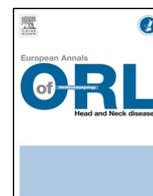




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## Case report

# Hyperparathyroidism in pregnancy and $^{99m}\text{Tc}$ -MIBI scintigraphy

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## ABSTRACT

**Introduction:** Primary hyperparathyroidism (PHPT) during pregnancy can be responsible for serious maternal and foetal complications and should be treated by elective low-risk, minimally invasive surgery. Preoperative assessment of hyperfunctioning parathyroid glands is classically based on high-resolution neck ultrasound (US) and  $^{99m}\text{Tc}$ -sestamibi/ $^{123}\text{I}$  scintigraphy. However, administration of any radiopharmaceutical during pregnancy must be limited and justified and US alone may be sufficient to localize an abnormal parathyroid gland.

**Case report:** We report the case of a 4-month pregnant woman with severe primary hyperparathyroidism, in whom US failed to localize the abnormal parathyroid gland.  $^{99m}\text{Tc}$ -sestamibi scintigraphy was performed in preference to  $^{18}\text{-F}$ -fluorocholine (FCH)-PET/CT on the basis of a multidisciplinary decision. As  $^{99m}\text{Tc}$ -MIBI demonstrated an hyperfunctioning right inferior parathyroid,  $^{123}\text{I}$  was not administered. A large right paravertebral parathyroid adenoma was successfully removed, as confirmed by decreased postoperative serum parathyroid hormone and calcium levels. The eutrophic newborn infant was delivered at term, with normal serum calcium and TSH levels.

**Discussion:** In pregnant women with primary hyperparathyroidism, US alone may be sufficient when it localizes the abnormal parathyroid gland, allowing elective low-risk minimally invasive surgery. Otherwise, a multidisciplinary approach is mandatory to select the radiopharmaceutical that can be safely used to identify the hyperfunctioning parathyroid gland with minimal risks for the foetus.

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## 1. Introduction

Primary hyperparathyroidism (PHPT) is uncommon during pregnancy, but can be associated with risks for both the mother and the foetus [1]. The diagnosis of PHPT is often delayed in pregnant women due to the nonspecific nature of the symptoms [2].

The risks of pre-eclampsia, early miscarriage, stillbirth, intrauterine growth restriction, and foetal hypocalcaemia and hypoparathyroidism associated with PHPT during pregnancy [3] justify surgical resection during the second trimester [1].

Preoperative localization of the abnormal parathyroid gland responsible for PHPT is essential to allow targeted surgery [4] and classically consists of high-resolution ultrasound of the neck and  $^{99m}\text{Tc}$ -sestamibi/ $^{123}\text{I}$  scintigraphy to identify the hyperfunctioning parathyroid (PT) gland(s) [4].

However, administration of radiopharmaceuticals, particularly Iodine-123, is not recommended during pregnancy due to radiation exposure of the foetal thyroid gland. Ultrasound examination may therefore be sufficient when it accurately identifies the abnormal PT gland [1].

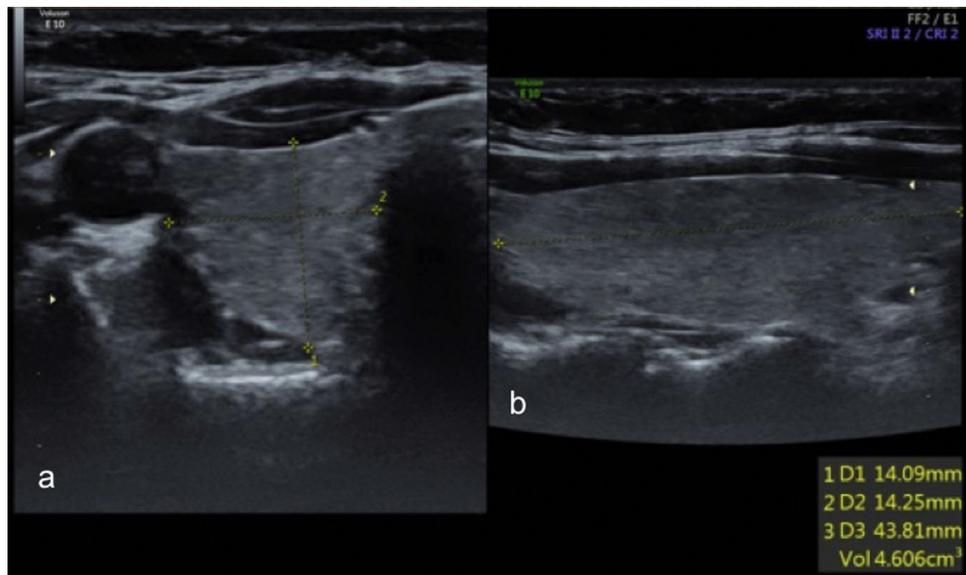
We report the case of a pregnant woman with PHPT in whom ultrasound failed to identify the abnormal parathyroid gland. A multidisciplinary meeting adopted the functional imaging strategy with an optimal benefit/risk balance, guided by the ALARA principle (radiation exposure as low as reasonably possible) applied to the foetus [5].

