein Inhibitor: PET/CT In the Diagnosis of Neurocysticercosis.

Abstract.

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F18-FDG (Fluorine18- fluoro-deoxyglucose) PET CT scan shows intense physiologic uptake in the brain parenchyma. This precludes 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. F-18-FDG PET/CT was suggestive of hypometabolic area in the right parietal lobe without any FDG avid lesions or lymph nodes in the body. Ga68-FAPI PET/CT was performed which showed increased tracer uptake within the right inferior parietal 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.

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Comment [U5]: There was a hypometabolic area in the right parietal lobe as revealed by F-18-FDG PET/CT, with no FDG avid lesions or lymph nodes identified in the body.

Introduction

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

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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 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 early phase. (2)

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Neurocysticercosis (NCC) is the commonest CNS helminthic infestation in humans and one of the common acquired causes of epilepsy. Diagnosis is best by multidisciplinary approach. On MRI, NCC has four stages: vesicular, colloid-vesicular, granular and calcified nodular stages. Vesicular stage shows 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

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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 quarter of initial size and calcifies with no peripheral edema. F18-FDG PET does not play significant role in the diagnosis of CNS infections. Ga68-FAPI PET has high target to background ratio in brain lesions and has an added advantage of detecting extra-cranial lesions as demonstrated in the present case report.

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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 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.

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On MR spectroscopy, there was a mild elevation

Patient was referred for whole body F18-FDG PET/CT to look for occult primary. 8.3 mCi-F18-FDG was administered intravenously in overnight fasting state and scan was acquired after 60 minutes on LSO detector based PET CT system. The scan showed hypometabolic area in the right temporoparietal 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.

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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 right inferior parietal 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 left gluteus medius muscle which was inconspicuous on FAPI scan. (Figure 4). Hence the diagnosis of NCC was made.

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Treatment

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

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Discussion

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Neurocysticercosis is one of the major causes of acquired epilepsy in around 29 % of the cases worldwide. Ingestion of raw or not properly 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

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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 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 located at the cortical sulci at the convexity of brain. Ventricular cysts are located within the ventricles. (8) The scolex are seen as "hole with dot" and considered to be pathognomonic. Diffusion weighted imaging (DWI) and fast imaging employing steady state acquisition (FIESTA) help in identifying scolex that are not seen on conventional imaging. (9) However, rarely a cystic neoplastic lesion may mimic scolex due to remnants of neoplastic cells in its interior. it can be mistaken by a space occupying lesion in some cases. Most NCC are less then 20mm, clearly demarcated from brain parenchyma, may show ring enhancing pattern. More than one lesion with different patterns including typical calcifications (solid, less then 10mm, evenly distributed in cerebrum) also suggest 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 are suggestive of 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 necessarily 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 large 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 fronto-parietal cortex. Previous studies have demonstrated 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 left internal oblique with central hypo intensity without surrounding edema. Features were characteristic of neurocysticercosis. Additional lesion with similar morphology was seen in left gluteus medius which was inconspicuous in FAPI scan. Patient responded to anthelminthic therapy. Ga68-FAPI is known to localize in various neoplasms by virtue of their property of cancer associated fibroblast activity.

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Fibroblasts are also known to be associated in 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 of 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.

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Conclusion

1 Neurocysticercosis is an important parasitic infestation of brain.
2. Both NCC and tuberculosis can present as ring enhancing lesions on MR.
3. FDG PET has limitations in brain lesions due to its physiologic uptake in brain parenchyma.
4. Ga68 FAPI has no brain uptake and hence provides high target to background localisation in benign and malignant diseases.
5. Ga68 FAPI helps detect distant muscular lesions in NCC that can be further targeted with MR for increasing the specificity as demonstrated in the present case.

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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.

Patient consent statement: - Informed consent to publish this case (including images and data) was obtained and is held on record.

