Comparison of Meta-Iodo-Benzyl-Guanidine scintigraphy and Computed Tomography for localization of phaeochromocytoma
Abstract

Objective: To compare the results of CT scanning and MIBG scintigraphy in the localization of phaeochromocytoma.
Design: Retrospective study.
Setting: University Hospital.
Results: In 21 out of 24 patients MIBG scintigraphy provided accurate localization. In 16 out of 18 patients who underwent CT scanning a correct localization was obtained.
Conclusion: Sensitivity of the two methods is about equal. In patients with non-familial phaeochromocytoma it is advisable to use MIBG scintigraphy as initial localization technique, combined with CT directed by scintigraphic results, if more anatomical information is needed.

INTRODUCTION

Since the first successful operation for phaeochromocytoma in 1926 by César Roux, complete surgical extirpation of all catecholamine-producing tumour tissue is still the only curative treatment\(^1\). Phaeochromocytoma is diagnosed on biochemical grounds by measurement of urinary catecholamines and catecholamine metabolites and plasma catecholamines. After the diagnosis has been confirmed, localization of the tumour is of utmost importance for adequate resection. Angiography with or without venous sampling is technically difficult and can provoke hypertensive crisis in these patients \(^3,4\). These techniques have therefore been abandoned and replaced by less invasive localization modalities. Ultrasonography is a non-invasive technique but its sensitivity is low in small adrenal lesions. Moreover, ultrasonography has a high inter-observer bias \(^3,5\). At present (1991), Computed Tomography (CT) and \(^123\)I meta-iodo-benzyl-guanidine (MIBG) scintigraphy are the methods of choice for localizing phaeochromocytoma \(^2,8-12\). CT can detect 85% to 95% of intra-adrenal lesions larger than 1 centimetre. Sensitivity decreases in smaller lesions or in case of extra-adrenal phaeochromocytoma \(^3,4\). Meta-iodo-benzyl-guanidine has a high affinity for chromafin granula of the adrenal medulla and sympathetic tissue. Tumours derived from these tissues, like phaeochromocytoma, neuroblastoma and paraganglioma, have a high up-take of this tracer, thereby using the functional characteristics of these tumours for their localization \(^7\). Sensitivity of \(^131\)I MIBG scintigraphy for detecting phaeochromocytoma is reported to be high (87%-91%). At present, \(^123\)I is the preferred isotope labeling compared to \(^131\)I because of the lower radiation load with \(^123\)I, which enables to use a higher dose. This study compares the advantages and disadvantages of MIBG scintigraphy and Computed Tomography for the localization of phaeochromocytoma.

PATIENTS AND METHODS

Between 1983 and 1990, MIBG scintigraphy was performed in all 24 patients with biochemically proven phaeochromocytoma at the University Hospital Groningen, The Netherlands.

The patient group comprised 13 women and 11 men with a mean age of 43 years (range 18-73). In 8 patients phaeochromocytoma was associated with the multiple endocrine neoplasia (MEN) type 2 syndrome. In all patients the diagnosis phaeochromocytoma was confirmed by detection of elevated levels of urinary catecholamines (metanephrines and normetanephrines) (Figure 1). Two patients had previous surgery for phaeochromocytoma; in both patients a unilateral adrenalectomy had been performed for phaeochromocytoma. The procedure for MIBG scintigraphy and CT is described in detail elsewhere (Chapter 4). All patients underwent MIBG scintigraphy
(before 1985 with $^{131}$I in 9 patients, from 1985 onwards with $^{123}$I in 15 patients). In 18 patients preoperative CT scans were obtained, directed by the scintigraphic outcome. Thus, in 15 patients only the adrenal glands were visualized by CT whereas in 3 patients with extra-adrenal MIBG uptake a CT scan of the entire abdomen was obtained. All 24 patients underwent surgery; in 21 patients adrenalectomy was performed (14 unilateral, 7 bilateral), in two patients extra-adrenal localized phaeochromocytoma was removed and in one patient only biopsy of the tumour was feasible because of aortic involvement. All patients underwent laparotomy and in all the diagnosis phaeochromocytoma was confirmed by histopathological examination. Three patients had malignant phaeochromocytoma as proven by metastases. In all patients urinary catecholamine metabolites were measured post-operatively (Figure 1). In three patients catecholamine excess persisted, and residual phaeochromocytoma was suspected. Re-exploration was undertaken in all three after MIBG scintigraphy and Computed Tomography. In two patients incompletely resected phaeochromocytoma was found and removed. The third patient showed no postoperative uptake of MIBG nor a lesion at CT. In this patient the contralateral adrenal gland was removed. Histological examination showed no pathology in this gland. All MIBG and CT studies were separately evaluated by an expert nuclear medicine specialist and a radiologist without prior knowledge of the histopathological diagnosis.

