# Does Horner's syndrome in infancy require investigation?

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**Abstract**

***Aims*—To evaluate whether isolated Horner's syndrome presenting in the first year of life warrants investigation.**

***Method*—Retrospective review of 23 children presenting with Horner's syndrome in the first year of life.**

***Results*—In 16 patients (70%) no cause was identified. Birth trauma was the most common identifiable cause (four patients). Twenty one children (91%) had urinary vanillylmandelic acid (VMA) measured and 13 patients (57%) underwent either computed tomography or magnetic resonance imaging of the chest and neck. These investigations revealed previously undisclosed pathology in only two—one ganglioneuroma of the left pulmonary apex and one cervical neuroblastoma. A further patient was known to have abdominal neuroblastoma before presenting with Horner's syndrome. There were no cases of Horner's syndrome occurring after cardiothoracic surgery. Long term follow up of the patients (mean 9.3 years) has not revealed further pathology.**

***Conclusions*—Routine diagnostic imaging of isolated Horner's syndrome in infancy is unnecessary. Infants should be examined for cervical or abdominal masses and involvement of other cranial nerves. If the Horner's syndrome is truly isolated then urinary VMA levels and follow up in conjunction with a paediatrician should detect any cases associated with neuroblastoma. Further investigation is warranted if the Horner's syndrome is acquired or associated with other signs such as increasing heterochromia, a cervical mass, or cranial nerve palsies.**

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Horner's syndrome occurs as a result of a lesion anywhere along the oculosympathetic pathway from the hypothalamus to the orbit.[1] The condition is not uncommon in adult neuro-ophthalmology practice and the site of the lesion may be localised by history, accompanying signs such as anhidrosis, and by pharmacological testing of pupils.[1 2] Further imaging of the pulmonary apices and cervical region may be undertaken as indicated by the site of the lesion.

However, an infant presenting with a Horner's syndrome leaves the physician with a diagnostic dilemma. It may not be clear whether the signs have been present from birth or are acquired. Heterochromia may appear to be progressive as the child develops normal pigmentation in the fellow iris. Furthermore, pharmacological testing of pupils in infants may be difficult to evaluate[2] or may yield false localising information.[3 4]

Childhood Horner's syndrome has been described in congenital varicella,[5 6] birth trauma,[7] tumours of the neck and mediastinum such as neuroblastoma,[8–10] ganglioneuroma[11 12] and neurilemmoma,[13] and vascular lesions of the internal carotid or subclavian artery.[14] Although many reports recommend extensive investigation of these children, they do not clearly distinguish congenital isolated Horner's syndrome from that acquired later in childhood accompanied by other signs at presentation.

We describe a series of 23 consecutive cases of Horner's syndrome presenting in the first year of life in order to evaluate the causes and necessary investigation of these patients.

## Patients and methods

Infants presenting to one paediatric neuro-ophthalmologist (CSH) between 1978 and 1995 with the diagnosis of Horner's syndrome in the first year of life were identified from a database. The diagnosis of Horner's syndrome was based on anisocoria, which was more obvious in the dark, and ptosis. Heterochromia was judged in room lighting. Facial anhidrosis was assessed by history from the parents and by feeling each side of the face.

A complete history was taken and severity of birth trauma was corroborated with the attending obstetrician. General examination was performed including palpation of the neck and abdomen for neuroblastoma, and auscultation of the chest. Pharmacological testing of the pupils was not performed routinely. Urinary vanillylmandelic acid (VMA) levels were measured in most cases. Computed tomography (CT) or magnetic resonance imaging (MRI) investigation of the head and neck was performed depending on the availability of these techniques at that time.

## Results

Twenty three children (12 male, 11 female) presenting with Horner's syndrome in the first year of life were identified (Table 1). Follow up ranged between 1 and 19 years (mean 9.3 years).

Horner's syndrome was right sided in 10 patients and left sided in 13 patients. All patients had obvious pupillary signs but in one (case 21) the ptosis was equivocal. There were 18 patients (78%) with iris heterochromia. Ipsilateral anhidrosis, indicating a preganglionic lesion, was present in 16 patients (70%).

