ELSEVIER

Seminars in
NUCLEAR
MEDICINE

Gender-Based Differences in Pediatric Nuclear Medicine

Adina L. Alazraki, MD, and Kiery A. Braithwaite, MD

Gender-based differences commonly encountered in pediatric nuclear medicine reflect both basic embryologic differences of the sexes, which are evident from infancy, and evolving physiological changes due to gender, which occur as the pediatric patient grows, undergoes puberty, and matures to adulthood. It is important for a nuclear medicine physician or radiologist to know both the gender and the age of a patient when interpreting her or his studies. It is also important that the reading physician be familiar with the normally evolving physiological changes that are specific for that patient's stage of development. It is particularly important that the reading physician consider such changes when comparing serial studies of the patient that are acquired during the patient's transitions through her or his different significant stages of development. Many pediatric nuclear medicine imaging protocols are modifications or adaptations of the protocols for adult imaging. Physicians reading pediatric studies must routinely incorporate knowledge on age and gender that is relevant to the patient for any given study. The age-defined gender-based subtleties of potential findings in pediatric nuclear medicine studies are often underrecognized. However, they are often of interest and at times important in the workup of both benign entities and pathologic processes of the pediatric patient.
Semin Nucl Med 44:451-460

Introduction

Gender-based differences specific to disease processes in the pediatric population are not uncommon. These differences are often inherent in the embryology of the fetus and in the sex-determination factors that influence development of male or female anatomy. Gender-based differences observed on nuclear medicine imaging of male and female individuals with disorders for which the management requires such imaging are few, but often critical. Sex plays a role in the evaluation of some abnormal structures and some normal structures. It is important to recognize when it does and why it does not play a role. The goal of this article is to highlight the more commonly encountered gender-specific physiological and pathologic differences one encounters when interpreting nuclear medicine studies in the pediatric population with hopes that this would provide the reader useful practical knowledge for application in the management of pediatric patients.

Department of Radiology and Imaging Sciences, Children's Healthcare of Atlanta, Emory University, Atlanta, GA.

Address reprint requests to Adina L. Alazraki, MD, Department of Radiology and Imaging Sciences, Children's Healthcare of Atlanta, Emory University, 1405 Clifton Rd, Atlanta, GA 30322. E-mail: adina.alazraki@choa.org

FDG-PET Imaging

Normal physiological patterns of FDG uptake have been extensively described in the medical literature.[1] The patterns of normal FDG uptake in the male and female population are largely similar, with a few notable exceptions that are more obviously distinct in the adolescent population.

Normal FDG uptake in the gonads is frequently seen, but it is more pronounced in the pediatric adolescent population than in the adult population. FDG uptake in the adult testis has been described as declining with age, even when corrected for testicular volumes.[1,2] Conversely, moderately intense FDG uptake is frequently noted in the pediatric testes and increases with age during adolescence. A study by Goethals et al,[3] although limited by a small sample size, found a statistically positive correlation between the mean bilateral testicular standardize uptake value (SUV) and patient age in young male individuals. In this study, which focused on male individuals aged 9-18 years, the mean SUV of the testes of its subjects steadily increased throughout late childhood and adolescence. The authors commented that the mean testicular volume also increased with age, and it was uncertain what percentage of change in SUV was secondary to increase in volume vs physiological uptake. It is important not to confuse this

http://dx.doi.org/10.1053/j.semnuclmed.2014.06.007
0001-2998/

age-related increase in FDG uptake in the testes during late childhood and adolescence with testicular malignancies, both primary and secondary. This may be especially important in patients with hematologic malignancies, such as leukemia and lymphoma, as the testis is well known to be a site with a relatively increased risk of relapse, because of the blood-testis barrier.

The endometrium and ovaries are the female analog to the testes. They also undergo, particularly during adolescence, both anatomical and physiological changes that can result in normal and abnormal FDG uptake. The endometrium and ovaries are dormant in the prepubescent child, but undergo significant change during puberty. The normal endometrium can have increased FDG uptake such that it tends to peak during menstruation.[4] During ovulation, increased metabolic activity within the ovaries could be misinterpreted as pelvic disease if it is not recognized as a normal physiological phenomenon.[4] Therefore, recording the last menstrual period of the female patient is pertinent to the interpretation of her FDG study.

Normal physiological uptake of FDG in the breast tissue is frequently identified in postpubertal adolescent girls and premenopausal women, with uptake generally higher during menstruation.[5,6] Dense breast tissues tend to have higher baseline FDG uptake and this is more common in the young, adolescent female population when compared with the adult population.[5] However, it can be noted that the average SUV in dense breast tissue is still less than 2.5, which is the accepted SUV for background.[7]

All the aforementioned findings are considered normal patterns of uptake, but the variations in the patterns by gender are important to recognize and to use so as to correctly interpret a pediatric nuclear medicine study (Fig. 1).

