Paediatric Horner Syndrome: How much further to investigate?

Manjushree Bhate, Maree Flaherty[1], Neil Rowe[1], Robert Howman-Giles[2,3]

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1603_20

Jasti V Ramanamma Children's Eye Care Centre L.V. Prasad Eye Institute, Hyderabad, Telangana, India, [1]Department of Ophthalmology Children's Hospital, Westmead, [2]Department of Nuclear Medicine Children's Hospital Westmead, [3]Division of Imaging Sydney Medical School, University of Sydney, Sydney, Australia

Correspondence to: Dr. Maree Flaherty, Children's Eye Centre, 73 Darcy Road Wentworthville 2145, Sydney, Australia. E-mail: flaherty@childrenseyecentre.com.au

Received: 23-May-2020 Revision: 02-Aug-2020
Accepted: 11-Sep-2020 Published: 26-Oct-2020

We report an infant with an early-onset Horner syndrome and normal urinary catecholamine levels. Further investigations with Nuclear medicine imaging with ^{123}I-MIBG (meta-iodo benzyl-guanidine) confirmed a right thoracic inlet mass consistent with a neuroblastoma, a tumor of neural crest origin. The authors emphasize the need for investigating idiopathic acquired pediatric Horner syndrome and the value of an MIBG scan as a diagnostic test for suspected neuroblastoma.

Key words: Horner syndrome, MIBG scan, neuroblastoma, urinary VMA levels

Our case discusses Horner syndrome presenting in the first month of infancy and the specific investigations which revealed an underlying neuroblastoma.

Case Report

An 18-day-old baby girl presented with a history of not opening her right eye fully for 1–2 weeks. The mother, a medical

Cite this article as: Bhate M, Flaherty M, Rowe N, Howman-Giles R. Paediatric Horner Syndrome: How much further to investigate? Indian J Ophthalmol 2020;68:2607-10.

