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CASE REPORT

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Tracer Accumulation in Relation to Venous Thrombus on ^{18}F-DOPA PET/CT in a Case of Persistent Hyperinsulinemic Hypoglycemia of Infancy

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Abstract

^{18}F-DOPA PET/CT is commonly done in patients with persistent hyperinsulinemic hypoglycemia of infancy (PHHI) to look for any focal lesion in the pancreas. We present the findings in a 20-day-old neonate with PHHI who underwent ^{18}F-DOPA PET/CT. The scan showed diffuse uptake in the pancreas with no focal lesion, physiologic excretion into the genito-urinary system, and interestingly tracer accumulation was seen in the inferior vena cava and ilio-femoral veins which is a non-physiological site for tracer accumulation. The uptake corresponded to a large venous thrombus which was confirmed by a venous Doppler.

Keywords Venous thrombus · 18F-DOPA PET/CT · Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) · Congenital hyperinsulinism

Introduction

Hypoglycemia is a common metabolic problem seen in neonates, which occurs because of failure of proper metabolic adaptation to maintain glucose concentration post delivery [1]. Normally, immediately after birth when the cord is clamped, the glucose supply from the materno-placental circulation stops and the glucose concentration falls rapidly. However, insulin secretion which occurs in the body of neonate from beginning continues in post birth period also. To maintain falling glucose concentration, counter regulatory hormones including glucagon and cortisol increase and metabolic changes including gluconeogenesis and glycogenolysis occur to create a balance and maintain glucose concentration. But if these metabolic changes do not occur properly, this results in hypoglycemia [2]. Transient hypoglycemia can occur in some neonate until the time these adaptations fully settle in, more so in at-risk neonates including pre-term, small for gestational age, intrauterine growth-retarded infants, infants of diabetic mothers, asphyxia, sepsis, or other medical conditions [2, 3]. Some causes result in prolonged hypoglycemia in neonates. Persistent hyperinsulinemic hypoglycemia of infancy (PHHI) is one such cause, which occurs due to inappropriate hypersecretion by pancreatic β-cells. Other conditions associated with persistent hypoglycemia are metabolic disorders including glycogen storage disorder, disorders of gluconeogenesis, and fat oxidation

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[4]. PHHI can present with two different patterns including focal or diffuse pancreatic involvement. This has clinical significance because patients which fail to respond to medical therapy surgical option can be tried and the type of surgical intervention varies in two different patterns. Focal lesion, if present, can be dealt with partial pancreatectomy and diffuse pancreatic involvement requires near-total pancreatectomy. Different imaging methods including anatomical and functional imaging methods are used to differentiate focal and diffuse involvement. ^{18}F-DOPA (3,4 dihydroxyphenylalanine) PET/CT has shown good results in studies to identify the focal lesions in these cases [5].

Case Report Here, we present the case of a 20-day-old pre-term neonate, born at 35 weeks of gestation by caesarian section (birth weight 3.6 kg). On day 1 of life, on routine investigation, he was found to have persistently low random blood sugar (RBS) of 35 mg/dl and the corresponding critical sample showed serum insulin level of 80 mIU/ml and cortisol level of 25 μg/dl. Clinical diagnosis of neonatal hypoglycemia was made and the child was started on hourly feeds and intravenous (I/V) dextrose initially through umbilical venous catheter (UVC) with maximum glucose infusion rate of 17.5 mg/kg/min on day 1. With no improvement in glucose levels, later oral diazoxide was added and increased up to 20 mg/kg/day but intermittent hypoglycemic episodes still persisted. Subsequently, injection octreotide was added and the dose was increased up to 22 μg/kg/day on which the child improved symptomatically.

The UVC developed thrombosis at tip, later right femoral and then left femoral catheter were placed which also developed thrombosis. Meanwhile, along with medical management of PHHI, ^{18}F-DOPA PET/CT was planned for localization of any surgically resectable focal lesion in the pancreas as part of the diagnostic workup. ^{18}F-DOPA PET/CT scan (as shown in Fig. 1) showed diffuse uptake in the pancreas with no focal pancreatic lesion (Fig. 1, black arrow). Also noted was physiologic excretion of radiotracer into the genito-urinary system. However, interestingly, tracer accumulation was also seen in the inferior vena cava (IVC) and ilio-femoral veins with left femoral catheter in situ (Fig. 1, white arrow). This is a non-physiological site for ^{18}F-DOPA uptake. Therefore, we correlated the findings by doing the Doppler scan (as shown in Fig. 2). Venous Doppler image showed distended right common femoral vein (Fig. 2, thick white arrow) with intra-luminal echogenic content suggestive of thrombus (Fig. 2, curved white arrow) and normal right common femoral artery (Fig. 2, thin