*Table 1 Clinical details of patients*

| Case | Sex | Eye | Miosis | Ptosis | Heterochromia | Anhidrosis | History | VMAs | CT or MRI | Follow up (years) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | R | + | + | + | − | Severe birth trauma | − | 0 | 19 |
| 2 | M | L | + | + | + | + | | 0 | 0 | 18 |
| 3 | F | L | + | + | + | + | | − | 0 | 18 |
| 4 | M | L | + | + | − | − | Forceps delivery but not thought traumatic | − | − | 17 |
| 5 | F | R | + | + | + | + | | − | − | 16 |
| 6 | F | L | + | + | + | + | | − | − | 16 |
| 7 | F | L | + | + | − | + | | − | 0 | 14 |
| 8 | M | R | + | + | − | − | | − | 0 | 13 |
| 9 | F | L | + | + | + | + | Known abdominal neuroblastoma | + | − | 11 |
| 10 | M | R | + | + | + | + | | − | − | 10 |
| 11 | F | L | + | + | − | − | | − | 0 | 9 |
| 12 | F | L | + | + | + | + | | − | − | 9 |
| 13 | F | L | + | + | + | + | | − | 0 | 8 |
| 14 | M | R | + | + | + | + | | − | 0 | 7 |
| 15 | M | L | + | + | + | + | | − | − | 7 |
| 16 | F | L | + | + | + | − | Severe birth trauma | − | 0 | 5 |
| 17 | M | L | + | + | + | + | Progressive heterochromia. Apical ganglioneuroma | 0 | + | 4 |
| 18 | F | R | + | + | − | + | | − | − | 4 |
| 19 | M | R | + | + | + | + | Cervical neuroblastoma | + | + | 3 |
| 20 | M | L | + | + | + | − | | − | 0 | 2 |
| 21 | M | R | + | +/− | + | + | | − | − | 2 |
| 22 | F | R | + | + | + | − | Severe birth trauma | − | − | 2 |
| 23 | M | R | + | + | + | + | | − | − | 1 |

+ = sign present or investigation abnormal; − = sign absent or investigation normal; 0 = investigation not performed.

No cause was identified in 16 patients (70%). Birth trauma was the most common identifiable cause, resulting from difficult vaginal delivery (three cases) or forceps delivery (one case). Twenty one patients (91%) had urinary VMA levels measured and 13 patients (57%) underwent either CT or MRI of the chest and neck. These investigations revealed previously undisclosed pathology in only two: case 17 was thought to have an acquired Horner's syndrome and increasing iris heterochromia prompted further investigation. A CT scan of the chest revealed a ganglioneuroma of the left pulmonary apex, which was subsequently resected. Case 19 had raised urinary VMA levels and was found to have a cervical neuroblastoma. A further patient (case 9) had already been diagnosed as having abdominal neuroblastoma before presenting with a Horner's syndrome. There were no cases of Horner's syndrome occurring after cardiothoracic surgery. Long term follow up of the patients has not revealed further pathology.

## Discussion

The investigation of Horner's syndrome in infants remains a contentious issue and previous reports have recommended varying degrees of investigation.[4 14 15] These reports have included a range of ages from birth to those acquiring the syndrome later in childhood. Furthermore, the distinction between an isolated Horner's syndrome and those with involvement of other cranial nerves, palpable masses in the neck, or postoperative Horner's syndrome has not been emphasised. In our series of 23 consecutive cases of Horner's syndrome presenting in children under 1 year of age, investigation with urinary VMA levels, CT, or MRI of the chest and neck revealed only two cases with previously undiagnosed pathology—one ganglioneuroma of the left pulmonary apex and one occult neuroblastoma. One other child had an abdominal mass and was diagnosed as having neuroblastoma before developing a Horner's syndrome. It could be argued that some cases which were not imaged may have had underlying pathology, but long term follow up of these cases has not shown any progressive disease.

Localisation of the Horner's syndrome to the pre- or postganglionic neuron by pharmacological testing of pupils is useful in adults,[1] as it provides prognostic information as well as directing the physician to further areas of investigation. However, we have not been impressed by the usefulness of pharmacological testing of the pupils in children and it was not performed routinely in this series. Other authors have reported equivocal results in children[3 4] and some series specifically exclude children owing to difficulties in pupillography.[2] Ipsilateral facial anhidrosis, which was present in 70% of our patients, localises the lesion to the preganglionic neuron.

The most common identifiable cause of Horner's syndrome in our series was birth trauma, resulting from a difficult vaginal delivery (three cases) or forceps delivery (one case). Ipsilateral facial anhidrosis was absent in all four patients, indicating a postganglionic location. In the only other series with a comparable age group with ours Weinstein *et al* used a combination of anhidrosis and response to hydroxyamphetamine in order to localise the site of the lesion in 11 patients.[3] They too found postganglionic lesions in 4/5 of their birth trauma cases. This may be the result of traction on the internal carotid artery sympathetic plexus during forceps delivery or due to torsion of the head and neck with a difficult vaginal delivery. Interestingly, some patients in Weinstein's series demonstrated ipsilateral anhidrosis indicative of a preganglionic lesion, but hydroxyamphetamine testing showed only partial mydriasis. They postulated that orthograde trans-synaptic degeneration of the

postganglionic neuron had taken place. Although the association of Klumpke's paralysis is well recognised,[16] this was not present in any of our patients.