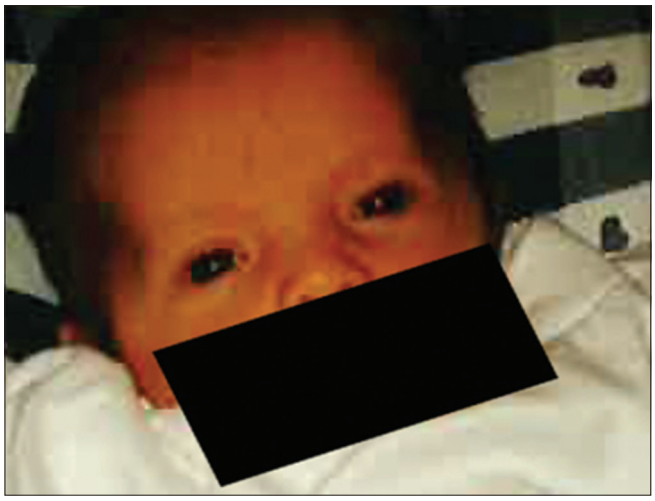

Figure 1: Child approximately 1 week old. No ptosis evident

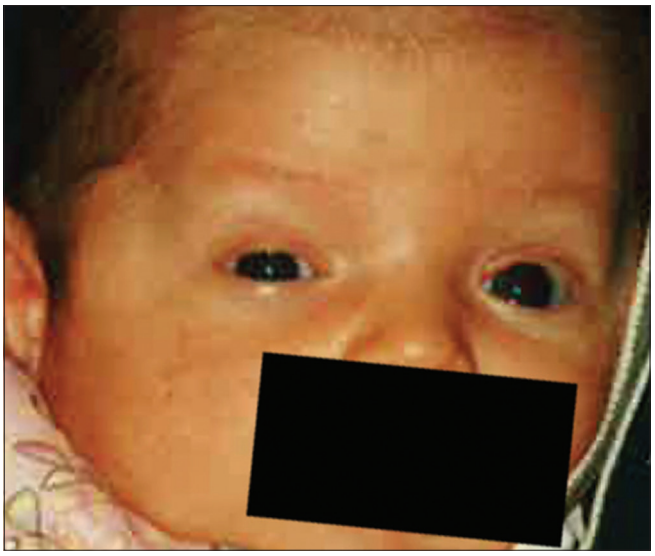

Figure 2: Upper and lower lid ptosis evident on right side at 1 month of age

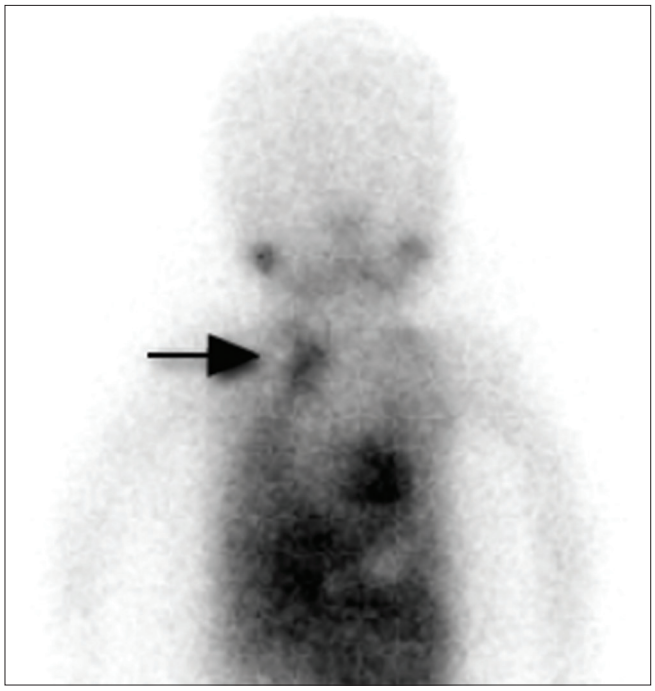

Figure 3: Focal increased accumulation of ^{123}I-MIBG into the right thoracic mass (arrow)

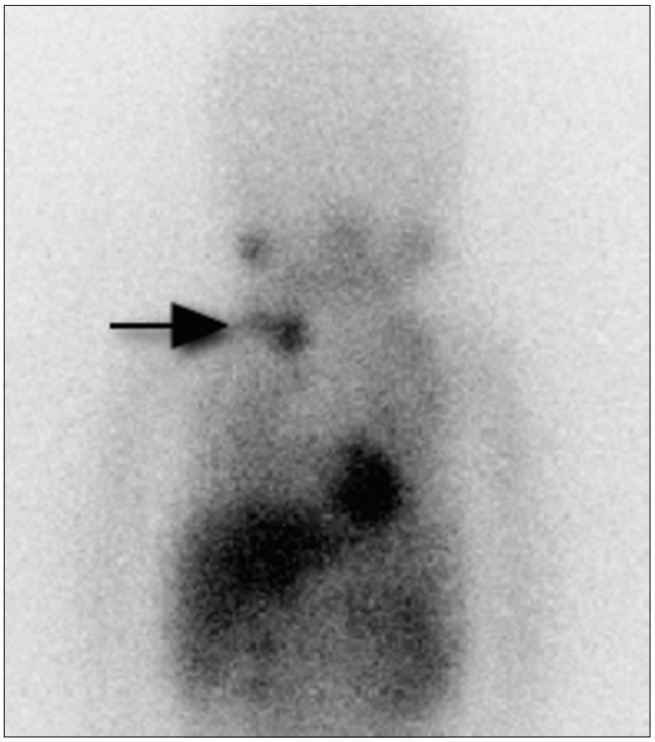

Figure 4: Residual tumor on side of primary neuroblastoma with extension into right supraclavicular area (arrow)

practitioner, had not noticed ptosis at birth nor within the first week [Fig. 1]. The baby was a product of a twin IVF pregnancy born at 36 weeks gestation by a normal vaginal delivery without the use of forceps. There was no evidence of birth trauma.

On examination at 18 days of age an upper and lower lid ptosis was noted on the right side [Fig. 2]. Anisocoria was evident with the right pupil being smaller. Both pupils reacted briskly to light. No heterochromia was noted, nor developed with time, and fundus examination was unremarkable. Cranial nerves were otherwise intact. A diagnosis of right Horner syndrome was made and the child was referred to a pediatric neurologist for further examination and investigations. Urinary vanillylmandelic acid (VMA) 24-h collection was normal. A scintigraphy with ^{123}I-meta-iodo benzyl-guanidine (MIBG) was performed which showed active uptake of tracer in a right thoracic inlet mass extending to the cervicothoracic junction [Fig. 3], indicative of a neural crest tumor. Computed tomography (CT) subsequently confirmed a non-calcified soft tissue lesion in the right thoracic outlet with extension to the cervicothoracic junction. Head, orbital and abdominal CT scans were normal. Whole-body bone scintigraphy was also normal. Debulking of the tumor was performed at 3 months of age. Histology showed a poorly differentiated neuroblastoma with foci of calcification. No chemotherapy or radiotherapy was given.