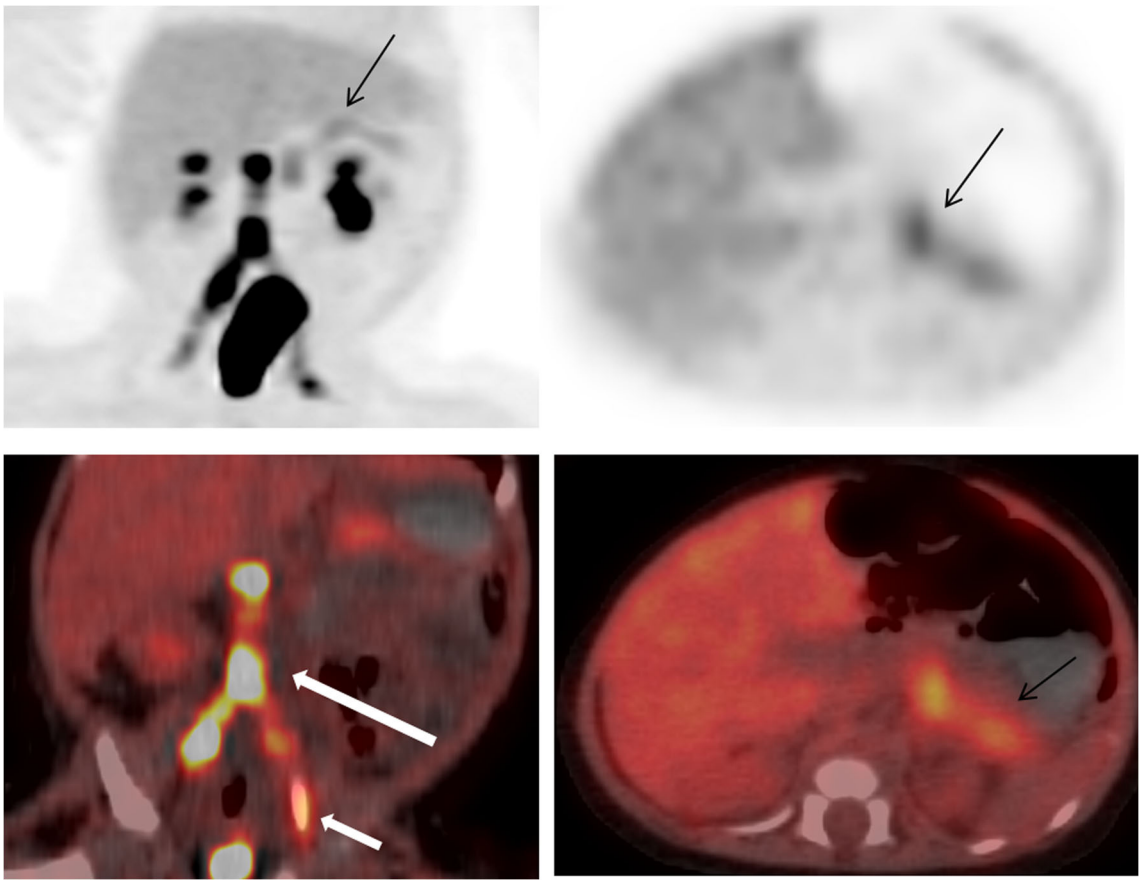

Fig. 1 MIP image, axial and coronal sections of ^{18}F-DOPA PET/CT. Scan shows diffuse uptake in the pancreas with no focal lesion (black arrow), physiologic excretion of radiotracer into genitor-urinary system and tracer accumulation in the inferior vena cava and ilio-femoral veins with left femoral catheter in situ (white arrow)

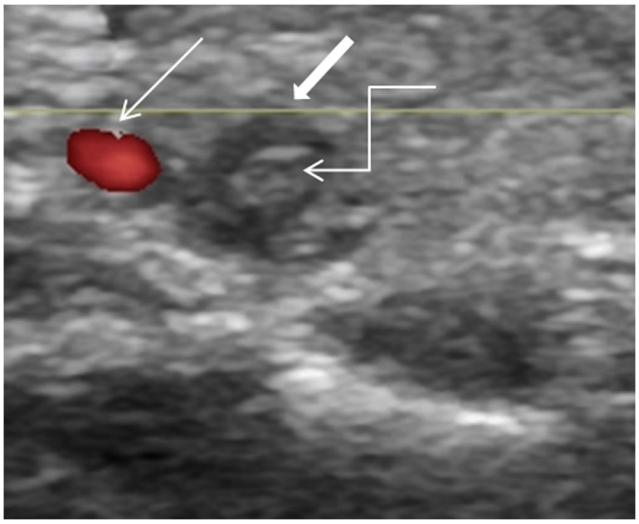

Fig. 2 Venous Doppler image showed distended right common femoral vein (thick white arrow) with intra-luminal echogenic content suggestive of thrombus (curved white arrow) and normal right common femoral artery (thin white arrow) confirming ilio-femoral venous thrombosis

white arrow) confirming ilio-femoral venous thrombosis. Finally, peripherally inserted central catheter (PICC) was placed in the upper limb and anticoagulant therapy with fractionated heparin was started which resulted in resolution of thrombus and child responded well to the medical management regarding hypoglycemia management.

