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EFFICACY OF DUAL PHASE PLANNER ^{99M}TC-SESTAMIBI PARATHYROID SCAN IN IDENTIFYINGPARATHYROID ADENOMA AS A CAUSE OF HYPERPARATHYROIDISM; A SINGLE CENTER EXPERIENCE

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ABSTRACT

AIM: The aim of this study was to review the experience of the Nuclear Medicine Department at Royal Medical Services (RMS) in assessing the efficacy of ^{99m}Tc-sestamibi scans in identifying parathyroid adenoma as a cause of hyperparathyroidism. **PATIENTS AND METHODS:** This is a retrospective study for 120 patients who underwent both ^{99m}Tc-sestamibi parathyroid scans followed by elective parathyroidectomy from 2017–2020 at King Hussein Medical Centre (KHMC). Visual analysis of early (10–20 minutes) and delayed (2–3 hours) images was done, and any focally progressive tracer accumulation on the early and delayed images was reported as positive for parathyroid adenoma. Histopathology reports were reviewed for final diagnosis. **RESULTS:** One hundred and twenty patients underwent sestamibi scans during the period of the study with a mean age of 48 years (range 27–82 years). One hundred and nine had an elective parathyroidectomy (102 patients with positive sestamibi scan findings and 7 patients with a negative sestamibi scan), while 99 patients had a parathyroid adenoma in postoperative histopathology reports, with 96.9% sensitivity, 71.4% specificity, 94% positive predictive value, 83.3% negative predictive value, and 92.5% accuracy. **CONCLUSION:** Dual-phase planner ^{99m}Tc-sestamibi parathyroid scintigraphy has proved its efficiency as a trustable diagnostic tool in identifying parathyroid adenoma as a cause of hyperparathyroidism, with highly concordant results found for surgery at KHMC.

KEYWORDS: Hyperparathyroidism, ^{99m}Tc-sestamibi, Parathyroid adenoma, Dual-phase imaging.

INTRODUCTION

Overproduction of parathyroid hormone (PTH) by the parathyroid glands is the main cause of hyperparathyroidism. Parathyroid adenoma, hyperplasia or parathyroid carcinoma are the main causes of primary hyperparathyroidism, which is characterised by high serum calcium and PTH levels and can lead to multiple complications including skeletal, cardiac, vascular, gastrointestinal, renal and nervous system complications.[1] A solitary parathyroid adenoma is the main cause of primary hyperparathyroidism in almost 80% of cases, while surgery (parathyroidectomy) is still the only curative treatment for symptomatic patients. "The traditional surgical approach was bilateral neck exploration with high cure rates of >95%"[2], but minimally invasive parathyroidectomy is currently preferred due to improvements in imaging and the availability of intraoperative PTH monitoring, which is also associated with high cure rates.[2, 3] Since an accurate preoperative localisation is necessary, a non-invasive imaging modality was a crucial issue. ^{99m}Technetium sestamibi parathyroid scintigraphy has an increasing role in assessing patients with primary hyperparathyroidism and is the imaging modality of choice for parathyroid adenoma localisation prior to surgery which is superior to US, CT and MRI.[4] However, the ^{99m}Tc sestamibi tracer is not specific for parathyroid tissue and is taken up by adjacent thyroid tissue. The problem of this non-specificity can be solved by using either a dual tracer or single tracer dual phase method which was first described and reported by O'Doherty et al. in 1992[5] and is the imaging protocol which is currently in use in our centre.

This implies the need to acquire planar images in the early phase (10–20 minutes) and delayed phase (2–3 hours), where there will be focally progressive tracer accumulation within the hyperfunctioning parathyroid tissue and washing out from adjacent thyroid tissue revealing thesite of parathyroid adenoma.

This protocol is still used at our Nuclear Medicine Centre/Royal Medical Services and the purpose of this study is to review our experience in assessing the efficacy of dual phase ^{99m}Tc- sestamibi parathyroid scintigraphy in identifying parathyroid adenoma as a cause of hyperparathyroidism and proper pre-surgical localisation.

PATIENTS AND METHODS

We conducted a retrospective study with a total of 120 patients who underwent both ^{99m}Tc- sestamibi parathyroid scan followed by elective parathyroidectomy at King Hussein Medical Hospital (KHMH) from 2017–2020. This study was approved by the Jordanian Royal MedicalServices ethics committee.

Dual phase ^{99m}Tc Sestamibi Scintigraphy: (740–925) MBq of ^{99m}Tc sestamibi was injected intravenously to the specified patients. The image acquisitions were performed on a double-head gamma camera equipped with 9.5mm sodium iodide crystal (Symbia; Siemens Medical Solutions).

Early and delayed planar high-count images were performed over the neck and mediastinum 10minutes and 2 hours after injection, respectively. The mediastinum was included in the field to detect ectopic parathyroid tissue; both images were acquired for 10 minutes, in a 128x128 matrix, with a 20% window centred on the 140 keV photopeak using a high-resolution parallel hole collimator.

