Pediatric Neuroblastoma: Application of MIBG Scintigraphy in Diagnosis, Staging, and Follow-up – Analysis of Three Cases

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Abstract

Introduction: *Neuroblastoma is the most common extracranial solid tumor in children, accounting for 8-10% of all pediatric cancers. Accurate diagnosis and management rely on imaging modalities and biological markers such as elevated urinary catecholamines. Among the various imaging techniques, Metaiodobenzylguanidine (MIBG) scintigraphy, often combined with SPECT/CT, provides high specificity for neuroblastoma cells. It is crucial for determining tumor extent, identifying metastatic disease, and monitoring therapeutic response.*

Materials and Methods: *This study presents three clinical cases illustrating the role of MIBG scintigraphy in the diagnosis, staging, and follow-up of pediatric neuroblastoma. The three patients underwent Iodine-131 labeled MIBG scintigraphy, with planar imaging, and in two cases, additional SPECT/CT imaging.*

Results:

Case 1: *A 3-year-old child with a right adrenal mass and diffuse bone marrow metastases, classified as stage IV neuroblastoma.*

Case 2: *An 11-year-old girl with recurrent retroperitoneal neuroblastoma identified during follow-up MIBG scintigraphy.*

Case 3: *An 11-year-old girl with no evidence of disease progression, confirmed by MIBG scintigraphy, indicating complete remission.*

Conclusion: *MIBG scintigraphy is an invaluable tool in the management of neuroblastoma, offering precise tumor localization, accurate staging, and effective monitoring of treatment response. Its integration into clinical practice helps guide therapeutic decisions and improves patient outcomes.*

Keywords: *Neuroblastoma; MIBG Scintigraphy; Pediatric Oncology; Tumor Staging; Metastasis Detection*

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Introduction

Neuroblastoma is the most common extracranial solid malignancy in children, primarily affecting those under the age of five years (1). It originates from neural crest cells, which are precursors of the sympathetic nervous system, and represents 8-10% of all pediatric cancers (2). Despite its relatively low incidence, neuroblastoma accounts for approximately 15% of cancer-related mortality in children (3). The clinical presentation of neuroblastoma is remarkably heterogeneous, ranging from localized disease that may spontaneously regress to highly aggressive forms with widespread metastases (4).

The variability in clinical behavior underscores the importance of accurate diagnosis, staging, and monitoring to tailor appropriate treatment strategies (5). Metaiodobenzylguanidine (MIBG) scintigraphy is an essential imaging modality in this context due to its high specificity for neuroendocrine tissue (6). MIBG is a norepinephrine analog that is actively taken up by neuroblastoma cells, allowing for precise localization of primary tumors and detection of metastatic lesions (7). Furthermore, MIBG scintigraphy plays a critical role in evaluating the extent of

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disease, guiding biopsy, and assessing response to therapy (8). The ability to visualize both primary and metastatic disease in a single examination makes MIBG scintigraphy a cornerstone in the management of neuroblastoma (9).

In addition to diagnosis and staging, MIBG scintigraphy is invaluable in the follow-up of patients to detect recurrence or residual disease after treatment (10). In cases where therapeutic MIBG is administered, diagnostic MIBG scans help evaluate treatment efficacy and plan subsequent interventions (11). Given its clinical utility, MIBG scintigraphy is often combined with other imaging modalities, such as CT and MRI, to enhance diagnostic accuracy (12).

In this study, we analyze three pediatric cases of neuroblastoma to illustrate the multifaceted role of MIBG scintigraphy in diagnosis, staging, and follow-up. Each case highlights specific aspects of how this imaging technique contributes to comprehensive patient management (13).

Materials and Methods

This retrospective analysis was conducted at the Department of Nuclear Medicine, CHU Hassan II, Fez, Morocco. The study included three pediatric patients who were diagnosed with neuroblastoma and underwent MIBG scintigraphy for diagnostic, staging, and follow-up purposes. Due to the unavailability of Iodine-123 (I-123) labeled MIBG in Morocco, all scintigraphic procedures were performed using Iodine-131 (I-131) labeled MIBG (14). Although I-123 MIBG is preferred for diagnostic imaging due to its superior imaging characteristics, including lower radiation dose and higher image resolution, I-131 MIBG remains a valuable alternative in regions where I-123 is not accessible (15).