Discussion

The common risk factors for venous thrombosis are trauma, malignancy, sepsis, inherited clotting disorders, pregnancy or recent delivery, varicose veins, use of central venous catheters, and implants like pacemakers [6, 7]. Use of high concentration of dextrose used in maintenance of glucose levels in patients with PHHI is also another risk factor for venous thrombosis [8].

Formation of thrombus involves complex mechanisms, involving interaction between platelets and multiple clotting factors [9]. Many different components of coagulation pathway which have been targeted by functional imaging include (radiolabeled antibodies targeting fibrin, activated platelets, plasminogen, plasmin, factor XIII, fibrin, platelet GP IIb/IIIa receptors, and ^{18}F-FDG (fluorodeoxyglucose) uptake in metabolically active inflammatory cells and platelets [10]. ^{18}F-FDG PET/CT can differentiate between bland versus tumor thrombus and its usefulness for response assessment after therapy has been described in few case reports [11]. ^{18}F-DOPA PET/CT is used preoperatively in PHHI to help differentiate focal from diffuse disease [12]. The mechanism of DOPA uptake at molecular level involves conversion to ^{18}F-fluorodopamine by enzyme amino acid decarboxylase in the pre synaptic terminals [13]. Also, DOPA uptake into tumor cells by amino acid transporters, which are over expressed in cancer cells, has been defined [14]. ^{18}F-DOPA uptake in thrombus has not been reported previously in any report, neither its mechanism of accumulation seems to be linked to any of the step in coagulation cascade. Accumulation of ^{18}F-DOPA in and around the thrombosed venous segment can be an artefactual finding, which could be because of sticking of particles in the blood circulation on the surface of the thrombus, but further research is warranted in this regard as it was just an observation in this study. This finding was communicated to the clinician, and after correlation with Doppler study, it was decided to place the PICC line through upper limb as the thrombosis involved bilateral ilio-femoral vessels extending up to IVC and anticoagulant treatment was started.

Compliance with Ethical Standards

Conflict of Interest Saurabh Arora, Nishikant Avinash Damle, Averilicia Passah, Rajni Sharma, Harish Goyal, Shreedharan Thankarajan Arunraj, Priyanka Gupta, and Manisha Jana declare that they have no conflict of interest.

Ethical Approval Statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent from parents of neonate was obtained to be included in the study.

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References

1. Sann L. Neonatal hypoglycemia. Biol Neonate. 1990;58:16–21.
2. Hawdon JM, Ward Platt MP, Aynsley-Green A. Prevention and management of neonatal hypoglycemia. Arch Dis Child. 1994;70:60–4.
3. Land JM. Hypoglycemia in the neonate: how and when is it important? Dev Neurosci. 1994;16:307–12.
4. Kahler SG. Metabolic disorders associated with neonatal hypoglycemia. NeoReviews. 2004;5:377–81.
5. Capito C, Khen-Dunlop N, Ribeiro MJ, et al. Value of 18F-fluoro-L-dopa PET in the preoperative localization of focal lesions in congenital hyperinsulinism. Radiology. 2009;253:216–22.
6. Lee Y. Current developments in imaging for deep vein thrombosis. Hong Kong Med J. 2015;21:96–7.
7. Prandoni P, Piccioli A. Venous thromboembolism and cancer: a two-way clinical association. Front Biosci. 1997;2:12–20.
8. Hessov I, Bojsen-Møller M, Melsen F. Experimental infusion thrombophlebitis. A comparison between glucose and frutcose and 5% and 10% glucose solution. Intensive Care Med. 1979;5:79–81.
9. Lowe GD. Virchow's triad revisited: abnormal flow. Pathophysiol Haemost Thromb. 2003;33:455–7.
10. Houshmand S, Salavati A, Hess S, et al. The role of molecular imaging in diagnosis of deep vein thrombosis. Am J Nucl Med Mol Imaging. 2014;4:406–25.
11. Miceli M, Atoui R, Walker R, et al. Diagnosis of deep septic thrombophlebitis in cancer patients by fluorine-18 fluorodeoxyglucose

positron emission tomography scanning: a preliminary report. J Clin Oncol. 2004;22:1949–56.
12. Meintjes M, Endozo R, Dickson J, et al. 18F-DOPA PET and enhanced CT imaging for congenital hyperinsulinism: initial UK experience from a technologist's perspective. Nucl Med Commun. 2013;34:601.
13. Garnett ES, Firnau G, Nahmias C. Dopamine visualized in the basal ganglia of living man. Nature. 1983;305:137–8.
14. Youland RS, Kitange GJ, Peterson TE, et al. The role of LAT1 in (18)F-DOPA uptake in malignant gliomas. J Neuro-Oncol. 2013;111:11–8.