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Potential diagnostic value of ^{131}I-MIBG myocardial scintigraphy in discrimination between Alzheimer disease and dementia with Lewy bodies

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ABSTRACT

Objectives: Clinical difficulty to discriminate between the Alzheimer disease (AD) and dementia with Lewy bodies (DLB) has led researchers to focus on highly sensitive functional imaging modalities. The aim of the present study was to assess ^{131}I-MIBG cardiac imaging to distinguish between AD and DLB.

Patients and methods: Seventeen patients who were known cases of dementia underwent ^{131}I-MIBG myocardial scintigraphy to differentiate AD from DLB. Planar and ^{131}I-MIBG SPECT were obtained 2 h after the injection of 1 mCi ^{131}I-MIBG on a dual head gamma camera. The visual assessment of the heart uptake compared with lungs and the quantification based on the heart to mediastinal ratio (HMR) were done. The cardiac receiver operating characteristic (ROC) curve was designed for the optimal HMR cut-off values to predict the diagnoses of the patients. The diagnoses were clinically confirmed during the follow up of 14 ± 8.2 months.

Results: Out of 17 patients (13 males; 76.5%), 10 patients had AD (7 males; 70%) and 7 patients had DLB (6 males; 85%). The pooled HMR was 1.74 ± 0.33 in the study population; with 1.95 ± 0.22 in the AD group and 1.43 ± 0.20 in the DLB group to demonstrate significantly different HMR scores between patients with AD and DLB (p value = 0.001). The visual interpretation was positive in 10 patients (accuracy of 88.2%). The shortest distance on the ROC curve to the optimal value corresponding to HMR = 1.57 identified 10 patients with a high HMR (positive cardiac uptake) and 7 patients with a low HMR (negative cardiac uptake), the accuracy calculated at 88.2%.

Conclusion: ^{131}I-MIBG myocardial scintigraphy is a potential alternative diagnostic modality for discrimination between AD and DLB when ^{123}I is not available.

1. Introduction

Alzheimer's disease (AD) has become the most common senile degenerative dementia in recent times, while dementia with Lewy bodies (DLB) has been acknowledged as the second most common etiology. Because of the significant overlapping symptoms in most patients, differentiation between these two types of dementia is difficult on the basis of clinical criteria. Decisive discrimination plays an important role to apply an appropriate pharmacological management [1–3]. Few imaging and laboratory assessments may assist the clinicians with specific indications. Nevertheless, in particular conditions including those cases with intractable or progressive disease without remarkable response to treatment further examinations may become necessary.

The metaiodobenzylguanidine (MIBG) enters the sympathetic synaptic cleft and reuptake into the presynaptic neuron via different reuptake mechanisms and accumulates within the neurons very similar to norepinephrine. Labeled ^{131}I or ^{123}I MIBG myocardial scintigraphy denotes cardiac sympathetic innervations, which is a diagnostic modality of suggestive features of consensus diagnostic criteria for dementia with Lewy bodies [1,2,4–6]. It is confirmed that in the Parkinson disease the reuptake of MIBG in sympathetic neurons of the heart is defective [4] and the cardiac uptake in these patients is decreased [7,4]. Cardiac uptake in the patients with DLB is also decreased possibly with the same mechanism [8] but the MIBG cardiac uptake in AD assumed to remain unchanged. The diagnostic value of ^{123}I MIBG scan is rather documented previously [12,13] but the accuracy and diagnostic performance of the ^{131}I MIBG scan is not yet verified. In Iran (6) and many other areas with limited resources [9] where the cyclotrons are

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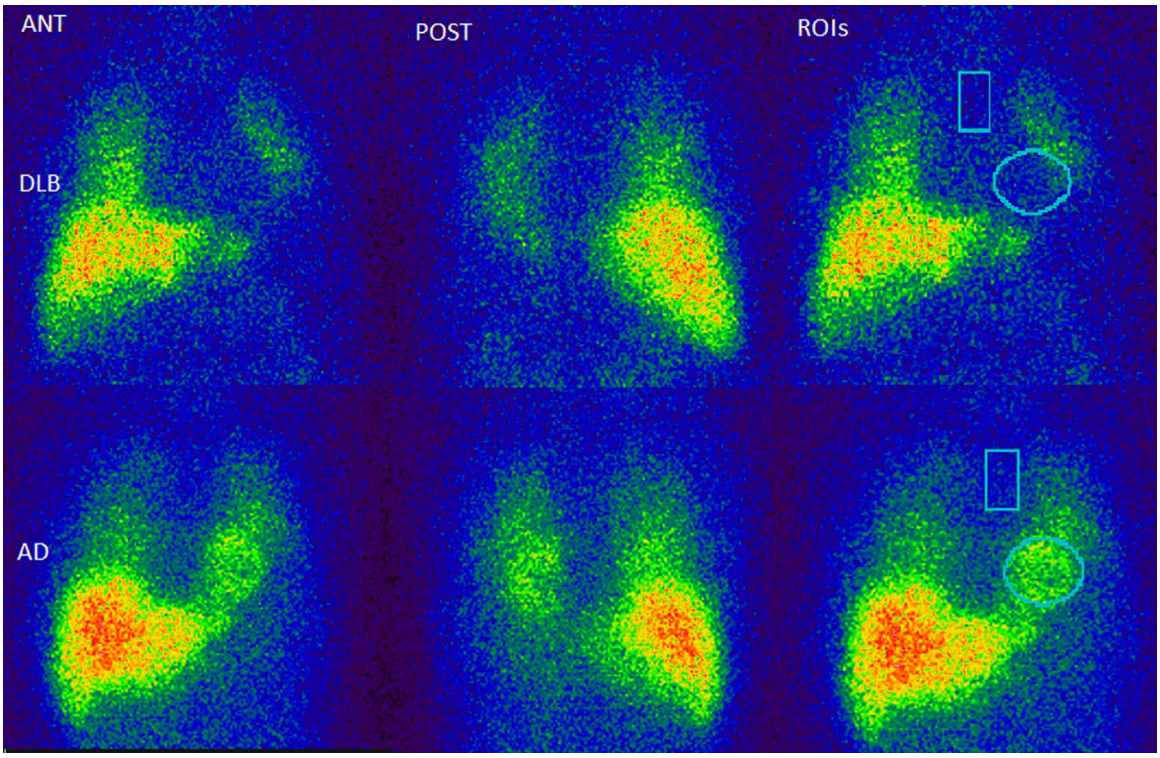