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

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Images

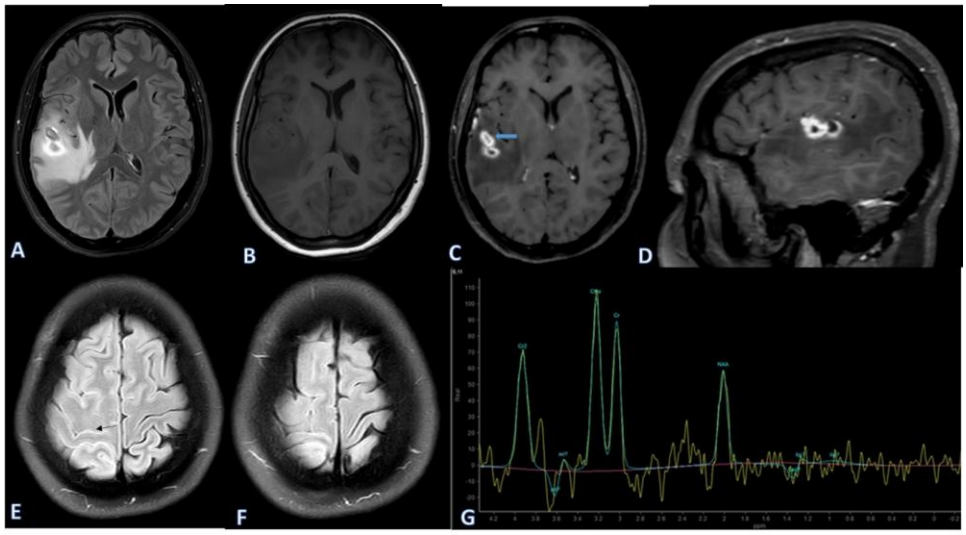

Figure 1- MRI Brain-

Comment [U68]: Brain MRI

(A) Non contrast T2 FLAIR shows coalescing lesions in right inferior parietal 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-parietal sulcal spaces (black arrow); (G) MR spectroscopy shows raised choline with mild decrease in NAA and creatine. No lipid lactate peak.

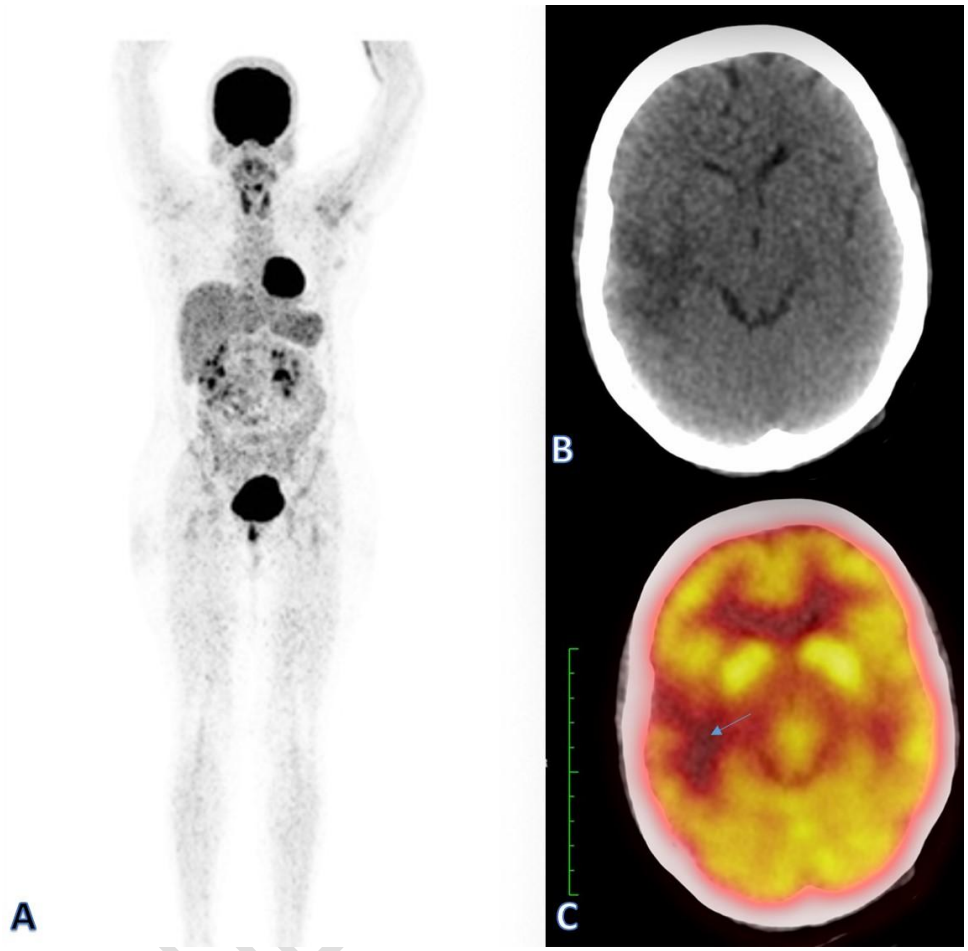

Figure 2. 18F-FDG PET/CT images showing the hypo-metabolic area (blue arrow) corresponding to the location of the lesion. No FDG avid lesions or lymph nodes were noted in rest of the study.