Patients received an intravenous injection of I-131 MIBG, and imaging was performed at 24, 48, and 72 hours post-injection to allow for optimal tumor uptake and background clearance (16). This multi-timepoint acquisition protocol helps to improve lesion detectability, as delayed imaging can reveal additional sites of disease not visible at earlier time points (17). Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) was performed at 48 hours to provide detailed localization and anatomical correlation (18).

To ensure optimal image quality and patient safety, thyroid blockade was administered using Lugol's iodine prior to the injection of I-131 MIBG to protect the thyroid gland from unnecessary radiation exposure (19). Lugol's iodine effectively reduces thyroid uptake of free radioactive iodine, minimizing the risk of long-term hypothyroidism (20). Additionally, patients were given laxatives to promote bowel clearance and reduce gastrointestinal activity, which can obscure abdominal lesions (21). This preparation is particularly important because delayed gastrointestinal clearance may interfere with the visualization of tumors in the abdominal and pelvic regions (22).

Clinical data, including patient demographics, clinical presentation, and treatment history, were collected from medical records. Biological parameters, such as urinary catecholamines, were also reviewed. Imaging findings from the MIBG scintigraphy were correlated with other imaging modalities, including CT and MRI, to ensure comprehensive evaluation (23). The response to therapy and disease progression were assessed based on follow-up imaging and clinical outcomes (24).

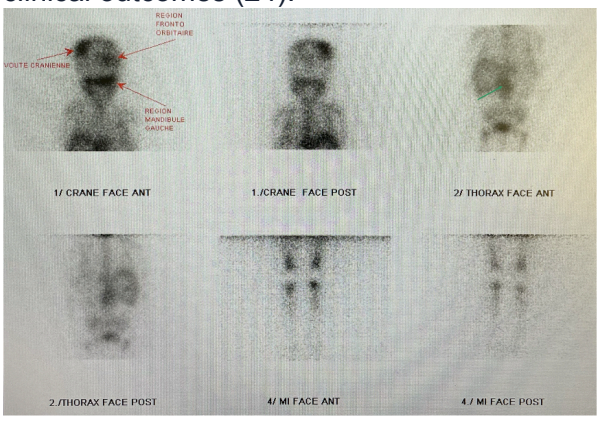

Figure 1: Whole-body static MIBG scintigraphy images showing intense uptake in the right suprarenal primary tumor (indicated by the green arrow) and metastatic bone lesions (indicated by the red arrows).

III. Case Presentations

Case 1

A 3-year-old boy from a non-consanguineous marriage, with no significant medical history, presented with a three-month history of diffuse abdominal pain. One month prior to consultation, the pain worsened and was accompanied by abdominal distension, prompting his parents to seek medical attention. Initial diagnostic workup, including abdominal ultrasound and CT scan, revealed a large retroperitoneal mass arising from the right adrenal region. The mass had regular contours, was heterogeneous in density, and contained areas of necrosis and calcifications. After the injection of contrast