At 6 months of age, a mass was noted on the right side of the neck. A ^{123}I-MIBG scan was positive, indicating residual tumor with extension into the right lower neck [Fig. 4]. Two discrete masses were subsequently excised and neuroblastoma confirmed on histopathology. Urinary VMA levels again were normal. Follow-up ^{123}I-MIBG and bone scans over the next two years were normal with no evidence of recurrence. The child has remained systemically well.

Discussion

This case highlights the association of neuroblastoma with Horner syndrome. Previous reports have mentioned this association presenting congenitally,[1] or in infancy.[2,3] Neuroblastoma is a malignant tumor of undifferentiated neuroectodermal cells with an incidence of 8–10 per million accounting for 8%–10% of all childhood cancers.[4] Oculo-sympathetic disruption can occur with cervical[1,3] or thoracic lesions[1] and rarely with distant tumor sites. Benign causes for infantile Horner syndrome are more common although no clinical distinctions differentiate between aetiologies. Various authors have examined the degree of investigations appropriate to exclude neuroblastoma as the underlying cause for infantile Horner syndrome. George *et al*. suggested that routine diagnostic imaging of an isolated Horner syndrome in infancy is unnecessary.[5] They recommend urinary VMA levels and follow-up with a pediatrician, despite in their series of 23 patients, two had previously undiagnosed tumors, including one with a cervical neuroblastoma.

Smith *et al*.,[6] in their study to determine the incidence of pediatric Horner syndrome with occult malignancy, reported no cases of associated neuroblastoma in 20 cases. In addition, they reported 10 of 14 patients with neuroblastoma having elevated urinary catecholamine metabolites[7] and recommended physical examination with urinary catecholamine studies as sufficient in idiopathic Horner syndrome and imaging studies reserved for cases demonstrating signs of worsening disease.

Mahoney *et al*. reported 28 children with idiopathic Horner syndrome, 24 of whom were tested for urine catecholamines and all had normal levels. Four had an underlying neuroblastoma, confirmed with MIBG scanning.[8] They recommended physical examination, head, neck, and chest magnetic resonance imaging (MRI), and urinary catecholamine testing. They suggested that an MIBG scan was better in screening for neuroblastoma and metastasis of unknown location and that future studies should clarify whether or not more sensitive functional imaging techniques such as ^{123}I-MIBG or positron emission tomography scintigraphy would identify occult lesions not detectable by standard anatomic imaging.

In our case, urinary VMA levels were normal on both occasions with metabolically active neuroblastoma. Woodruff *et al*. noted that while elevated VMA levels are suggestive of the presence of neuroblastoma, normal VMA values do not exclude a tumour[2]. As approximately 60%–70% of neuroblastomas diagnosed in the perinatal period are non-secretory;[3] hence, screening with urinary VMA levels is not a sensitive test in this age group.

A review by Kanagalingam and Miller recommended physical examination, MRI of the brain, neck and chest, and urinary catecholamine assay in evaluating infants and children of idiopathic Horner syndrome.[9] While Kembhavi and colleagues have reported that imaging plays a central role in the diagnosis, staging, response evaluation, and follow-up of neuroblastoma, they considered ^{123}I MIBG scintigraphy as essential for evaluating metastatic disease to marrow and other sites and recommend it be obtained prior to tumor excision.[10] Xia Bai *et al*. have also considered the MIBG scan an important imaging modality in the evaluation of suspected or confirmed neuroblastoma with high accuracy.[11] The International Neuroblastoma Risk Group (INRF) recommends an MRI/CT scan, I^{123}MIBG scan, chest radiology as mandatory work up in neuroblastoma.[12,13] It is proposed MRI/CT scan to be obtained before proceeding with the MIBG scan as it still remains a standard imaging modality. Certain precautions are advised while performing ^{123}I-MIBG scan. A slow injection of the drug is advisable and injecting via a central venous catheter must be avoided if possible for potential adverse effects including tachycardia, pallor, and vomiting.[14,15] Pertaining to infants, breastfeeding should be discontinued for at least 48 h after injection.[14]

Any child with an acquired Horner syndrome suggests the onset of pathology, warranting investigation unless there is a known preceding cause. In our case, the Horner syndrome was not noted at birth but within the first few weeks of life. However, the exact time of onset of infantile Horner syndrome may not always be apparent at presentation; hence, there is a risk of underlying neuroblastoma.

