Paediatric Horner Syndrome: How much further to investigate?

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We report an infant with an early-onset Horner syndrome and normal urinary catecholamine levels. Further investigations with Nuclear medicine imaging with ¹²³I-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

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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.

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)
At 6 months of age, a mass was noted on the right side of the neck. A 123I-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 123I-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, or in infancy. 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. Oculo-sympathetic disruption can occur with cervical or thoracic lesions 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. 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., 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 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. 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 123I-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. As approximately 60%–70% of neuroblastomas diagnosed in the perinatal period are non-secretory; 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. 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 123I MIBG scintigraphy as essential for evaluating metastatic disease to marrow and other sites and recommend it be obtained prior to tumor excision. 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. The International Neuroblastoma Risk Group (INRF) recommends an MRI/CT scan, 123I MIBG scan, chest radiography as mandatory work up in neuroblastoma. 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 123I-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. Pertaining to infants, breastfeeding should be discontinued for at least 48 h after injection.

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 123I-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, 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.

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Conflicts of Interest

There are no conflicts of interest.

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