INITIAL EXPERIENCE WITH I^{131} MIBG IMAGING IN PATIENTS WITH NEUROBLASTOMA

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SUMMARY

Metaiodobenzyl guanidine was synthesized from metaiodobenzyl amine hydrochloride and cyanamide at different temperatures. The yield was found to be 60-70%. The product was characterized by UV, IR, and NMR spectroscopic techniques. The characterized product was labelled with Iodine-131 and labelling efficiency was determined by radio-TLC technique. Labelling yield upto 95% was achieved. Five patients with biopsy proven neuroblastoma were imaged. In two patients intrabdominal primary tumor was successfully localized and a thoracic metastatic site was detected in one of them. MIBG scanning was normal in remaining three patients.

INTRODUCTION

Radio-iodinated metaiodobenzyl guanidine is a relatively new radiopharmaceutical that has gained an accepted role in the localization of neural crest tumors like pheochromocytomas, neuroblastomas, paragangliomas and carcinoid tumors.[1,4] MIBG is a physiological analogue of guanethidine and noradrenaline. I^{131} MIBG is taken up and retained in the tumor cells by the catecholamine uptake mechanism and as a result enables scintigraphic imaging.[1,2] Neural crest tumors may be functionally active when still small in size and thereby elude methods of localization that are based on anatomical changes. Moreover they may be multiple and extra-abdominal extending from the brain to the floor of pelvis. When present at sites other than the usual, it will be impossible to determine the nature of these tumor masses without biopsy. As such I^{131} MIBG whole body imaging provides a safe, non-invasive, sensitive and specific method for localization of neural crest tumors and metastatic sites.

MATERIAL AND METHODS

Synthesis and Labelling of I^{131} MIBG

All the chemicals used in this work were 98-99% pure from Aldrich and E.Merk. The I^{131} was obtained from Amersham International U.K as an aqueous solution of NaI^{131}. Radioactivity was quantified with Picker isotope calibrator N0.63507-2. The MIBG sulphate was prepared by Wieland method.[5] The product was characterized by UV, IR, NMR spectroscopic methods. Radioiodination of the characterized product was done with I^{131} using Cu^{++} assisted exchange reaction.[6]

Sympathoadrenal Imaging With I^{131} MIBG

Five patients of neuroblastoma have been included in this study all of which were diagnosed on biopsy and other investigations (Table 1).

Patients thyroid was blocked by lugol's iodine one day prior to imaging and continued for 8 days post injection. Patient was also instructed to stop all

medication prior to imaging which are known to interfere with I^{-131} MIBG scanning.[7]

1 mCi of radioiodinated MIBG was injected and serial imaging was done at 24, 48, 72 hrs. The whole body was scanned in multiple overlapping anterior and posterior views. Each view was acquired for 110K counts. Patient was asked to empty his bladder before each imaging.

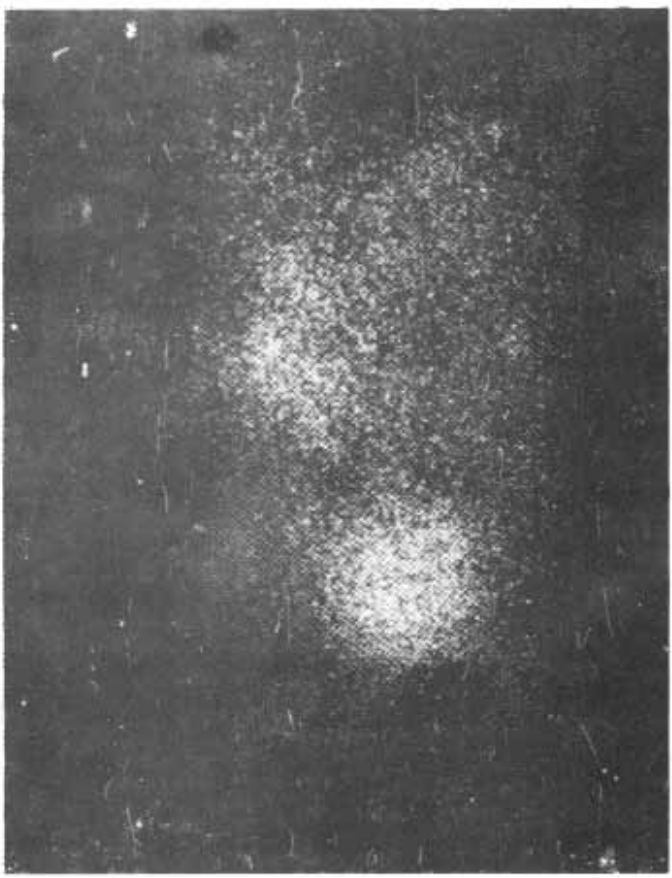
RESULTS

The yield of MIBG was found to be 67-70%, and was comparable with reported literature values.[5]

The results of I^{131} MIBG imaging and other investigations are shown in Table 1.