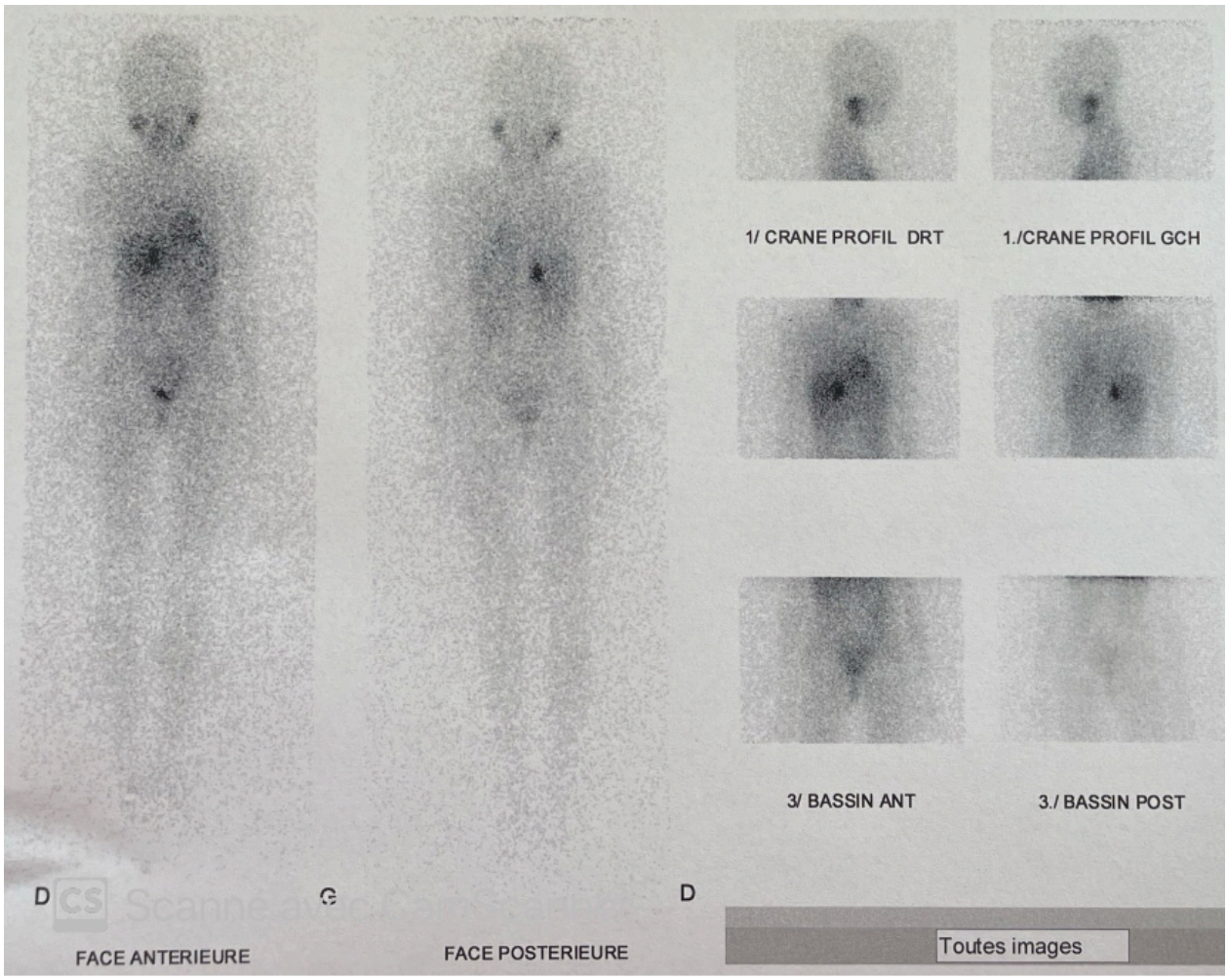

Figure 2: Whole-body MIBG scan and whole-body static MIBG acquisitions in anterior and posterior projections at 24 hours.

agent, a heterogeneous and progressive enhancement was noted. The mass measured 10 x 7.9 x 11 cm (Transverse x Anteroposterior x Height) and displayed the following relationships and extensions: superiorly and anteriorly, it displaced the visceral surface of the liver, with loss of the fat plane at segment I; inferiorly, it displaced the kidney, coming into contact with its upper pole with a regular interface; medially, it compressed the inferior vena cava (IVC), which remained patent, and came into contact with the right diaphragmatic pillar, with loss of the fat plane. The mass remained separate from the aorta and the right paravertebral space. A biopsy of the mass was performed on the same day, and histopathological analysis confirmed the diagnosis of neuroblastoma. The patient was subsequently referred to our Department of Nuclear Medicine, for further staging. A scintigraphy with Iodine-131 labeled MIBG showed intense pathological uptake in the known right suprarenal mass, confirming the primary tumor. Additionally, the examen revealed distant pathological uptakes suggesting bone metastases in the cranial vault, the left fronto-orbital region, and the right mandibular region. These findings were consistent with secondary bone lesions, and a bone biopsy confirmed their metastatic nature. Based on these results, the diagnosis of stage IV neuroblastoma was established. The patient was started on systemic chemotherapy to manage the primary tumor and metastatic disease (Fig.1).

Case 2

An 11-year-old girl was diagnosed at the age of 4 years and 7 months with a retroperitoneal and thoracic neuroblastoma, classified as stage IV due to bone and bone marrow metastases. She was treated

