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The predictive value of preoperative fluorine-18-L-3,4-dihydroxyphenylalanine positron emission tomography–computed tomography scans in children with congenital hyperinsulinism of infancy

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Abstract

Background/Purpose: In congenital hyperinsulinism (CHI) of infancy, the use of preoperative fluorine-18-L-3,4-dihydroxyphenylalanine–positron emission tomography–computed tomography (^{18}F-DOPA-PET-CT) scan has recently been reported. The aim of this study was to evaluate the accuracy of this technique in discriminating between diffuse and focal CHI and the anatomical localization of focal lesions.

Methods: Between 2006 and 2010, ^{18}F-DOPA-PET scan was performed in 19 children with CHI (median age, 2 months; range, 1-12 months) who were not responding to medical therapy and underwent laparoscopic or open surgery. The findings of ^{18}F-DOPA-PET scan were correlated with histology.

Results: In 5 children, ^{18}F-DOPA-PET scan showed diffuse pancreatic uptake, confirmed at histology and supporting the genetic suspicion of diffuse disease. In 14 children, ^{18}F-DOPA-PET scan indicated focal pancreatic uptake, which corresponded to histology. However, in 5 patients (36%), ^{18}F-DOPA-PET scan was inaccurate in defining the location of the lesion (n = 3), size of the lesion (n = 1), or both location and size (n = 1), leading to an inaccurate pancreatic resection.

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Conclusions: Fluorine-18-L-3,4-dihydroxyphenylalanine–positron emission tomography–computed tomography scan discriminates between diffuse and focal forms of CHI. In focal forms, ^{18}F-DOPA-PET scan is useful in 2/3 of patients in defining the site and dimension of the focal lesion. Intraoperative histologic confirmation of complete focal lesion resection is needed.

Congenital hyperinsulinism (CHI) is the most frequent cause of persistent hypoglycemia in infants, and it is associated with a high risk of neurologic complications [1]. Histologically, 2 subtypes of CHI have been described, focal and diffuse [2]. Both forms share a similar clinical presentation, but result from different pathophysiological mechanisms and are managed differently. The diffuse form, which affects the whole pancreas, is medically treated, and surgery (near-total pancreatectomy) is required only when medical therapy is unsuccessful. Conversely, the focal form (40%-50% of cases), which is localized to one region of the pancreas, can be completely cured by partial pancreatectomy including the focal lesion, which minimizes the risk of diabetes mellitus or exocrine insufficiency [3]. Because of these differences, the preoperative identification of those children with a focal form is critical. In the past, methods for identifying children with a focal CHI included intrahepatic pancreatic portal venous sampling, arterial calcium stimulation/venous sampling, acute insulin response testing to intravenous glucose, calcium, and tolbutamide and biopsy of the tail of the pancreas. However, these investigations are technically difficult and do not reach maximal accuracy. A more recent method to identify pancreatic focal lesions is fluorine-18-L-3,4-dihydroxyphenylalanine positron emission tomography (^{18}F-DOPA-PET) combined with computer tomography (CT) scan [4].

The aim of the present study was to evaluate the predictive value and accuracy of the ^{18}F-DOPA-PET scan in (i) the discrimination between diffuse and focal pancreatic lesions and (ii) the anatomical localization of the focal lesions. To answer these questions, we compared the preoperative ^{18}F-DOPA-PET scan results with the macroscopic and histologic findings in our cohort of patients with CHI who were not responding to medical therapy and underwent surgery.

1. Methods

1.1. Patients

Institutional ethical approval was obtained (institutional review board reference: 06/Q0508/58). Our institution is a tertiary referral center for CHI, where a prospective database of all children with CHI is maintained. Our diagnostic pathway of children suspected of having CHI has been previously reported [5]. Diagnosis of CHI is based on the following parameters: glucose infusion rate greater than 8 mg/kg per minute, laboratory blood glucose, greater than 3 mmol/L, detectable insulin/C-peptide, hypoketosis, undetectable/low free fatty acids, and a positive glycemic response to glucagon. Children with established CHI are then commenced on diazoxide (±chlorothiazide), nifedipine, and glucagon/octreotide. To distinguish between diffuse and focal forms of CHI, we first rely on genetic analysis [6]. In children with genetically confirmed diffuse disease, ^{18}F-DOPA-PET scan was not performed. The ^{18}F-DOPA-PET scan was performed only in those children with a diagnosis or a suspicion of focal disease based on our genetic studies, that is, (i) children with no characteristic mutations to differentiate between focal and diffuse CHI [4,7,8] and (ii) children with genetic mutations characteristic of focal CHI to localize the focal lesion.

Children with diffuse CHI are treated according to our protocol [1,5]; medically unresponsive cases who continue to require intravenous glucose infusion despite maximal medical therapy undergo a laparoscopic near-total pancreatectomy. All children with focal CHI are treated by laparoscopic or open segmental pancreatectomy with complete excision of the focal lesion as confirmed by intraoperative frozen-section histology. In children with focal CHI in the head of pancreas, the lesion is resected, and usually a pancreaticojejunostomy is performed to obtain drainage of the distal remaining pancreas. In children with distal focal lesions, a laparoscopic limited distal pancreatectomy is performed.

All our patients but 1 (patient 6; Table 1) had the ^{18}F-DOPA-PET scan done at the same center. The investigation followed a modified protocol as previously described [9]. Investigations were performed without discontinuation of diazoxide or octreotide. All the ^{18}F-DOPA-PET scan results were analyzed and interpreted jointly by the same multidisciplinary team (1 nuclear physician, 1 radiologist, 1 pediatrician). A 3-phase high-resolution CT scan was part of the scan procedure; a high-resolution PET scanner (Siemens biograph) was used for acquisition of the PET signals.

Histologic studies on resected pancreatic specimens occurred both intraoperatively and postoperatively. Intraoperative specimens were collected and sent for analysis of frozen sections, to confirm the presence, nature, and subtype of the pancreatic disease (diffuse or focal). In case of diffuse CHI, the first resected specimen was the tail of the pancreas and was sent for urgent frozen-section histologic analysis to confirm the diagnosis of diffuse CHI. No further resection