Fig. 1. The cardiac ^{131}I MIBG scintigraphy in two patients with low and normal cardiac uptake; DLB, dementia of Lewy body; AD, Alzheimer disease; ANT, anterior; POST, posterior; and ROI, region of interests.

unavailable or cyclotrons are set to produce more clinically demanded isotopes [9,10], ^{123}I is not available routinely and the use of ^{131}I −MIBG with a long half-life is practical and logistically convenient [10,9,11]. In the current study we assessed the diagnostic accuracy of cardiac ^{131}I MIBG scintigraphy.

2. Material and methods

2.1. Patients

Seventeen patients diagnosed by the clinical criteria (i.e. Dubois Diagnostic Criteria for AD and Consensus Diagnostic Criteria for DLB) were enrolled in this study from December 2013 until October 2015 in the Department of Neurology of Imam Khomeini Hospital Complex (IKHC), Tehran University of Medical Sciences, Tehran, Iran. Routine clinical examination and blood tests were performed. By meeting the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition* (DSM-V) criteria, each of the patients was confirmed as a case of dementia. Patients underwent MIBG myocardial scintigraphy at the Department of Nuclear Medicine, IKHC, Tehran, Iran. The exclusion criteria were malignancy, thyroid disease, head injury, cardiovascular disease, pregnancy, breastfeeding, cerebrovascular disease, diabetes, and taking medications known to affect MIBG concentrations [14–18]. This study was approved by the Ethics Committee of Tehran University of Medical Sciences. Informed consents were obtained from all included patients prior to entry and following a detailed explanation of the study protocol.

2.2. Imaging and quantification

After the blockage of thyroid, patients were treated with injection of 1 mCi ^{131}I-MIBG (Pars Isotope Co., Tehran, Iran) and subsequently scanned 2 h later. A dual head gamma camera (Mediso, Budapest, Hungary) with mounted high energy collimators performed the entire imaging. In the thoracic area, both planar and SPECT ^{131}I MIBG images were obtained with the patient lying in the supine position [5,7]. Planar images were taken for 12 min in the anterior and posterior views at the nearest position of the camera head to the chest wall with 128 × 128 matrix size. The SPECT images were recorded in the 64 × 64 matrix size at every 3°-intervals with 45-s projection time. The automatic body contour least distance mode was employed.

The normal heart uptake was reported for the visual interpretation of whether uptake in the heart was higher than the lungs in planar images or uptake of the heart at the transverse sections of SPECT images was detectable. For quantitative analysis, two regions of interest (ROI) were generated manually over the heart and mediastinum and the heart to mediastinum ratio (HMR) was calculated by the ratio of count per pixel in each of the two ROIs. The gold standard for the diagnosis was the clinical diagnosis over the time by the neurologist. This diagnosis was made at the time of final analysis based on inpatient and outpatient files according to the clinical course and response to treatment 14 months (range: 3–29) after scan.

2.3. Data analysis

The receiver operating characteristic (ROC) curve was designed for the HMR to predict the diagnoses of the patients. The shortest distance on the ROC curve was computed as the square root of (1- sensitivity) ^{2}+ (1-specificity) ^{2}. The accuracy related indices were estimated for visual and quantitative interpretations. The optimal HMR cutoff for discrimination between the AD and DLB diagnoses was obtained by the shortest distance on the ROC curve [7,5]. One expert nuclear medicine physician (M.A) reviewed all imaging records without knowing the suggestive diagnoses. Analyses were performed in the IBM SPSS statistics 19 and the curve of shortest distance on the ROC curve was drawn in Microsoft Office Excel 2007 in order to detect optimal cutoff point. One of the figures is plotted with SigmaPlot.12.3. HMR values were studied for normal distribution with the Kolmogorov Smirnov (K-S) test. Analysis of the correlation and pattern of distribution was run by the Pearson coefficients of correlation, independent *t* test, and the