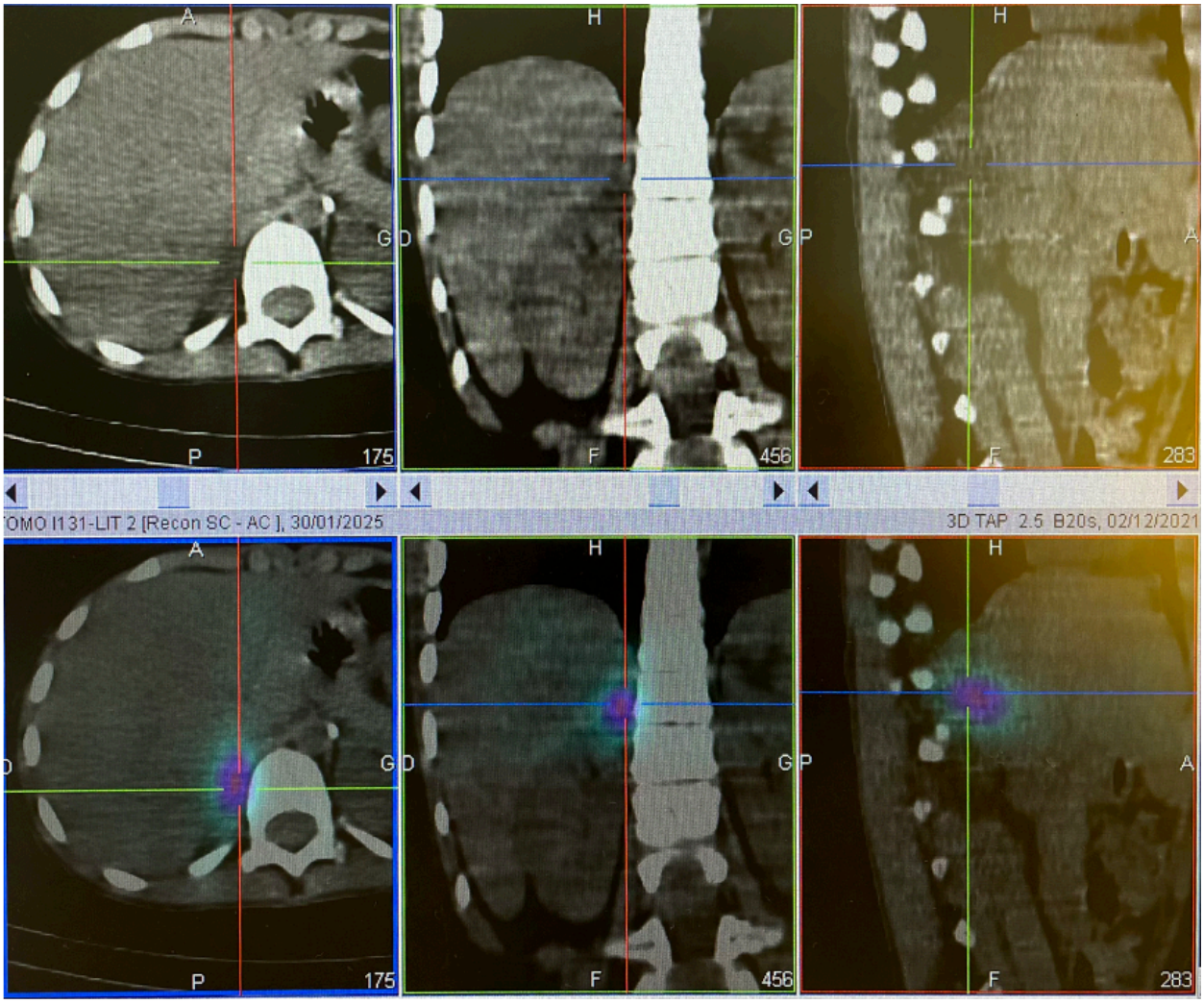

Figure 3: Complementary MIBG SPECT/CT imaging.

The MIBG scintigraphy images in Figures 2 and 3 demonstrate a pathological focus of increased uptake in the right adrenal gland, indicative of recurrent neuroblastoma. This uptake highlights the presence of metabolically active neuroblastoma cells, guiding the decision for further surgical intervention.

according to the protocol of a multicenter clinical trial for high-risk neuroblastoma.
Initial management included surgery with an incomplete resection of the retroperitoneal mass. Immediately postoperatively, she received chemotherapy and external radiotherapy. Despite this aggressive treatment, imaging revealed persistence of the retroperitoneal mass. The patient was subsequently placed on cis-retinoic acid therapy, but adverse effects after the third cycle led to its discontinuation. Due to the stability of the 19 mm retroperitoneal mass, the decision was made to transition to metronomic chemotherapy.

She received multiple cycles of metronomic chemotherapy with regular evaluations through CT scans, which showed a stable appearance of the mass with no new suspicious anomalies.
During follow-up, the patient was referred to our department for further assessment. An MIBG scintigraphy was performed, revealing a non-avid lesion at the retroperitoneal surgical site. However, the scan identified a new uptake in the right adrenal gland, suggesting disease recurrence.
This finding prompted the decision for further surgical intervention to manage the recurrence (Fig.2 and 3).

