The use of PET/CT in pregnancy: A case report of malignant parathyroid carcinoma and a review of the literature

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Abstract

Positron emission tomography scanning is not commonly performed in pregnancy but can be done if required. Fetal doses of radiation can be minimized, and our case exemplifies the safe application of positron emission tomography/computed tomography in pregnancy. A 38-year-old woman in her first ongoing pregnancy presented at 28 weeks' gestation with symptomatic hypercalcemia. Given a history of parathyroid carcinoma, recurrence was suspected. Ultrasound and magnetic resonance imaging failed to locate the lesion. However, positron emission tomography/computed tomography identified a culprit supraclavicular lymph node. This was excised under local anesthesia resulting in normalization of parathyroid hormone and calcium levels. A term, healthy baby was delivered. The literature provides support that the use of positron emission tomography/computed tomography is acceptable when indicated, and there are modifications to protocols that can further limit risk.

Keywords

Pregnancy, positron emission tomography, FDG, malignancy, hypercalcemia, parathyroid

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Introduction

The use of radiological modalities for the pregnant population can be anxiety provoking for physicians. Weighing the risks and benefits of any one test becomes more difficult with advancing technology and increasing options, while information about their effects on fetal tissues may be scarce. Guidelines such as those published by the American College of Obstetricians and Gynecologists¹ can be helpful to navigate common diagnostic imaging concerns, but lack detail about less common modalities in pregnancy. In this article, a case of a woman with recurrence of malignant parathyroid carcinoma in pregnancy is presented. Currently, positron emission tomography/computed tomography (PET/CT) is one of the gold standard modalities with which malignancy is detected and staged. The literature provides data supporting its use as acceptable when indicated, with modifications to protocols to further limit risk. This case exemplifies the safe application of PET/CT in pregnancy, and how it changed the management for this patient. In addition to the case report, the results of a literature review of papers that provide dosimetry data in the use of PET in pregnancy is provided. Finally, an approach for the appropriate use of PET in pregnancy is suggested.

Case report

A 38-year-old woman, gravida 3, para 0 gestation presented at 28 weeks with left flank pain, nausea, vomiting, and diarrhea. Parathyroid carcinoma had been diagnosed eight years prior, and she had been treated with surgery and radiation therapy. Four years later, there was local recurrence in the mediastinum, which was again treated with surgery and radiation therapy. The patient had been disease free for four years until she presented with her current symptoms.

At presentation, parathyroid hormone (PTH) was 18.3 pmol/L (normal range: 1.4–6.8 pmol/L) and total calcium was 3.24 mmol/L (normal range: 2.10–2.60 mmol/L). The patient's symptoms were partially improved with intravenous (IV) normal saline and subsequent loop diuretic therapy, but calcium levels remained high (corrected

calcium: 3.2 mmol/L). The cause of the hypercalcemia was presumed to be a recurrence of parathyroid carcinoma.

A multidisciplinary meeting was held to discuss imaging/staging modalities, surgical options, and timing of delivery to facilitate further oncological treatments. A watch and wait approach was considered to be suboptimal due to the potential deleterious effects of antenatal hypercalcemia on the neonate. High maternal calcium concentrations, left untreated, can cause an initial hypercalcemic state in the fetus leading to fetal PTH suppression that subsequently results in hypocalcemia after birth. Neonates can experience neuromuscular irritability, laryngospasm, tetany, and seizures.

Localization of the presumed recurrence was challenging. Initially, after an ultrasound of the neck failed to detect any abnormality, a magnetic resonance imaging (MRI) scan was performed in hopes of locating the recurrence without exposing the patient and her fetus to unnecessary radiation. Unfortunately, the MRI was nondiagnostic, and a low-dose ¹⁸F-FDG (fluorodeoxyglucose)-PET/CT was undertaken on a Philips Gemini TF scanner (whole body scan with dedicated neck scan). Dose-reduction techniques included lowering the dose (administered activity) of ¹⁸F-FDG to 173 MBq, IV hydration before and during the hour of uptake, and bladder catheterization of our patient prior to uptake, during the scan, and for 2 h postscan. The estimated average fetal dose was 2.8 mGy from 173 MBq of ¹⁸F-FDG, based on the six-month gestation phantom with a 2-h void, including crossover of FDG to the placenta.² Additionally, a low-dose CT scan without contrast

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Figure 1. (a) PET, CT, and fusion image showing solitary, left supraclavicular lymph node that is ^{18}F -FDG avid. (b) PET, CT, and fusion image demonstrating ^{18}F -FDG accumulation in fetal myocardium, head, renal tissue, and lower extremity (perhaps fetal bladder). Tracer is also seen in the maternal bladder, which lies in close proximity to the fetus.