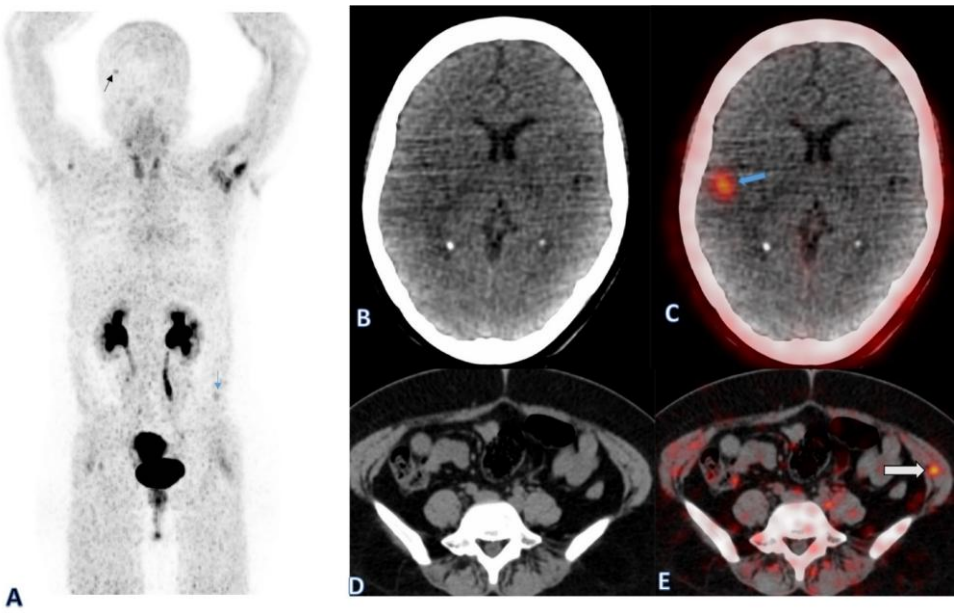

Figure 3. (A) MIP image of FAPI scan showed increased uptake in region of brain (black arrow) and (B and C) FAPI avid lesion in right inferior parietal lobe (blue arow); (D and E) focal tracer uptake corresponds to the hypodense lesion in left internal oblique muscle at the level of iliac crest. (white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

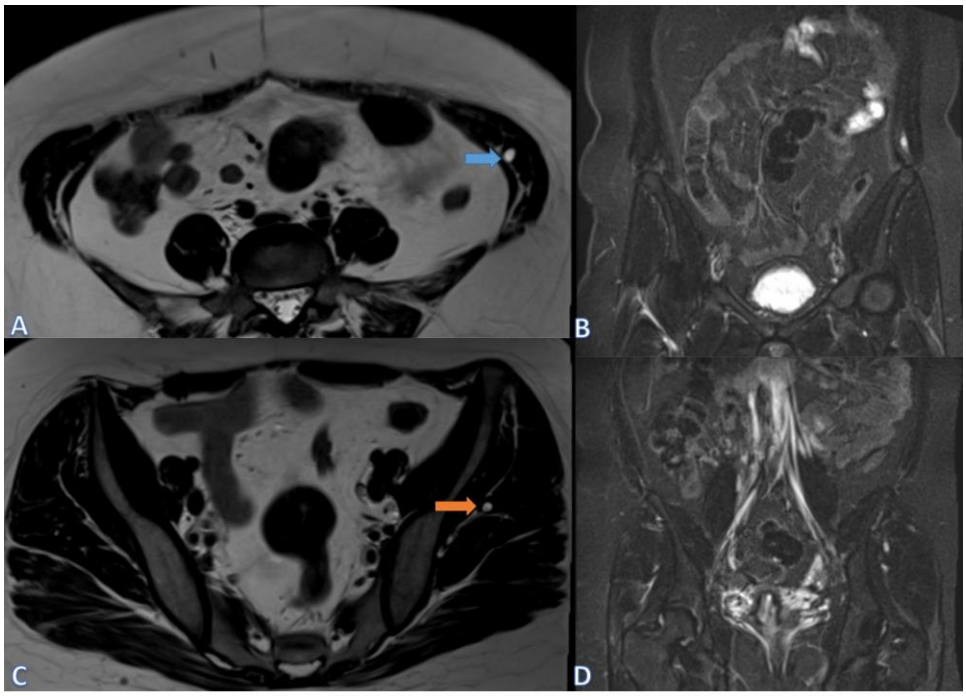

Figure 4. (A) Axial T2w (B) Coronal T2W small showing tiny hyperintense intramuscular lesion in left internal oblique (blue solid arrow); (C) Axial T2w (D) coronal T2W image showing tiny hyperintense intramuscular lesion left gluteus medius muscles (orange solid arrow). A hypointense focus is noted within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

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