Images were interpreted by a board-certified nuclear medicine physician. The scan was considered positive when there is a focal area of radiotracer retention in the neck or in the mediastinum and the specific location was also mentioned, whether the left or right side and the upper or lower positions in relation to the thyroid gland. The scan was considered negative when there was no focal radiotracer retention on early or delayed images.

After positive ^{99m}Tc sestamibi scintigraphy for adenoma as a reason for the high PTH levels, patients underwent surgery or were followed-up. In patients who underwent surgery, where the histopathological results of resected specimens were obtained from the patient's medical records,a comparison was done.

A true positive result was considered if the sestamibi scan findings matched the surgical outcome. A false positive result was considered when surgery did not reveal a parathyroid pathology, while scintigraphy was positive. A true negative result was considered when the sestamibi scan was negative and either PTH levels normalised or the surgery did not reveal anyadenoma. A false negative result was considered when an adenoma was found during surgery with negative sestamibi scintigraphy.

Statistical analysis

Categorical data were expressed as frequencies and percentages, while quantitative data wereexpressed as the mean ± SD. The sensitivities, specificities, positive predictive values (PPV), negative predictive values (NPV) and accuracies were calculated using SPSS version 22.

RESULTS

This study included 120 patients, with the majority (90, or 75%) being women and the minority (30, or 25%) being men. The mean age of the study population was 54.8 years, with a range of 27–82 years and a median of 56 years. The mean serum PTH level was 177 pg/mL (range: 49- 3119 pg/mL). Of the 120 99mTc-sestamibi studies, 102 (85%) were positive for a single focus of radiotracer retention, while 18 (15%) were reported as negative. The positive scans identified the adenoma as being in the right superior gland in 6 patients, right inferior gland in 43 patients, left superior gland in 7 patients, left inferior gland in 40 patients and ectopic in the mediastinum in 6 patients. Of the 120 patients, 109 underwent elective parathyroidectomy (102 patients with positive scan findings and 7 patients had a negative sestamibi scan). Reviewing the histopathology reports from these patients revealed that 96 had adenomas (2 had 2 adenomas each), yielding a true positive rate. There were also 6 false positive results, where the sestamibi scan was positive but surgery revealed findings other than a parathyroid adenoma (such as parathyroid carcinoma, hyperplastic thyroid nodule, thymic tissue, Hurthle cell thyroid cancer, or multiple endocrine neoplasia type 1). Of the 18 patients with negative sestamibi scans, 7 eventually had surgery, with 3 being found to have parathyroid adenomas (false negatives) and the remaining 11 patients being true negatives. The sestamibi scan had a sensitivity of 96.9%, specificity of 71.4%, positive predictive value of 94%, negative predictive value of 83.3% and accuracy of 92.5%.

DISCUSSION

Detecting hyperfunctioning parathyroid tissue can be challenging and it was once believed that the only reliable method for locating it was to have an experienced parathyroid surgeon explore the neck region.[6] However, it is now known that most patients with primary hyperparathyroidism (PHPT) have a single parathyroid adenoma[7, 8], making minimally invasive parathyroidectomy (MIP) a preferred option. MIP involves a targeted approach to the pathologic parathyroid gland and has a lower risk of complications, shorter operation time, faster recovery and more favourable cosmetic results compared to conventional bilateral neck exploration.[8-10] Preoperative localisation is an important part of MIP, as it helps the surgeon gain direct access to the abnormal gland. In cases of persistent or recurrent disease where re- operation is planned, positive preoperative imaging is also essential for planning the re-operative parathyroidectomy, as the abnormal glands may be in ectopic locations.[3, 11]

In 1989, Coakley et al. first described the use of ^{99m}Tc-sestamibi scintigraphy as a means of detecting parathyroid lesions.[12] Today, it is the gold standard radiotracer for this purpose.[3] ^{99m}Tc-sestamibi is a lipophilic cationic radiotracer that accumulates in tissues with high levels of mitochondria, such as adenomatous or hyperplastic parathyroid tissue, due to the large number of mitochondria in oxyphil cells. Its clearance is slower in parathyroid tissue compared to thyroid tissue due to the lower levels of P-glycoprotein expression[13], a transmembrane protein that acts as an energy-dependent influx and efflux pump, which is also involved in the transport of ^{99m}Tc-sestamibi across the cell membrane.[13]

Sestamibi scintigraphy is a widely available and relatively inexpensive method for imaging the parathyroid glands. It has a wide field of view, allowing for the detection of ectopic glands.[14] However, it may produce false-positive results due to the presence of thyroid nodules, inflammatory thyroiditis, or lymphadenopathy[15, 16] and false-negative results may occur in cases of small parathyroid adenomas (weighing less than 600–800 mg).[17] The sensitivity of ^{99m}Tc-sestamibi scans has been reported to range from 60–90%, with variations depending on study protocols and disease characteristics.[4, 18] In patients with parathyroid hyperplasia or multiple adenomas, sensitivity may be as low as 30–45%.[19]

CONCLUSION

In conclusion, this study found that ^{99m}Tc-sestamibi parathyroid scintigraphy is an effective diagnostic tool in identifying parathyroid adenoma as the cause of hyperparathyroidism, withhigh concordance between the scan results and surgical findings with an excellent positive predictive value and acceptable negative predictive value.

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