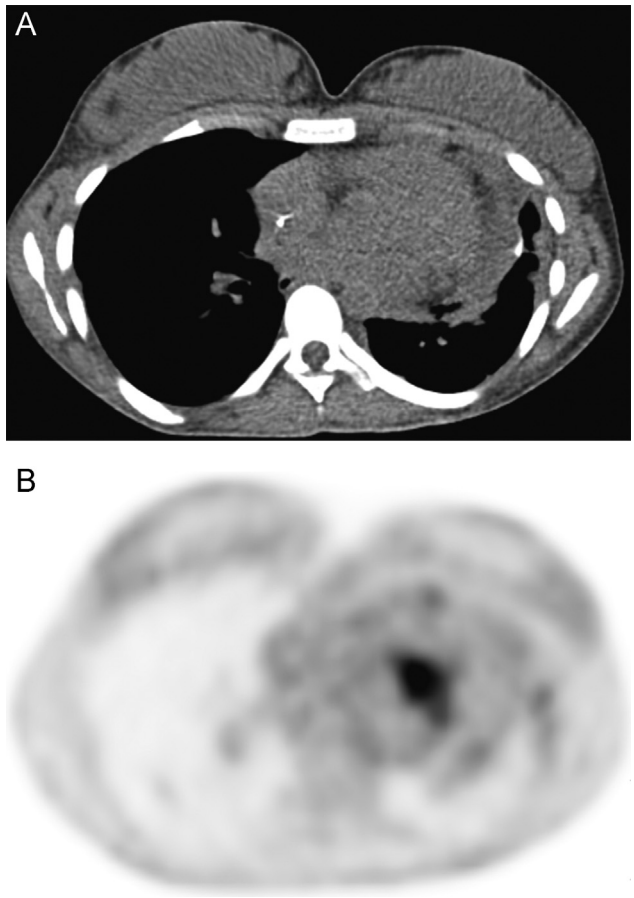

Figure 1 (A) CT and (B) PET axial images at the level of the breasts in a female adolescent patient. Dense breast tissue on the CT image and corresponding FDG uptake on the PET image can be noted.

Brown fat is a type of adipose tissue that is involved physiologically in heat generation and the regulation of body temperature. It is present in humans from infancy through adulthood. Brown adipose tissue is frequently encountered as hypermetabolic on FDG-PET scans in both pediatric and adult patients. The literature suggests that these depots of active brown fat are more common in adult women than in adult men.[8] However, this finding has not been substantiated in children. It has instead been shown that FDG uptake in brown fat in children is more dependent on age and adolescent development, that is, the Tanner stage. In a study by Drubach et al,[9] involving 385 scans of 172 patients, no significant difference was found between the FDG uptakes in brown fat in boys and the uptakes in brown fat in girls (aged 5.3-20.8 years). In the same study, the frequency of identification of brown adipose tissue increased through childhood, reaching a maximum frequency near the age of 13 years in both male and female individuals. In the study, the uptake of FDG in brown fat was identified in nearly half of the adolescent patients, a frequency that is much higher than that reported for the adult population. Similar findings were reported in a smaller study (73 patients) by Gilsanz et al, which compared the volume of brown fat in pediatric patients that was detected using PET with the Tanner stage. Younger prepubescent children (Tanner stage 1) were shown to have less uptake in the brown fat than that in older children undergoing physiological changes of puberty. The greatest volume of brown fat detected using PET/CT by Gilsanz et al was that detected in the later stages of puberty (Tanner stages 4-5) for both adolescent girls and boys. Furthermore, a gender–based difference in the volume of brown fat was identified in the study by Gilsanz et al,[10] but only in the aforementioned later stage of puberty. The volume was greater in male than in female individuals.[10] Both studies demonstrate that brown adipose tissue is more reliably relatable to the inverse body mass index and that peak identification of metabolically active brown fat in adolescence correlates with the age of physiological development that is associated with less body fat and a marked increase in skeletal muscle mass.[9,10]

Brown fat is activated by exposure to cold. The result of such exposure can be a 5-fold increase in the uptake of FDG.[11] Controlling the uptake of FDG within brown fat stores is important for accurate staging of disease. A number of pharmacologic and practical solutions have been suggested. Gelfand et al reported a significant decrease in the uptake of FDG within brown fat in children when fentanyl was administered before FDG. Gelfand et al[12] reported no visible reduction following administration of low-dose diazepam. Similarly, other studies have shown a reportable decrease in brown adipose tissue activity when a beta-adrenergic antagonist, that is, propranolol, is administered before uptake.[13,14] The most important factor in diminishing uptake in brown fat