CASE REPORT

False-positive radio-iodinated metaiodobenzylguanidine (^{123}I -MIBG) accumulation in a mast cell-infiltrated infantile haemangioma

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ABSTRACT. Radio-iodinated metaiodobenzylguanidine (^{123}I -MIBG) is used for the detection and staging of neuroblastoma, pheochromocytoma and other neuroendocrine tumours in diagnostic nuclear medicine. A specific uptake and storage mechanism provides the basis for imaging with ^{123}I -MIBG. Nevertheless, cases of false-positive ^{123}I -MIBG scintigraphy with accumulation in non-chromaffin tumours have been described. Here, we present a case of a false-positive ^{123}I -MIBG scan in a case of a mast-cell infiltrated infantile haemangioma and discuss the possible uptake mechanism.

Received 12 May 2009
Revised 3 August 2009
Accepted 1 September 2009

DOI: 10.1259/bjr/40750533

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Radio-iodinated metaiodobenzylguanidine (^{123}I -MIBG) has been used for several years for the detection and staging of neuroblastoma, pheochromocytoma and other neuroendocrine tumours. ^{123}I -MIBG is transported across the plasma membrane by the human norepinephrine transporter (NET); a smaller amount enters the cell by passive diffusion. Intracellularly, the vesicular monoamine transporters (VMATs) accumulate ^{123}I -MIBG in catecholamine storing granules [1, 2]. This specific uptake and storage mechanism provides the basis for the imaging of neuroendocrine tumours such as pheochromocytomas and neuroblastomas. Nevertheless, cases of false-positive ^{123}I -MIBG scintigraphy with accumulation in non-chromaffin tumours such as angiomyolipoma [3], adrenocortical carcinoma [4], adrenocortical adenoma [5], juvenile capillary angioma [6] or cavernous haemangioma [7] have been described. Here, we present another case of a false-positive ^{123}I -MIBG scan of a tumour within the adrenal gland area and discuss the possible mechanism.

A 3-month-old girl presented with constipation. Abdominal ultrasound showed a round, strictly delineated, inhomogeneously hypoechogenic structure with a diameter of 18 × 30 mm at the upper renal pole. On the basis of these findings, adrenal haemorrhage was suspected. A follow-up ultrasound examination 6 weeks later confirmed the structure. The inhomogeneous appearance of the structure was increasing; the diameter was unchanged. An MRI examination of the abdomen was performed on a 1.5 T system (Avanto; Siemens, Erlangen,

Germany). The following imaging sequences were applied: coronal T_2 weighted (w) STIR-BLADE [8], repetition time/echo time (TR/TE) 4500/47 ms; transversal T_{2w} BLADE (TR/TE, 5640/118 ms); coronal T_{1w} BLADE (TR/TE, 1280/55 ms); transversal T_{1w} BLADE (TR/TE, 1400/55 ms) and transversal T_{1w} TSE (TR/TE, 510/9.5 ms). On T_{2w} images, the tumour mass proved to be only of moderate hyperintensity. The size was 34 × 22 × 28 mm, located in the area of the right adrenal gland. After application of 1 ml gadoteridol (Prohance; Bracco Diagnostics, Princeton, USA), the tumour showed an intensive contrast media enhancement (Figure 1). A ^{123}I -MIBG scan was obtained, which showed focal tracer uptake in the area of the right adrenal gland (Figure 2), corresponding to the tumour mass in the MRI examination (Figure 3) and suggestive of neuroblastoma. On the basis of the imaging data, neuroblastoma with negative urine vanillylmandelic acid and positive ^{123}I -MIBG scintigraphy was assumed and an open biopsy was performed. During surgery, a highly vascularised tissue was found in the adrenal gland. The histological examination revealed a compact vascular lesion with morphological and immunohistochemical criteria (Figure 4a,b) consistent with infantile haemangioma. Within the tumour, mast cell infiltration, which was positive upon VMAT2 staining, was seen (Figure 4c,d).

Discussion

The high specificity of ^{123}I -MIBG accumulation is useful for the classification of tumours, such as pheochromocytomas, neuroblastomas or carcinoids, in the area of the

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Figure 1. Transversal T_1 weighted BLADE MRI image (repetition time/echo time 1400/55 ms, after injection of 1 ml gadoteridol), showing a tumour mass (red arrow) in the area of the right adrenal gland. See the intensive contrast enhancement of the tumour.

Figure 2. ^{123}I -MIBG scintigraphy (SPECT) in transversal, sagittal and coronal projections. See the intensive accumulation of the radiotracer in the area of the right adrenal gland (blue crosshairs).

Figure 3. Coronal and transversal fusion images obtained after automatic coregistration using the mutual information method of the ^{123}I -MIBG SPECT and the T_1 weighted BLADE MRI data (Esoft; Siemens, Erlangen, Germany). The fused images confirm the almost identical localisation of the radiotracer uptake in the SPECT and the tumour in the MRI examination (red arrows).

Figure 4. Staining. (a) Hemotoxylin (HE) for tumour histology. (b) GLUT1 (brown) for glucose transporters, confirming the diagnosis of infantile haemangioma. (c) VMAT2 (brown) for amine transporters. (d) Giemsa (blue) for mast cells. Magnification throughout $\times 20$.

adrenal glands. Other tumours with ^{123}I -MIBG uptake have been described, including haemangiomas [6, 7].

Mast cells are frequently found in haemangiomas [9]. Several studies showed that the number of mast cells is highest during the involuting phase in haemangioma, lower in the involuted phase and lowest in the proliferating phase. The role of mast cells in the life cycle of haemangiomas is, however, likely to be complex as mast cells can secrete both stimulators of angiogenesis in the proliferative phase and inhibitors in later phases.

The expression of VMAT2 in mast cells has been described before; this protein is known to be an excellent marker for mast cells [10]. ^{123}I -MIBG is a substrate of VMAT2, which is of importance for the uptake and retention of ^{123}I -MIBG in tumours [2], and so the expression of this protein by mast cells may explain the strong ^{123}I -MIBG accumulation within the tumour mass in this case. So, mast cell infiltration of tumours such as haemangiomas must be considered as a reason for ^{123}I -MIBG accumulation.

The presented case is additionally remarkable owing to the combination of ^{123}I -MIBG accumulation in an infantile haemangioma and its localisation within the

area of the adrenal gland, which led to the assumed diagnosis after MRI and ^{123}I -MIBG examination of a neuroblastoma in the typical localisation.

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