## 2. Case report

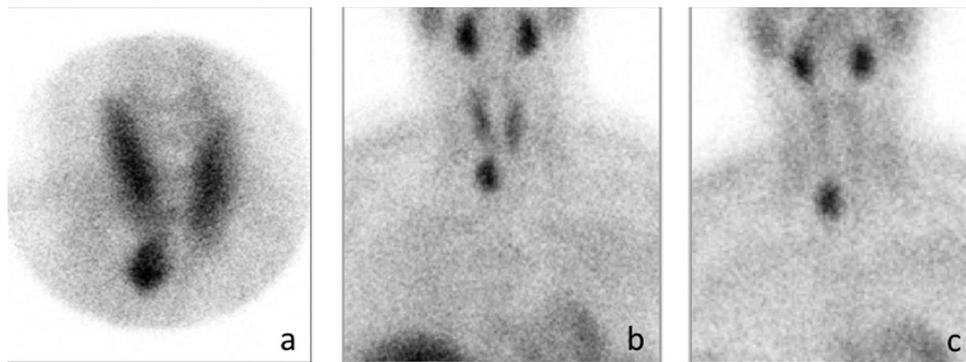
A 31-year-old primigravida woman was referred, at 16 weeks of amenorrhoea, for management of PHPT known for 3 years, but neglected. She presented hypercalcaemia with serum calcium: 2.95 mmol/L, serum PTH (serum intact PTH 1–84): 160 pg/mL and urinary calcium: 823 mmol/24 h. It was decided to perform resection of a probable parathyroid adenoma. High-resolution

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**Fig. 1.** High-resolution ultrasound examination of the thyroid gland. Axial (a), and longitudinal (b) sections of the right side. Normal appearance of the right lobe of the thyroid, and no parathyroid gland identified.



**Fig. 2.**  $^{99m}\text{Tc}$ -MIBI scintigraphy: early images (a, b) and late image (c). Site of increased uptake suggestive of hyperfunctioning parathyroid gland, situated inferiorly to the physiological uptake of the right lobe of the thyroid gland (uptake by salivary glands, myocardium and the dome of the liver is also observed on the large field image in the center). At the late phase (image acquired 3 hours after injection), MIBI has left the thyroid gland but not the suspicious site, an additional criterion in favour of parathyroid adenoma (c).

ultrasound examination was performed, but failed to localize the abnormal PT (Fig. 1).

The practical modalities of functional imaging were discussed at a multidisciplinary meeting (otorhinolaryngologist, nuclear physician, endocrinologist, obstetrician and the teratogenic agent reference centre) based on foetal radioprotection, the approved indications for the available radiopharmaceuticals and the sensitivity of the examination. It was decided to perform  $^{99m}\text{Tc}$ -MIBI scintigraphy alone, with subsequent administration of  $^{123}\text{I}$  only in the event of doubtful localization.

The early and late phases of  $^{99m}\text{Tc}$ -MIBI scintigraphy demonstrated a site of increased uptake below the right base of the thyroid, in favour of a single parathyroid adenoma (Fig. 2).

A minimal right retrothyroid neck incision was performed with preoperative and postoperative foetal monitoring. A PT measuring  $3 \times 3$  cm was found on the posterior surface of the middle third of the right lobe of the thyroid, in a posterior paravertebral plane, corresponding topographically to a superior PT (Fig. 3). Histological examination confirmed a benign parathyroid adenoma.

Vitamin D and calcium replacement therapy (Cacit<sup>®</sup> [calcium carbonate] and Unalfa<sup>®</sup> [alfacalcidol]) was instituted for 1 month to limit postoperative hypocalcaemia. The fall in serum PTH to 4.6 pg/mL on postoperative day 1 confirmed the success of the



**Fig. 3.** Macroscopic appearance of the resected parathyroid gland.

operation. The woman gave birth, at 41 weeks of amenorrhoea, after an otherwise uneventful pregnancy, to an eutrophic infant weighing 3250 g with normal serum TSH. Six months after surgery, PTH was 49 pg/mL and the calcium assessment was normal

(total calcium: 2.43 mmol/L, ionized calcium: 1.24 mmol/L, vitamin 25OH-D3: 35.6 ng/mL).