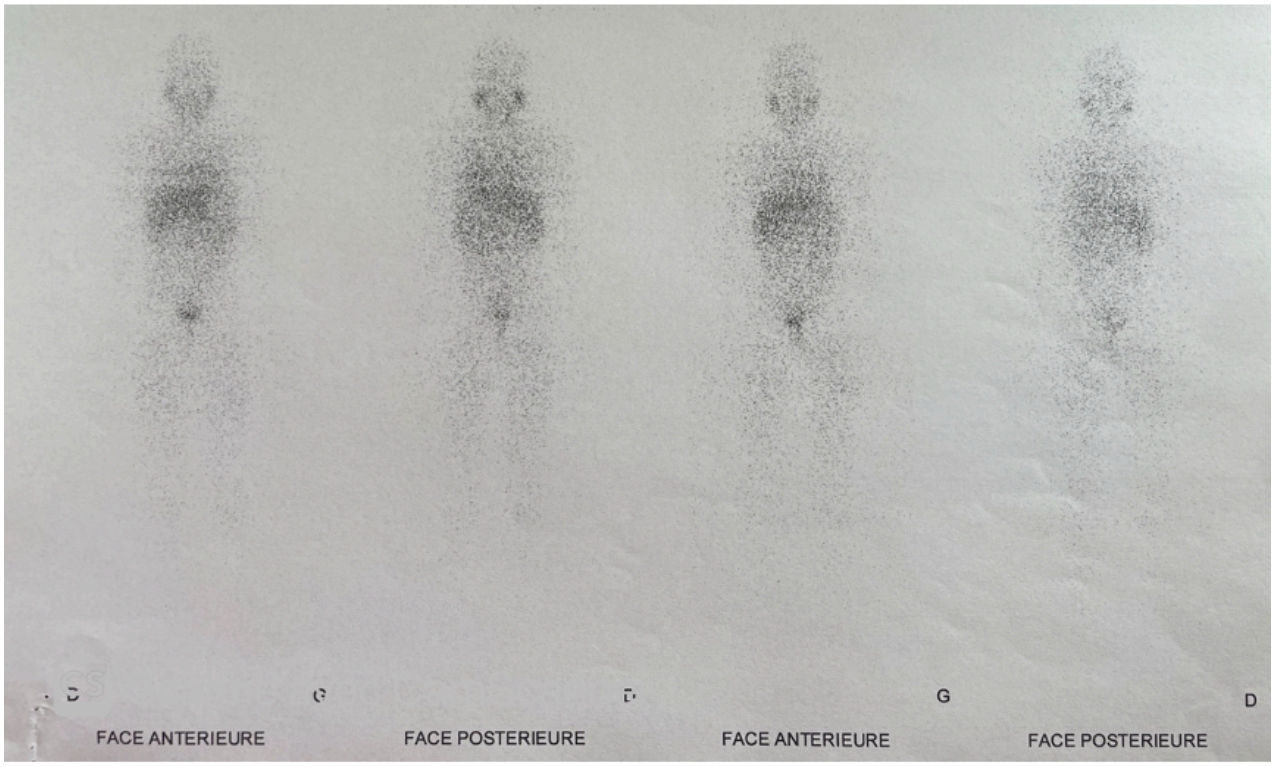

Figure 4: Whole-body MIBG scintigraphy scans at 24 hours and 48 hours.