Iris heterochromia, present in 78% of our patients, is typical of congenital Horner's syndrome but may also develop in Horner's syndrome acquired before 2 years of age.[7] Acquired or increasing heterochromia should alert the physician to further investigation. In case 17, the child's mother had felt that the Horner's syndrome was not present at birth. Increasing heterochromia prompted further investigation, which revealed a large mass of the left pulmonary apex. This was subsequently resected and proved to be a benign ganglioneuroma. Ganglioneuroma has been reported as a rare cause of infantile Horner's syndrome.[11 12] These tumours are thought to represent a regressed form of neuroblastoma and if left untreated the outcome would probably have been good.[17] However, imaging alone will not distinguish benign ganglioneuroma from neuroblastoma and a tissue diagnosis was therefore required.[18]

Vascular lesions have also been reported to cause Horner's syndrome, leading authors to recommend angiography in these children.[14] Sauer and Levinsohn reported subclavian artery aneurysm and internal carotid artery thrombosis in two children. However, both presented in later childhood (aged 7 and 5 years respectively) with an acquired Horner's syndrome and in one this was associated with VI nerve palsy.[14]

Cervical or mediastinal neuroblastoma is the most significant treatable cause of Horner's syndrome in children. Jaffe *et al* noted a Horner's syndrome at diagnosis in 4/30 cases.[9] Musarella *et al* described 14 cases of Horner's syndrome from a series of 405 children with neuroblastoma and emphasised the good prognosis associated with this presentation.[10] In nine children the Horner's syndrome was the presenting feature. Woodruff *et al* reported neuroblastoma in 2/10 cases of childhood Horner's syndrome.[4] Some reports include significant numbers of children where the Horner's syndrome had occurred as a result of surgical resection of cervical neuroblastoma or other malignancy rather than as a presenting sign.[3 9 14] The most common site for neuroblastoma is the abdomen (60%), followed by thorax (15%), pelvis (5%), and cervical sympathetic chain (5%). Although CT scanning[19] or MRI[18] are the most sensitive techniques for detecting neuroblastoma at any site, urinary VMAs are raised in 95% of cases[20] and in one series a plain chest *x* ray detected all cases of thoracic neuroblastoma.[19] We found neuroblastoma in only two of 23 cases of Horner's syndrome. In case 19 a Horner's syndrome was the presenting feature and raised urinary VMA levels prompted further imaging. Case 9 was known to have an abdominal neuroblastoma before developing a Horner's syndrome. Interestingly, a CT scan of the neck and thorax showed no evidence cervical neuroblastoma. This phenomenon has been noted in two previous cases.[8 10] Possible explanations of this phenomenon could be that of a paraneoplastic effect, spontaneous regression of the tumour, or simply that CT scanning missed a small focus of neuroblastoma in the cervical sympathetic chain. Spontaneous regression of neuroblastoma is well documented and may occur in up to one third of cases.[21 22] Additionally, small foci of adrenal neuroblastoma have been demonstrated at necropsy in up to 2–3% of infants dying from non-malignant causes.[23] It should be emphasised that our series includes only patients presenting under 1 year of age and may therefore underestimate the true incidence of neuroblastoma presenting with Horner's syndrome. Although neuroblastoma usually presents at around 2 years of age, there are at least five cases in the literature where the development of a neuroblastoma has been associated with a congenital Horner's syndrome.[4 8–10]

This series of patients demonstrates that Horner's syndrome presenting in the first year of life is usually a benign entity. In most cases no cause is identified. Birth trauma is the most common identifiable cause followed by neuroblastoma. In the present climate of cost effective medicine we have found that routine CT or MRI scanning of the neck and chest in isolated Horner's syndrome in infancy is unnecessary. Infants should therefore be examined for cervical or abdominal masses and involvement of other cranial nerves. If the Horner's syndrome is truly isolated then a urinary VMA level and follow up in conjunction with a paediatrician should detect any cases associated with neuroblastoma. Further investigation is warranted if the Horner's syndrome is acquired or associated with other signs such as increasing heterochromia, a cervical mass, or cranial nerve palsies.

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