Whole-body imaging with ^{123}I-MIBG is a sensitive diagnostic test for assessing neuroblastoma as the agent is incorporated into the catecholamine pathway and accumulates in neuroblastoma in 90%–95% of cases,[4] thus showing a high specificity and detection rate, making it a targeted therapeutic agent and ideal for neural crest tumors.

Conclusion

We emphasize the need of investigating idiopathic pediatric Horner syndrome and the value of an MIBG scan as an important diagnostic test in the initial and follow-up management of suspected neuroblastoma.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of Interest

There are no conflicts of interest.

References

1. Musrella MA, Chan HSL, DeBoer G, Gallie BS. Ocular involvement in neuroblastoma: Prognostic implications. Ophthalmology 1984;91:936-40.
2. Woodruff G, Buncic JR, Morin JD. Horner's syndrome in children. J Pediatric Ophthalmol Strabismus 1988;25:40-4.
3. Cardesa-Salzmann TM, Mora-Graupera J, Claret G, Agut T.

Congenital cervical neuroblastoma. Pediatric Blood Cancer 2004;43:785-7.

4. Howman-Giles R, Shaw PJ, Uren RF, Chung DKV. Neuroblastoma and other neuroendocrine tumors. Semin Nucl Med 2007;37:286-302.
5. George NDL, Gonzalez G, Hoyt CS. Does horner's syndrome in infancy require investigation? Br J Ophthalmol 1998;82:51-4.
6. Smith SJ, Diehl N, Leavitt JA, Mohney BJ. Incidence of pediatric Horner syndrome and the risk of neuroblastoma: A population-based study. Arch Ophthalmol 2010;128:324-9.
7. Smith SJ, Diehl NN, Smith BD, Mohney BJ. Urine catecholamine levels as diagnostic markers for neuroblastoma in a defined population: Implications for ophthalmic practice. Eye 2010;24:1792-6.
8. Mahoney NR, Liu GT, Menacker SJ, Wilson MC, Hogarty MD, Maris JM. Pediatric horner syndrome: Etiologies and roles of imaging and urine studies to detect neuroblastoma and other responsible mass lesions. Am J Ophthalmol 2006;142:651-9.
9. Kanagalingam S, Miller N. Horners syndrome: Clinical perspectives. Eye Brain 2015;7:35-46.
10. Kembhavi SA, Shah S, Rangarajan V, Qureshi S, Popat P, Kurkure P. Imaging in neuroblastoma: An update. Indian J Radiol Imaging 2015;25:129-36.
11. Bai X, Yang H, Zhuang H. Asymmetric thoracic metaiodobenzylguanidine (MIBG) activity due to prior radiation therapy. Clin Nucl Med 2015;40:e338-40.
12. Monclair T, Brodeur GM, Ambros PF, Brisse HJ, Cecche o G, Holmes K, *et al.* INRG Task Force. The International Neuroblastoma Risk Group (INRG) staging system: An INRG Task Force report. J Clin Oncol 2009;27:298-303.
13. Brisse HJ, McCarville MB, Granata C, Krug KB, Woo on-Gorges SL, Kanegawa K, *et al.* International Neuroblastoma Risk Group Project. Guidelines for imaging and staging of neuroblastic tumours: Consensus report from the International Neuroblastoma Risk Group Project. Radiology 2011;261:243-57.
14. Emilio B, Giammarile F, Aktolun C, Baum RP, Delaloye AB, Maffioli L, *et al*. $^{131}I/^{123}I$-Metaiodobenzylguanidine (MIBG) Scintigraphy: Procedure guidelines for tumour imaging. Eur J Nucl Med Mol Imaging 2010;37;2436-46.
15. Agarwal A, Rangarajan V, Shah S, Puranik A, Purandare N. MIBG (metaiodobenzylguanidine) theranostics in pediatric and adult malignancies. Br J Radiol 2018;91:20180103.