(120 kVp, 3 mm slices, z-modulation) was conducted for attenuation correction and anatomical localization purposes, yielding an estimated fetal dose of 3.1 mGy.³ A solitary left supraclavicular lymph node was identified as the culprit lesion (Figure 1(a)). Figure 1(b) demonstrates the distribution of the tracer in the fetal tissues and maternal bladder.

At 30 weeks' gestation, the patient underwent excision of the affected node under local anesthesia, which resulted in immediate suppression of PTH and normalization of calcium levels. She had an induced vaginal delivery at the 41st week. Her baby weighed 3210 g and had APGARs of 9 and 9 at 1 min and 5 min, respectively. The baby's calcium was not checked, as the mother's calcium had been normal for many weeks. The patient has remained normocalcemic since the excision, and her baby is healthy.

Discussion

Our patient's lesion could not be initially localized using modalities traditionally considered "safe" in pregnancy. This potentially could have led to more invasive exploratory surgery, exposing her to the risks associated with the use of general anesthesia in pregnancy. Instead, management of this case was significantly changed by using PET/CT, and an excellent outcome was achieved.

The primary risks involved in PET/CT are thought to be from ionizing radiation and the potential toxicity of the radiopharmaceuticals. Many experts recommend that total fetal radiation exposure should not exceed 50 mGy (5 rad)¹ to mitigate risk; the International Commission on Radiological Protection lists the threshold for adverse

effects as 100 mGy.^{4,5} Deterministic adverse outcomes of radiation, such as pregnancy loss, congenital malformation, microcephaly, intellectual disability, and fetal growth restriction, are not seen below this threshold. These outcomes typically are not a concern with the amounts of radiation that a fetus would be exposed to with most known diagnostic imaging techniques. Cancer induction is believed to be a probabilistic risk: there is no threshold for adverse events, but the risk increases with increasing dose. For example, the background risk of leukemia is estimated to be 1/3000, and this risk is thought to increase by a factor of 1.5 to 2.0 per 10 to 20 mGy fetal exposure,¹ but the absolute risk remains low for any single radiologic procedure commonly used in pregnancy. Clinicians must weigh the risks and benefits to pregnant women when radiologic studies expose the fetus to ionizing radiation. Given the low absorbed doses received in utero from properly performed diagnostic procedures, radiologic imaging techniques should not be withheld in settings where they are the gold standard. If the potential radiation dose of a particular investigation falls below the recommended thresholds in pregnancy, and the imaging could change patient management, such investigations should not be withheld. Once a diagnostic imaging procedure is clinically justified in a pregnant patient, its administration should then be optimized for diagnostic quality and dose reduction.

Traditionally, there have been concerns for the use of PET and ¹⁸F-FDG in pregnancy due to concerns about radiation risk and fetal uptake of radiopharmaceuticals. A literature search in MEDLINE for positron emission tomography and pregnancy limited to humans, where dosimetry is available was performed on 13 April 2016. The references from these articles were also reviewed, and in total there was one abstract⁶ and eight papers⁷⁻¹⁴ where PET scans were performed in pregnancy with dosimetry data published. One of these papers⁸ reported on the same patient (with slightly different calculations) as a previous paper⁷; therefore, 8 publications from 2004 to 2015 describing a total of 19 examinations in 18 pregnant women were reviewed. Almost all of these scans were performed for the evaluation of malignancy. Table 1 summarizes these scans including gestational ages at the time of the scan, doses, dose reduction strategies, and the dosimetry data provided. It is evident that PET, with or without CT, has been successfully used in all trimesters in the published literature for well over a decade, particularly for oncological indications. In 2004, Stabin² published fetal dose estimates per administered activity for ¹⁸F-FDG, and these values have been used in several of these publications. Although these are based on theoretical models, they are helpful at generally estimating risk and can be compared against the protocols used by individual centers. The dosimetry data published in these reports provide some basis with which to counsel patients and help gauge the tangibility of these risks when weighing them against the potential benefits.