### 3. Discussion

PHPT in a pregnant woman raises the problem of the optimal treatment strategy. Surgery is the treatment of choice, but, in the absence of preoperative localization of the adenoma, bilateral exploration must be performed, with a risk of a bilateral recurrent laryngeal nerve injury and long or even negative exploration. Prescription of Mimpara® (cinacalcet) during pregnancy is an alternative, but its efficacy and its effects on the foetus have not been adequately studied [6].

In this setting, ultrasound constitutes the first-line examination, and may be sufficient when it localizes the abnormal PT. A negative or doubtful ultrasound examination raises the problem of the most appropriate nuclear medicine functional imaging protocol: scintigraphy or PET. We have previously described the value of <sup>18</sup>F-fluorocholine PET/CT in HPT [7], which has the advantage of providing better detection and topographic localization of hyperfunctioning PT glands, with a shorter examination time than scintigraphy [7]. Radiation exposure due to the radiopharmaceutical is similar to that of <sup>99m</sup>Tc-MIBI, but the essential fusion with CT adds a low dose of x-rays to foetal exposure (less than 1 mGy) [5]. Although less sensitive, <sup>99m</sup>Tc-sestamibi/<sup>123</sup>I scintigraphy can be performed without associated CT scan [7,8]. Precise localization of the abnormal PT may be more difficult, but it is generally possible to identify the side of the neck in which the hyperfunctioning PT is situated. In the absence of specific data for <sup>99m</sup>Tc-MIBI, we deliberately maximized the risk by taking into account recent results concerning <sup>99m</sup>Tc-pertechnetate [9]; for a dose of 679 MBq, the estimated dose delivered to the foetus at 6 months of pregnancy is 10.7 mGy, considered to be devoid of any risk of foetal malformation. The dose of <sup>123</sup>I absorbed by the foetal thyroid gland is inverse to uptake by the maternal thyroid; according to recent data at the end of pregnancy [10], for a dose of 8 MBq, the maximum total dose to the foetus would be 0.12 mGy with a maximum dose of 58 mGy to the thyroid gland. <sup>99m</sup>Tc-sestamibi/<sup>123</sup>I scintigraphy performed at the 2nd trimester of pregnancy delivers a radiation dose to the foetus much lower than known to induce non-stochastic effects such as malformations or hypothyroidism [8]. The currently approved indications for <sup>99m</sup>Tc-MIBI and Iodine-123 include the possibility of administration to pregnant women, after confirmation of a favourable benefit/risk balance. However, this is not the case for <sup>18</sup>F-fluorocholine, which is currently not indicated for the investigation of HPT.

In the case reported here, we simplified the usual scintigraphy protocol [7]. As ultrasound failed to demonstrate any abnormality in the thyroid, <sup>99m</sup>Tc-MIBI scintigraphy (679 MBQ) was performed. MIBI was preferred to <sup>18</sup>F-fluorocholine on the basis of the approved indications and also in view of the possibility of performing a simple planar examination without CT and with MIBI alone without Iodine-123 for the early phase to decrease exposure of the foetal thyroid. The foetal thyroid probably also concentrates MIBI, as in adults, but with a shorter wash-out, and a half-life one half that of Iodine-123. Subsequent ingestion of Iodine-123 was planned only in the case of doubtful uptake on MIBI, with

dual-energy image acquisition at 3 hours. If scintigraphy had been negative, <sup>18</sup>F-fluorocholine PET/CT would have been preferred to complementary tomoscintigraphy coupled with CT in order to maximize the probability of detection.

### 4. Conclusion

The decision to medically or surgically treat HPT during pregnancy must be based on assessment of the risks by obstetricians and endocrinologists. Preoperative localization is mandatory, and ultrasound may be sufficient. When preoperative ultrasound fails to localize an abnormal PT, our case illustrates that nuclear medicine functional imaging can be performed according to the technique preferred by the nuclear physician, as the results of this examination are essential for surgical management [8]. The choice of imaging protocol was therefore essentially based on 3 elements in this pregnant woman: reduction of radiation of the foetal thyroid and whole body as low as reasonably possible, compliance with approved indications, and ensure the most sensitive imaging possible. This decision must be based on multidisciplinary consultation.

### Disclosure of interest

The authors declare that they have no competing interest.

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