Cocaine test results in children with anisocoria

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Introduction
To establish a diagnosis of Horner syndrome, pharmacological pupillary testing using diluted cocaine eye drops is recommended. Horner syndrome in children has important systemic associations such as underlying neuroblastoma and brainstem pathology or can be caused by trauma or previous surgery [1]. Reported incidences of underlying mass lesions responsible for Horner syndrome vary from none to 33% in different pediatric collectives [2-4]. Presently, we aimed to identify the portion of positive cocaine test results in children with anisocoria and to describe the extent of systemic workup and the underlying etiologies.

Methods
We retrospectively reviewed all medical records of pediatric patients (<18 years old) that underwent cocaine testing for evaluation of anisocoria between August 2007 and August 2015 at our tertiary referral center. Positive cocaine tests were defined by an increase in anisocoria and/or a resulting anisocoria of >1mm (example given in Fig. 1). If cocaine drops did not show any effect on either pupil, the test was classified as inconclusive.

Results
Thirty-eight pediatric patients with anisocoria that underwent cocaine testing were identified. The patient characteristics are listed in Tab. 1. Cocaine testing was positive, negative, or inconclusive in 12/38 (32%), 23/38 (60%) and 3/38 (8%), respectively. Eleven children with a positive test result and three other cases were referred for further neurological and systemic workup. Fig. 2 illustrates the studies performed. Mediastinal non-Hodgkin lymphoma was diagnosed in one patient. A history of birth trauma and thoracic surgery might be causative in two other patients.

Discussion
The majority of children undergoing cocaine testing for evaluation of anisocoria had a negative test result, presumably including a large portion of physiological anisocoria. For the children with anisocoria and a positive cocaine test, no underlying etiology could be determined in most cases despite comprehensive medical workup. Only one patient was diagnosed with a malignant disease. As a limitation, children with Horner syndrome who were not subject to cocaine testing might have been missed in the present report. In our study population, other diagnostic signs of Horner syndrome (ptosis, facial anhidrosis, iris heterochromia) were usually absent. Therefore, a certain rate of false-positive cocaine test results cannot be excluded. Cocaine testing is susceptible to different sources of error such as pharmacological quality, dilution procedure and drop instillation. Ways to improve diagnostic accuracy might include taking standardized photographs for pupil measurements, possibly the alternative use of apraclonidine in older children and additional testing with direct-acting adrenergic agonists.

Conclusions
Special diagnostic challenges are encountered in suspected pediatric Horner syndrome. Cocaine test results are sometimes equivocal especially in small children and adjunctive tests may be useful. Serious underlying disease was rare in our population, however, careful evaluation regarding the need of further systemic workup is essential.

References

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Fig. 1. 4-months old girl with ptosis and miosis on the right side. Anisocoria is more pronounced in dark (b) than in light (a) condition. 60 minutes after instillation of 5% cocaine eye drops there is evidence of increased anisocoria (dilation deficit on the right side), suggestive of right sided Horner syndrome (c).

Tab. 1. Characteristics, examination findings and etiologies of pediatric patients evaluated for anisocoria subdivided into positive, negative and inconclusive cocaine test results.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Positive</th>
<th>Negative</th>
<th>Inconclusive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anisocoria</td>
<td>12</td>
<td>23</td>
<td>3</td>
<td>38</td>
</tr>
<tr>
<td>Anisocoria greater in dark</td>
<td>11</td>
<td>12</td>
<td>1</td>
<td>24</td>
</tr>
<tr>
<td>Pupil size</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Heterochromia</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Harlequin sign or anhidrosis</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

Fig. 2. Studies performed in patients with suspected Horner syndrome. Radiologic examination includes different combinations of conventional X-ray, CT, MRI and sonography. Urine studies refer to catecholamine testing (VMA and HVA).