Total fetal radiation dose is calculated by adding the amount of internal exposure from the tracer used for the PET scan to the external dose from the CT scan. Some authors have used PET only¹⁰ with a ⁶⁸Ge rod source for attenuation correction (which has negligible additional radiation dose), to limit the radiation dose to the fetus. However, no anatomical data are provided in a PET-only technique, which may result in fetal radiation exposure without appropriate benefit. Zanutti et al.¹⁴ had the unique experience of performing PET/MRI on two patients. Since MRI does not involve ionizing radiation, PET/MRI can be used as an alternative to provide detailed imaging without additional radiation. Not all centers have the capability for PET/MRI; regardless, even with CT, the total radiation dose to the fetus is still well below the recommended limits.

Early reports of the use of PET during pregnancy were in cases where they were imaged inadvertently during an unknown pregnancy.^{7,9} Despite no attempts to limit radiation, estimated doses were still below the 50 to 100 mGy recommended limit. Several sites used various methods to reduce fetal radiation exposure such as using a lower dose of radiotracer, hydration (oral or IV saline infusion) prior to ¹⁸F-FDG, IV furosemide administration to promote rapid excretion of ¹⁸F-FDG, and bladder catheterization. Since ¹⁸F-FDG is excreted

by the kidney and concentrates in the bladder, diuretics and catheterization would limit the dwell time of ¹⁸F-FDG, reducing fetal exposure. Finally, Zanutti et al.¹⁴ calculated the exposure to the fetus from the maternal bladder based on different void times. More frequent and early voiding led to lower fetal radiation doses.

There are large uncertainties involved in dosimetry, especially since every dose calculation relies on a mathematical model of a person. The majority of the radiopharmaceutical distributions are obtained from animals and men, and the biological distribution can vary significantly between normal versus pathological conditions. Additionally, an internal dose calculation for a pregnant patient is complicated by the stage of pregnancy and the change in the body's functions/metabolic processes. It should be noted that the dosimetric values presented in this and other papers are only estimates but are considered valid assessments for the patients under consideration. Some authors^{7-11,14} have made some patient-specific adjustments in determining ¹⁸F-FDG fetal doses. Even with these adjustments, the ¹⁸F-FDG fetal dose values are extraordinarily low. The average dose to the fetus across the literature reviewed, including the patient represented in this paper, is 4.06 ± 3.22 mGy. The uncertainties in estimating doses are such that the accuracy that could be expected for any dose value calculated for a patient would be within about a factor of 2 (i.e., either half or double the estimated dose).¹⁵⁻¹⁸ Regardless of the uncertainties, all the published fetal ¹⁸F-FDG doses are still well below the threshold for deterministic risks from radiation.

Initially, nondiagnostic imaging modalities were pursued for our patient, as our center did not have experience using PET scanning in pregnancy. The management of our patient was profoundly changed by utilizing a multidisciplinary approach, which led to conducting a PET/CT scan. She was appropriately staged, underwent a minimally invasive surgical strategy with local anesthesia, and went on to deliver a healthy baby at term. Other authors have also found that the results from PET changed the management for their patients. In the paper by Calais et al.,¹³ a 26-year-old woman at 26 weeks' gestation with sclerodermoid Hodgkin's lymphoma underwent a low-dose PET/CT scan which demonstrated stage IIIA disease. With this information, she was able to receive corticosteroids until delivery at 36 weeks, avoiding potentially being incorrectly staged and the pursuit of more harmful treatment options.