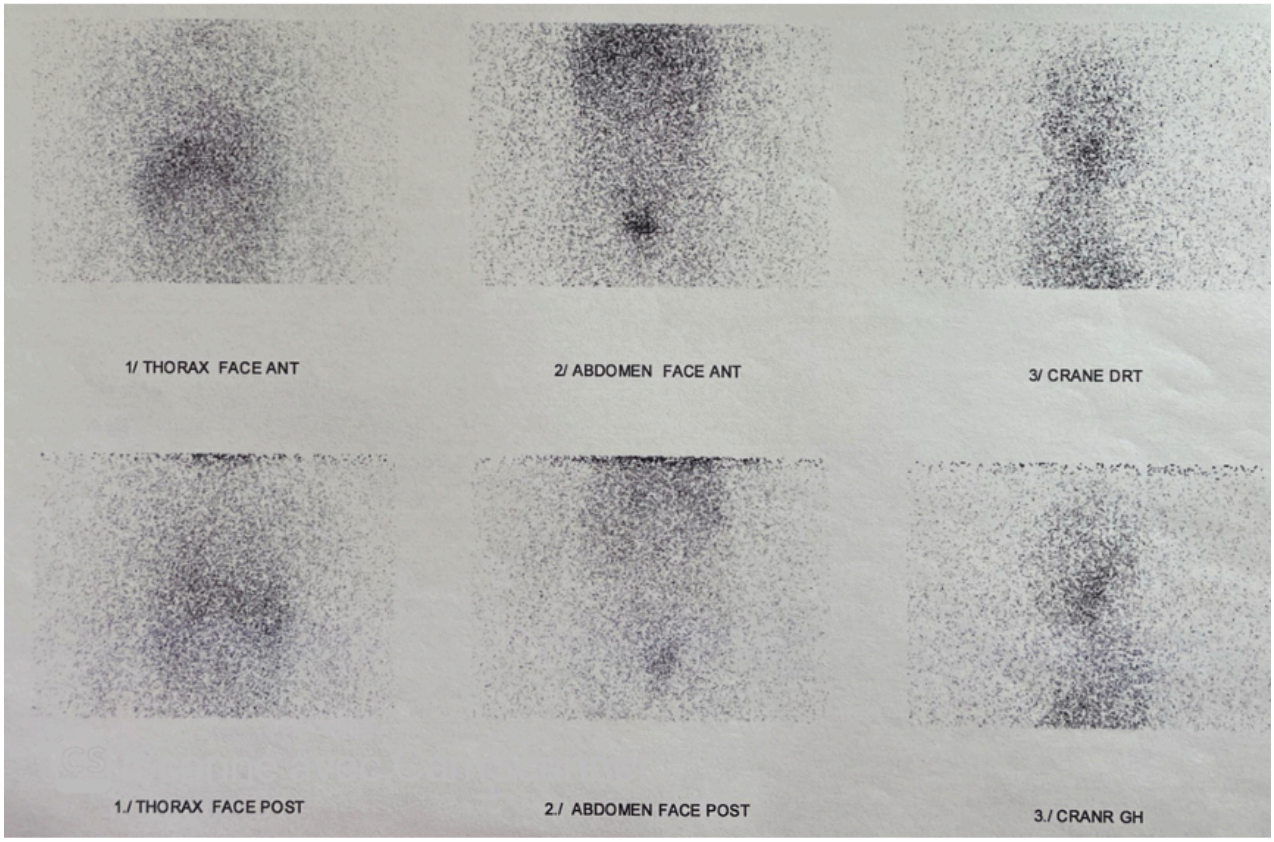

Figure 5: Whole-body static MIBG scintigraphy images at 24 hours.

The MIBG scintigraphy images in Figures 4 and 5 demonstrate the absence of pathological uptake, indicating no evidence of active neuroblastoma and confirming complete remission.

Case 3

An 11-year-old girl, with no notable medical history, was diagnosed with a right adrenal neuroblastoma, classified as stage IV high-risk neuroblastoma due to bone and bone marrow metastases. The illness began with right flank pain and vomiting, which worsened over several days, leading to referral to the Pediatric Oncology Department at CHU Hassan II, Fez.

A CT scan confirmed the presence of a right adrenal neuroblastoma. A bone scintigraphy revealed osteolytic lesions in the right humeral head, suggesting secondary bone involvement.

Initial treatment included multimodal therapy following a high-risk protocol, and the patient underwent tumor resection. Despite this, bone marrow involvement persisted, and the patient was placed on metronomic chemotherapy for palliative care.

An MIBG scintigraphy was performed to assess disease status. The scan showed no pathological uptake, confirming complete remission with a SIOPEN score of 0. Based on these results, the decision was made to discontinue metronomic chemotherapy (Fig.4 and 5).

Discussion

MIBG scintigraphy plays a pivotal role in the comprehensive management of neuroblastoma, providing high specificity for diagnosing, staging, and monitoring this aggressive pediatric malignancy. Neuroblastoma, originating from neural crest cells, often presents with metastatic disease, making precise imaging crucial for effective patient care.

In Case 1, a 3-year-old boy presented with abdominal pain and a palpable mass. MIBG scintigraphy confirmed the diagnosis of a right adrenal neuroblastoma and revealed diffuse bone marrow metastases, establishing the disease as stage IV. This aligns with studies showing that MIBG scintigraphy achieves a diagnostic sensitivity of 85% to 95% for neuroblastoma, significantly aiding in differentiating it from other pediatric tumors (6, 12). The ability of MIBG to detect bone marrow involvement is particularly crucial in young children where early intervention can improve outcomes (5).