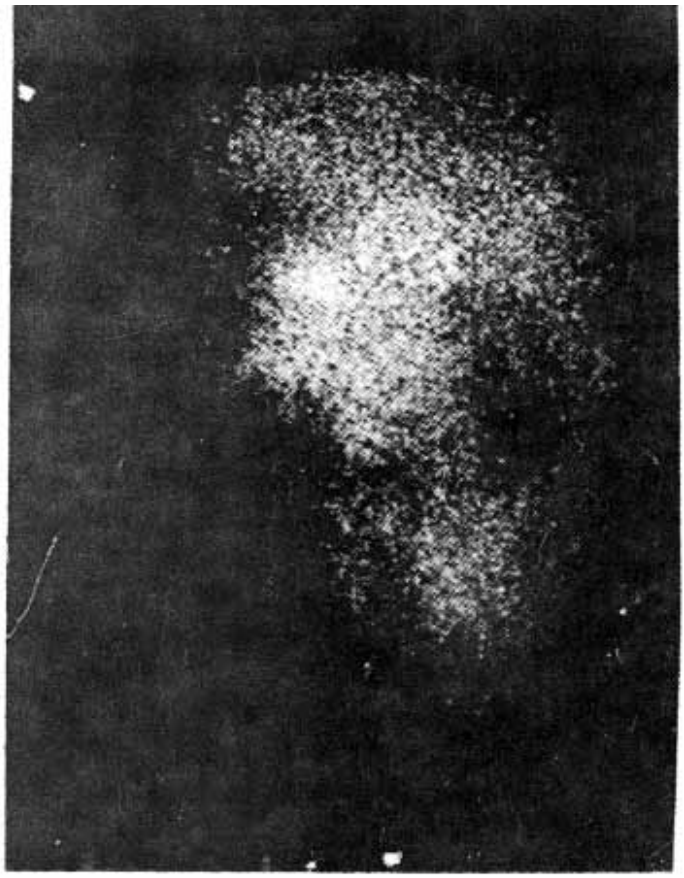
As an illustration we have included representative scans (Fig.1) of a patient aged 5 years (patient No. 1, Table 1).

Images taken at 24 hours post injection show normal distribution of MIBG in liver and bladder. Only a faint image of the tumor is seen at this stage (Fig.1a). Images taken at 72 hrs show large tumor mass in the left side of abdomen crossing the midline, Stage III tumor (Fig.1b).



(a) 24 hrs post injection scan

Fig. 1. I^{131} MIBG scans of patient with neuroblastoma.



(b) 72 hrs post injection scan

DISCUSSION

Neuroblastoma is among the common tumors of childhood. Other imaging modalities may be able to localize the tumor; however, only I^{131} MIBG imaging allows non-invasive exploration to detect the primary tumor and its metastases. I^{131} MIBG imaging is also a specific technique as it concentrates preferentially in tumors of neural crest origin.

In patients with neuroblastoma we were able to localize primary tumor mass in two cases and a metastatic site in lower chest in one of them. The thoracic metastatic site was not localized by other techniques.

I^{131} MIBG imaging was unsuccessful in localizing the primary site detected on ultrasonography in one case. In remaining two cases where I^{131} MIBG imaging was negative primary tumor had already been removed. In one of these two cases skeletal metastases seen on Tc^{99m} MDP bone scan were not detected on I^{131} MIBG imaging.

False negative results have been reported in all series published so far.[1-4] The reason for this is not very clear. The

Table - 1

SUMMARY OF THE RESULTS OF MIBG SCANS AND OTHER INVESTIGATIONS.

SNo	AGE	SEX	DIAGNOSIS	MIBG SCAN	SITE SEEN ON SCAN	OTHER INVESTIGATIONS
1	5yrs	F	NEUROBLASTOMA (BIOPSY)	+ive	LARGE TUMOR MASS IN ABDOMEN CROSSING MIDLINE (STAGE III)	U/S: Echodense mass of irregular shape measuring 54*78 mm adjacent to upper pole of left kidney. IVU: Lft. kidney and upper ureter displace laterally soft tissue mass which is not obliterating the psoas shadow. Enlarged lymph nodes can't be excluded. VMA: NORMAL.
2	8yrs	F	GANGLIONEUROMA (BIOPSY)	+ive -ive -ive -ive	1) LARGE TUMOR MASS FILLING THE WHOLE ABDOMEN. 2) RIGHT CHEST ABOVE DIAPHRAM SHOW INTENSE UPTAKE (PROBABLY METS)	U/S: Large tumor mass in abdomen of irregular shape with heterogeneous echoes and degenerative changes. X-RAY CHEST: an opacity obliterating Rt. costophrenic angle. BONE SCAN: normal uptake in skeleton. VMA: NORMAL.
3	10mth	M	NEUROBLASTOMA (BIOPSY)		NORMAL ADRENALS VISUALIZED	U/S: showed a horse shoe shaped kidney with an echogenic solid mass attached to the right upper pole.
4	14yr	F	NEUROBLASTOMA (OPERATED)		NORMAL ADRENALS VISUALIZED	BONE SCAN: showed multiple skeletal metastases in skull, lft. shoulder joint, multiple thoracic and lumber spines, lft. S.I joint and both femoral shafts. VMA: NORMAL
5	2yrs	M	NEUROBLASTOMA (OPERATED)		NORMAL ADRENALS VISUALIZED	U/S: Show residual tumor mass in abdomen. VMA: NORMAL

most probable explanation is the low dose of I^{131} that can be injected because of radiation dosimetric constraints. Replacement of I^{131} MIBG with I^{123} MIBG which has more favorable physical characteristics has provided better results .[8]

However in Pakistan we do not have artificial means of I^{123} production, and its import is not feasible because of its short half life of 13.2 hrs.

As far as skeletal metastases are concerned false negative results have been reported on I^{131} MIBG imaging and a bone scan has been advised in suspected cases.[9] Because of false negative results in all series a combined modality approach has been stressed.[9]

We conclude that in addition to other investigations I^{131} MIBG imaging provides specific information about the primary and secondary sites in neuroblastomas. I^{131} MIBG imaging being non-invasive and a safe technique it can be employed in all suspected cases.

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