Our recommendations for the use of PET or PET/CT in pregnancy for the evaluation of a malignancy are as follows:

1. All standard imaging modalities should be considered when evaluating a pregnant woman for malignancy, particularly if it will change the management.
2. A multidisciplinary approach is preferable. In particular, a nuclear medicine physician and medical physicist (if available) should be consulted to obtain information regarding protocols, dosimetry, and methods by which to limit radiation exposure.
3. Delaying investigation until later in pregnancy should only be considered if it would not affect the risk and prognosis for the mother or limit her options for termination of pregnancy if this is an option that she would consider.
4. Adequate hydration should be achieved by using oral and/or IV fluids judiciously. Volume overload should be avoided, particularly since pregnant women are predisposed to third spacing.
5. Women should be counseled to void prior to image acquisition, thereby avoiding a prolonged dwell time of the tracer in the bladder due to its close proximity to the uterus. One could also consider the use of diuretics or catheterizing the patient to minimize exposure of the fetus to the tracer, although the risks of causing bacteriuria or a urinary tract infection should be weighed. Catheterization can be done prior to arrival for the scan, kept in during image acquisition, and not removed until sometime after the scan to maximize voiding/elimination of the tracer.
6. Women should be counseled that ¹⁸F-FDG does accumulate in the fetus, but that the benefit of the information obtained likely outweighs any potential risk to the fetus.

Table 1. Published dosimetry data from cases in which PET scanning was performed in pregnancy.

Author	Gestational age	Imaging modalities	Injected activity (MBq)	FDG dose (mGy)	Transmission scan dose (mGy)	Fetal FDG-avid structures	Dose reduction and safety measures
Towson et al. ⁶	5 months	PET/CT	355	6.4	6	Whole fetus (noted head and body)	Just mentioned optimization for dose
	6 months	PET/CT (cerebral only)	188	3.2	Considered negligible	No specific organs mentioned	
Zanotti et al. ^{7,8}	8 weeks	PET/CT	320	10.7	8.3	Whole fetus	Urination before scanning (unknown pregnancy)
Zanotti et al. ⁹	10 weeks	PET/CT	296	11.8	10	Whole fetus	No contrast (unknown pregnancy)
Takalkar et al. ¹⁰	~6 weeks	PET	583	9.0	Considered negligible	Whole fetus	Oral + IV hydration, furosemide IV, multiple voids (unknown pregnancy)
*same patient scanned twice							
	18 weeks*	PET	200	1.4	Considered negligible	Whole fetus; sometimes myocardium	Oral + IV hydration, furosemide IV, multiple voids, reduced activity, no CT
	30 weeks*	PET	229	2.4	Considered negligible		
	23 weeks	PET	181	1.1	Considered negligible		
	25 weeks	PET	337	2.1	Considered negligible		
	28 weeks	PET	174	1.0	Considered negligible		
Zanotti et al. ¹¹	21 weeks	PET/CT	181	3.6	5	Whole fetus; brain	Low-dose CT scan, no contrast
Hsieh et al. ¹²	26 weeks	PET/CT	370	6.3	3.6	Myocardium and kidneys	Low-dose CT scan
Calais et al. ¹³	26 weeks	PET/CT	Not reported	4.1	3.2	Myocardium	Reduced activity, low-dose CT
Zanotti et al. ¹⁴	5 weeks	PET/CT	296	5.1	Not reported	Later trimesters: myocardium and likely kidneys and bladder	IV hydration, bladder catheterization, low-dose CT
	12 weeks	PET/CT	385	2.8	Not reported		
	~3 months	PET	350	2.7	Considered negligible		IV hydration, bladder catheterization
	19 weeks	PET/MR	296	1.4	N/A		IV hydration, bladder catheterization
	19 weeks	PET/MR	348	1.4	N/A		
	7 months	PET	296	1.8	considered negligible		IV hydration, bladder catheterization
Our case	28 weeks	PET/CT	173	2.8	3.1	Myocardium and likely kidneys, bladder, and head	IV hydration pre-scan, bladder catheterization pre-, during, and post-scan, no contrast

FDG: fluorodeoxyglucose; PET: positron emission tomography; CT: computed tomography; IV: intravenous; MR: magnetic resonance; N/A: not applicable.

*This is the same patient who was scanned twice at two different times in the pregnancy.

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