Accurate staging through MIBG scintigraphy is essential for risk stratification and treatment planning. In Case 2, an 11-year-old girl with a history of retroperitoneal neuroblastoma underwent follow-up imaging after initial treatment. MIBG scintigraphy identified a new pathological uptake in the right adrenal gland, suggesting recurrence. This prompted timely surgical intervention, consistent with the importance of MIBG scans in detecting disease recurrence and guiding therapy (7). The SIOPEN scoring system applied to MIBG imaging provides a standardized assessment of metastatic burden, which has been shown to correlate strongly with prognosis and therapeutic response (10). Studies have reported a sensitivity exceeding 90% for detecting bone marrow metastases, highlighting MIBG's role in assigning high-risk categories (8).

Monitoring patients for recurrence or confirming remission is another critical application of MIBG scintigraphy. In Case 3, an 11-year-old girl diagnosed with right adrenal neuroblastoma and humeral metastasis achieved complete remission following multimodal therapy. Follow-up MIBG scintigraphy demonstrated no pathological uptake, confirming remission with a SIOPEN score of 0. This justified discontinuation of metronomic chemotherapy. The ability to confirm remission through MIBG imaging aligns with findings by Kushner et al., who emphasized the role of surveillance MIBG scans in detecting subclinical recurrence and guiding therapeutic decisions (18). Complete remission indicated by the absence of pathological uptake supports better long-term outcomes and reduces unnecessary treatment exposure (11).

While CT and MRI provide detailed anatomical information, they lack the specificity of MIBG scintigraphy for neuroblastoma cells. For example, in Case 1, although CT identified a right adrenal mass, MIBG scintigraphy detected widespread bone marrow metastases, essential for accurate staging and guiding systemic therapy (23). In Case 2, despite CT scans showing stable residual retroperitoneal masses, MIBG scintigraphy revealed new adrenal uptake, indicating recurrence and prompting surgical intervention. These examples highlight the advantage of MIBG in identifying metabolically active

disease that may be missed by anatomical imaging (17). FDG-PET can serve as a useful adjunct in MIBG-negative neuroblastoma cases, particularly for poorly differentiated tumors, but its lower specificity limits its use in routine practice (13).

However, MIBG scintigraphy does have limitations. The sensitivity for detecting small or early lesions can be lower, and the need for specialized facilities and radiopharmaceuticals poses logistical challenges (16). In regions where Iodine-123 (I-123) MIBG is unavailable, Iodine-131 (I-131) MIBG serves as an alternative, as was the case in all three patients. While I-123 provides superior image quality and lower radiation exposure, I-131 remains effective for diagnosing and staging neuroblastoma (15). Advances in radiopharmaceutical production and imaging technology are needed to mitigate these challenges and improve diagnostic access (14).

In conclusion, these cases demonstrate the multifaceted role of MIBG scintigraphy in neuroblastoma management. It provides superior specificity for diagnosis, accurate staging through standardized scoring systems like SIOPEN, and effective monitoring for recurrence or remission. Integrating MIBG with other imaging modalities enhances diagnostic accuracy and supports informed clinical decision-making, ultimately improving patient outcomes.

Conclusion

MIBG scintigraphy is a fundamental tool in the diagnosis, staging, and follow-up of neuroblastoma, offering high specificity for neuroendocrine tissue (6). It allows precise localization of primary tumors and metastatic lesions, contributing to accurate risk stratification and treatment planning (12, 5). The use of standardized scoring systems like SIOPEN enhances the consistency and reliability of disease assessment (7).

In follow-up, MIBG scintigraphy plays a key role in detecting recurrence and confirming remission, ensuring timely intervention and improved outcomes (18, 19). Although it has limitations, such as reduced sensitivity for small lesions and the availability of I-123 MIBG, ongoing advancements in imaging technology are addressing these challenges (15).

Incorporating MIBG scintigraphy into clinical practice, alongside other imaging modalities, optimizes neuroblastoma management and contributes to better patient care and outcomes (10).

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Conflict of interest:

The authors declare that there were no conflicts of interest within the meaning of the recommendations of the International Committee of Medical Journal Editors when the article was written.

