CASE REPORT

Sestamibi scintigraphy for parathyroid localisation: a reminder of the dangers of false positives

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Accepted 17 January 2014

SUMMARY

Surgical parathyroidectomy is the only curative treatment for primary hyperparathyroidism. As minimally invasive parathyroidectomy increases in popularity, so does reliance on preoperative parathyroid localisation techniques. One such technique is sestamibi scintigraphy. We report a case of false-positive sestamibi scintigraphy caused by follicular variant of papillary thyroid carcinoma. Subsequent completion thyroidectomy was not possible due to widespread postoperative fibrosis. This case, therefore, highlights the potential dangers of false-positive results due to thyroid carcinoma and encourages surgeons to consider this possibility when faced with intrathyroidal or otherwise ambiguous parathyroid localisation results.

BACKGROUND

Primary hyperparathyroidism is an increasingly diagnosed endocrinopathy. It has been estimated to affect up to 1% of the UK population and is frequently discovered incidentally during routine blood tests.¹ While often asymptomatic, studies have shown that untreated hypercalcaemia may lead to long-term risk of cardiovascular disease, cerebrovascular disease and cancer, as well as direct sequelae such as bone and renal disease.²

Surgical parathyroidectomy is the only curative treatment for primary hyperparathyroidism. Traditionally, this was performed using bilateral neck exploration through a collar incision, with inspection of all four glands and removal of the clinically abnormal parathyroid(s). However, following observation that more than 85% of cases are attributable to a single adenoma, surgeons have been working to develop 'minimally invasive' parathyroidectomy techniques. These techniques have become increasingly common over the past decades and are made possible by developments in preoperative parathyroid localisation studies. Currently, the most commonly used localisation technique is 99m Technetium-sestamibi ('sestamibi') dual-phase scintigraphy.

In the following report, we describe a case presented to our institution in which sestamibi scanning produced a 'false-positive' result, found intraoperatively to be attributable to a thyroid nodule which was later shown to be a follicular variant of papillary thyroid carcinoma. Also we present a review of the current literature regarding sestamibi scintigraphy and highlight the risks of false-positive scan results in the age of minimally invasive parathyroidectomy.

CASE PRESENTATION

A 65-year-old woman was referred by her general practitioner, with hypercalcaemia on routine blood tests. She had a history of fatigue, urinary tract infections, anxiety and depression but no other symptoms of hypercalcaemia. Her medical history included hypothyroidism, hypercholesterolaemia, asthma and hearing loss. She had no known history of radiation exposure.

INVESTIGATIONS

On initial investigation, her corrected calcium was 2.70 mmol/L, vitamin D 105 nmol/L, parathyroid hormone 5.1 pmol/L and 24 h urinary calcium was elevated. A diagnosis of primary hyperparathyroidism was made and the patient was referred for dual-phase sestamibi scintigraphy. This showed a focus of delayed tracer washout over the left inferior pole in keeping with a left-sided parathyroid adenoma on planar images (figure 1). A departmental ultrasound scan was additionally performed which showed a large hypoechoic nodule of 2.6 cm in the longest axis (figure 2). This nodule showed echogenicity and vascularity typical of a parathyroid adenoma, but appeared to be partially intrathyroidal at the lower pole. These images were reviewed by a senior radiologist, who suggested, in conjunction with the sestamibi results, a left inferior parathyroid adenoma.

TREATMENT

The patient was listed for parathyroidectomy via a unilateral neck exploration.

Intraoperatively, left inferior and superior parathyroid glands appeared normal. In view of this finding, the operation was converted to a bilateral cervical exploration and an enlarged right inferior parathyroid was identified and removed. A 2 cm nodule was additionally identified at the inferior pole of the left lobe of the thyroid gland, consistent in location with the positive finding on sestamibi scanning. This nodule appeared abnormal intraoperatively and given that the patient was on thyroxine replacement, it was decided to remove the nodule via a left thyroid lobectomy.

OUTCOME AND FOLLOW-UP

Histological reports later confirmed the presence of a right inferior parathyroid adenoma. Biochemically her hyperparathyroidism resolved. The thyroid nodule removed via lobectomy was shown to be a follicular variant of papillary thyroid carcinoma of maximum extent of 21 mm, which had been incompletely excised (pT2, pNx).

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To cite: Whitcroft KL, Sharma A. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-203225

Figure 1 Sestamibi scan showing delayed tracer washout over the left inferior pole.

The patient was consequently listed for a completion thyroidectomy and level VI neck dissection. However, intraoperatively, she was found to have wide-spread postoperative fibrosis with no clear surgical planes for safe dissection. In order to prevent unnecessary morbidity, her operation was abandoned. She experienced no surgical complications.

Following discussion at the head and neck multidisciplinary team meeting, she is currently undergoing thyroid-stimulating hormone suppression therapy, and a watch and wait policy with regular follow-up has been adopted.