**Figure 1A.** Logarithmic reflection of median values (nmol/mol creat.) of metanephrines in urine samples of 24 patients with phaeochromocytoma. Normal value (N) = < 70 nmol/mol creat.
RESULTS

Scintigraphy was true positive in 21 of 24 patients. In two out of three patients with false negative scintigraphic results (both patients with MEN type 2), only unilateral uptake of the tracer was seen. Computed Tomography showed in one of these patients a small contra-lateral lesion. The third patient had a unilateral phaeochromocytoma with a diameter of 2.5 centimetre that was detected only by CT. In 16 patients CT was correctly positive. In two patients, CT scanning was not able to detect intra-adrenal lesions smaller than 1 centimetre. Both lesions were detected by MIBG scintigraphy. Table 1 compares the results of MIBG scintigraphy and CT in 18 patients who underwent both localization techniques.

DISCUSSION

Approximately 90% of phaeochromocytomas are located intra-adrenal. These tumours also occur in 10% of cases associated with a number of familial neurocrestopathic syndromes, including the MEN type 2 syndrome. Ten percent of phaeochromocytomas are located extra-adrenal or are malignant. At present, there is no consensus about the optimal pre-operative localization strategy. In the present patient group, MIBG scintigraphy localized the tumour correctly in 85% of patients. This percentage

\[ \text{Figure 1b. Logarithmic reflection of median values (nmol/mol creat.) of normetanephrines in urine samples of 24 patients with phaeochromocytoma.} \]

\[ \text{Normal value (N) = } < 260 \text{ nmol/mol creat.} \]
is in accordance with other reports. The cause of the three false negative results is not clear. A possible explanation is the wide range in uptake of MIBG in phaeochromocytoma. This uptake correlates with the content of neuro-secretory granula, and is not related to plasma levels of catecholamines. Large tumours with an intensive uptake of the tracer (as seen in solitary phaeochromocytoma) offer an unambiguous scintigraphic appearance. Scintigraphic differentiation between small phaeochromocytoma and normal or hyperplastic adrenal glands is often difficult as seen in this series. Mean tumour diameter in correctly positive scintigraphic results was 6 cm. Tumour localization was correctly detected in 90% of patients with CT scanning. These data match those of previously reported series (sensitivity 85% - 95%) CT was not able to detect an adrenal lesion smaller than 1 cm in MEN type 2 patients. These familial tumours differ from their solitary counterpart by development out of hyperplasia and moreover their presentation is different. The impact of these differences on localization strategy in MEN type 2 patients will be further discussed in chapter 4.

In conclusion, MIBG scintigraphy and CT both yield a high accuracy for the detection of phaeochromocytoma. Routine usage of both modalities in all patients is not warranted. In patients with non-familial phaeochromocytoma it is advisable to use MIBG scintigraphy as initial localization technique because of the possible extra-adrenal location of these tumours. CT can be directed by the scintigraphic results, if more anatomical information is needed. In familial phaeochromocytoma, MIBG is the most sensitive method for detecting hyperfunctioning adrenal tissue, but scintigraphy can not differentiate between hyperplasia and small phaeochromocytoma. Therefore, localization strategy in these patients may be different from preoperative localization in sporadic phaeochromocytomas.

<table>
<thead>
<tr>
<th>Tumour and localization</th>
<th>MIBG CP</th>
<th>MIBG FN</th>
<th>CT CP</th>
<th>CT FN</th>
</tr>
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<tr>
<td>Benign</td>
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<tr>
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<td>9</td>
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<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Extra-adrenal</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Familial (MEN 2)</td>
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<tr>
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<td>1</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>2</td>
<td>20</td>
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</tr>
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</table>

CP= Correct Positive, FN =False Negative
MIBG scintigraphy is the technique of choice for localization of post-operative residual tumour, because these tumour deposits are often small and the anatomical relations have been disturbed by previous surgery\textsuperscript{11}.

\textbf{Addendum}

In 1991 Magnetic Resonance Imaging was not yet widely available and the results of MRI for detecting phaeochromocytoma therefore were not included in this study. At present, Magnetic Resonance Imaging (MRI) can be regarded as being preferable over computed tomography for detection of adrenal lesions. MRI has a high sensitivity for detecting adrenal lesions due its multiplanar scan technique \textsuperscript{17,18}. Sensitivity and specificity of MRI equals the results obtained by computed tomography in detecting adrenal lesions \textsuperscript{6,7}. 
REFERENCES