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References

1. Park JR, Eggert A, Caron H. Neuroblastoma: biology, prognosis, and treatment. Pediatric Clinics of North America. 2008;55(1):97-120.
2. Maris JM. Recent advances in neuroblastoma. New England Journal of Medicine. 2010;362(23):2202-2211.
3. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. Journal of Clinical Oncology. 2010;28(15):2625-2634.
4. Brodeur GM. Spontaneous regression of neuroblastoma. Cell and Tissue Research. 2018;372(2):277-286.
5. Kushner BH. Neuroblastoma: a disease requiring a multitude of imaging studies. Journal of Nuclear Medicine. 2004;45(7):1172-1188.
6. Shulkin BL, Thompson NW, Shapiro B, et al. Pheochromocytomas and neuroblastomas: diagnostic imaging with 131-I MIBG. Radiology. 1986;161(3):491-495.
7. Matthay KK, Shulkin B, Ladenstein R, et al. Criteria for evaluating disease extent by 123I-MIBG scans in neuroblastoma: a report from the International Neuroblastoma Risk Group (INRG) project. Pediatric Blood & Cancer. 2010;56(1):50-56.
8. Taggart DR, Han MM, Quach A, et al. Comparison of 123I-MIBG and 18F-FDG PET scans in patients with relapsed neuroblastoma. Journal of Nuclear Medicine. 2009;50(8):1237-1243.
9. Sisson JC, Frager MS, Valk TW, et al. Scintigraphic localization of pheochromocytoma. New England Journal of Medicine. 1981;305(1):12-17.
10. Brisse HJ, McHugh K, Owens CM, et al. Guidelines for imaging and staging of neuroblastic tumors: consensus report from the International Neuroblastoma Risk Group Project. Radiology. 2011;261(1):243-257.
11. Gaze MN, Chang YC, Flux GD, et al. Feasibility of dosimetry-based high-dose 131I-MIBG therapy for neuroblastoma. Nuclear Medicine Communications. 2005;26(8):725-732.
12. Sharp SE, Gelfand MJ, Shulkin BL. Pediatrics: diagnosis of neuroblastoma with 123I-MIBG scintigraphy. Radiographics. 2011;31(6):1637-1646.
13. Kembhavi SA, Shah S, Rangarajan V, et al. Imaging in neuroblastoma: an update. Indian Journal of Radiology and Imaging. 2015;25(2):129-136.
14. Sgouros G, Kolbert KS, Sheikh A, et al. Patient-specific dosimetry for 131I-MIBG therapy of neuroblastoma. Medical Physics. 2001;28(11):2155-2165.
15. Buckley SE, Gaze MN. The role of MIBG therapy in the treatment of neuroblastoma. Advances in Therapy. 2006;23(5):728-736.
16. Shapiro B, Sisson JC, Shulkin BL. The current status of metaiodobenzylguanidine and analogues in the diagnosis and treatment of neuroblastoma. Quarterly Journal of Nuclear Medicine. 1995;39(2):114-121.
17. Monsieurs MA, Brans B, et al. Dosimetric considerations in 131I-MIBG therapy for neuroblastoma. European Journal of Nuclear Medicine and Molecular Imaging. 2002;29(1):102-111.
18. Kushner BH, Yeh SJ, Kramer K, et al. Impact of surveillance studies on prognostication and treatment of high-risk neuroblastoma. Journal of Clinical Oncology. 2003;21(17):3404-3410.
19. Gaze MN. The role of thyroid blockade in 131I-MIBG therapy. Nuclear Medicine Communications. 2008;29(2):109-112.
20. Sisson JC, Wieland DM. Radiopharmaceuticals for the diagnosis and treatment of pheochromocytoma. Nuclear Medicine and Biology. 1986;13(3):237-242.
21. Kushner BH, LaQuaglia MP, Modak S, et al. Neuroblastoma in children: clinical presentation and diagnostic considerations. Seminars in Pediatric Surgery. 2004;13(3):188-194.
22. McEwan AJ, Shapiro B, Sisson JC, et al. Gastrointestinal activity in MIBG scintigraphy: challenges and solutions. Journal of Nuclear Medicine. 1995;36(5):857-863.
23. Ladenstein R, Philip T, Lasset C, et al. Prognostic factors in metastatic neuroblastoma: correlation of MIBG imaging with other diagnostic modalities. European Journal of Cancer. 2003;39(5):635-641.
24. Villablanca JG, Matthay KK, et al. The role of imaging in assessing therapy response and disease progression in neuroblastoma. Journal of Clinical Oncology. 2009;27(7):1020-1025.