DISCUSSION

^{99m}Tc sestamibi is a lipophilic cationic compound that was first used for parathyroid imaging in the late 1980s. Diffusing down its electrochemical gradient, it is sequestered intracellularly within mitochondria. Parathyroid oxyphil cells contain high numbers of mitochondria, thereby causing prolonged retention of sestamibi relative to surrounding tissues.³

It has been theorised that malignant cells may retain sestamibi due to inherent mitochondrial dysfunction. Indeed, as preoperative sestamibi scanning emerged as a comparatively sensitive and

specific new technique, several case reports were published documenting ‘false-positive’ parathyroid localisation due to uptake in follicular, Hurthle cell and, as was the case here, papillary thyroid carcinomas.^{4–6} Despite these reports, use of sestamibi scintigraphy gained an increasing favour.

In a recent study at the Mayo Centre in the USA, Onkendi *et al* performed a retrospective analysis of 374 patients who had undergone thyroidectomy and parathyroidectomy following scintigraphy. They recorded a false-positive rate of up to 22% in patients with benign thyroid disease and up to 45% with malignant thyroid disease. While it should be noted that Onkendi *et al* used a slightly less common dual isotope technique (radioactive iodine and sestamibi subtraction method), these false-positive rates are, nevertheless, substantial. Indeed, they went on to characterise a dual isotope phenotype for identifying thyroid carcinoma using scintigraphy.⁷

False positives due to thyroid nodules are of particular interest given the increasingly acknowledged association between primary hyperparathyroidism and thyroid pathology, independent of familial syndromes or previous radiation exposure. Rates of association up to 75% have been quoted in the literature.⁷

Figure 2 Ultrasound scan showing hypoechoic nodule within the left inferior pole.

Specifically, with regard to malignancy, quoted figures vary but are often in the range of 2–6%.⁸ Whether these malignancy rates are sufficient to necessitate routine preoperative surveillance of the thyroid before parathyroidectomy for primary hyperparathyroidism is debated. However, given the aforementioned false-positive rates, it is clear that care is needed when interpreting the results of preoperative sestamibi scans in this patient group.

Various methods have been suggested to reduce the likelihood of false-positive results, including use of oblique views on sestamibi scintigraphy, single-photon emission CT or the concurrent use of ultrasound, the latter of which is recommended by the British Association of Endocrine and Thyroid Surgeons. Where results are ambiguous, it seems logical that further testings be undertaken. Despite this, many surgeons advocate use of sestamibi scintigraphy alone for preoperative localisation, as is often the case in the USA.⁷ As was shown in this case study, even where ultrasonography is used, sestamibi results suggestive of the location of a parathyroid adenoma can bias the interpretation of potentially ambiguous ultrasonography. Here, use of fine-needle aspiration to sample apparent intrathyroidal parathyroid tissue may have aided in correct preoperative diagnosis.

The current trend towards minimally invasive parathyroidectomy, in addition to producing greater reliance on localisation studies, affords less opportunity to the surgeons to inspect the thyroid during surgery. By their nature, false-positive scan results are often discovered intraoperatively. In the case of minimally invasive procedures, conversion to bilateral cervical exploration may be necessary. Failure to do so may result in missed parathyroid adenomas and, as in the case here, thyroid nodules. Awareness of the possibility of thyroid nodules producing false positives is, therefore, important in influencing the decision to convert to an open, bilateral explorative procedure.

Further intraoperative dilemmas are encountered following inspection and palpation of the thyroid, where the sestamibi scan has been falsely positive. If a thyroid nodule is evident, decisions must be made regarding its removal. If a thyroid nodule is not evident, more difficult decisions regarding thyroid sampling must be made. In either case, appropriate consideration of consent and the ethical implications of action and inaction in individual cases should be undertaken. It is, therefore, important that the operating surgeon is aware of the possibility of false-positive sestamibi scans and of the potential sequelae of the different available surgical options.

The case reported here highlights the long-term danger of false-positive sestamibi scans. Where false-positive results are due to malignant thyroid nodules, it is likely that further surgery may later be considered. Completion thyroidectomy and neck dissection in patients who have already undergone parathyroidectomy (and possible nodulectomy/thyroid lobectomy) carry increased risk of morbidity including damage to the recurrent laryngeal nerves and remaining parathyroid glands. In this case, postoperative fibrotic change was so significant that

the risk of morbidity outweighed the benefits of proceeding with completion thyroidectomy. Given the higher rate of false positives seen in malignant thyroid disease, as shown by Onkendi *et al*, some may argue that thyroid lobectomy as a minimum procedure is indicated in these cases.

In conclusion, it is important that surgeons are aware of the possibility of false-positive sestamibi scans due to malignant thyroid nodules. Such awareness may influence their interpretation of preoperative localisation scans and intraoperative management of false-positive cases, with consequent impact on patient outcomes.

Learning points

- ▶ Sestamibi-avid malignant thyroid nodules can produce false-positive parathyroid localisation scans.
- ▶ Ambiguous preoperative parathyroid localisation results should prompt further investigation with different localisation modalities and consideration of fine-needle aspiration cytology.
- ▶ Intraoperative decision-making in the context of false-positive sestamibi results should include consideration of malignant thyroid nodules, in addition to the potential sequelae of the surgical strategies available.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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