False Localizing Signs in Neurology

JOBIN V JOSEPH

ABSTRACT
False localizing neurological signs reflect dysfunction distant from the site of the pathology. They pose considerable difficulties to the treating neurologist as they are unreliable when attempting to localize the lesion, which challenges the traditional clinicoanatomical correlation. It is important to be aware of false localizing signs and the situations in which they occur as they may be indicative of a serious, even life-threatening, pathology for appropriate and timely investigations and management.

Keywords: False localizing signs, raised ICP, intracranial pathology

Neurological signs have been described as ‘false localizing’ if they reflect dysfunction distant or remote from the expected anatomical locus of pathology and hence challenging the traditional clinicoanatomical correlation paradigm on which neurological examination is based.

HISTORY
The notion false localizing signs was first elucidated by James Collier in 1904 on the basis of clinical examination during life and subsequent postmortem studies. Gassel noted false localizing signs to be more common in patients with raised intracranial pressure (ICP). Structural imaging, particularly magnetic resonance imaging (MRI), which gives an opportunity to study pathological anatomy contemporaneous with clinical examination, has provided some new insight into the causes of these signs.

PATHOGENESIS
The pathogenesis of false localizing signs remain uncertain. False localizing signs occur in two contexts: As a consequence of raised ICP, which is symptomatic of intracranial pathology (tumor, hematoma, abscess) or idiopathic (idiopathic intracranial hypertension [IIH]) and with spinal cord lesions. Associated lesions may be intra- or extraparenchymal. The course of the associated disease may be acute (cerebral hemorrhage) or chronic (IIH, tumor). Disturbance of higher mental functions, cranial nerve palsies, hemiparesis, sensory features and muscular atrophy, may all occur as false localizing signs.

FALSE LOCALIZING SIGNS
Cortical Functions
Signs traditionally thought to be of cortical origin, such as aphasia and inattention, may some times occur with exclusively subcortical pathology; conversely exclusively cortical lesions may results in dysarthria. Hemineglect is much commoner with right rather than left parietal lobe lesions. False localizing ipsilateral hemineglect has been reported in patients with posterior fossa tumors like meningioma causing left pontine compression, despite normal imaging of cerebral hemispheres.

Cranial Nerves
Oculomotor Nerve
Unilateral fixed dilated pupil (Hutchinson’s pupil) may occur with an ipsilateral lesion such as an intracerebral hemorrhage, due to transtentorial herniation of the brain compressing the oculomotor nerve against the free edge of the tentorium. Because of the fascicular organization of the fibers within the oculomotor nerve, the externally placed pupillomotor fibers are most vulnerable. Very occasionally, fixed pupil may occur contralateral, and hence false localizing, to cranial
pathology. The exact mechanism for this clinical observation is not known. The mechanism for this third nerve palsy has traditionally been ascribed to extrinsic compression of the third nerve on the margin of the tentorium. An alternative explanation, possibly relevant to false-localizing third nerve palsy, is that raised ICP causes kinking of the nerve over the clivus, just posterior to the clinoid. Another suggestion is that a central mechanism might be responsible, supratentorial pressure causing the brainstem to buckle as it descends because of caudal tethering of the neuraxis at the first dentate ligament (“dynamic axial brainstem distortion”).

Divisional third nerve palsy is usually associated with lesions at the superior orbital fissure or anterior cavernous sinus, where the superior division of the oculomotor nerve passes to the superior rectus and levator palpebrae, and the inferior division to the medial and inferior recti and inferior oblique muscles. Divisional third nerve palsies may sometimes occur with more proximal lesions, presumably as a consequence of the topographic arrangement of the fascicles within the nerve, for example with intrinsic brainstem disease (e.g. stroke) or with pathology in the subarachnoid space where the nerve rootlets emerge from the brainstem (e.g. malignant infiltration).

**Trochlear Nerve**

False localizing fourth nerve palsies, causing diplopia on downward and inward gaze, have occasionally been described in the context of IIH. Trochlear nerve palsy might be overlooked in cases in which other cranial nerves are affected (sixth, third) because the signs are subtle.

**Trigeminal Nerve**

Trigeminal nerve hypofunction (trigeminal sensory neuropathy) or hyperfunction (trigeminal neuralgia) may on occasion be false-localizing, for example in association with IIH or with contralateral pathology, often a tumor. For example, trigeminal neuralgia has been associated with a contralateral chronic calcified subdural hematoma, which caused rotational displacement of the pons, with resolution after removal of the hematoma.

This dysfunction may be hypoactive or hyperactive, manifesting with negative or positive Jacksonian symptoms, respectively; hence there may be trigeminal neuropathy or trigeminal neuralgia. Gassel found motor involvement in only two of eight patients with false-localizing fifth nerve involvement. Arsava et al reported both clinical and electrophysiological evidence of left trigeminal neuropathy in a patient with IIH: Examining the blink reflex, no response was elicited either ipsi- or contralaterally when stimulating the left supraorbital nerve, and although trigeminal motor function was clinically intact, no response was elicited from the left masseter muscle when measuring the latency of the jaw reflex.

As with the idiopathic condition, there has been debate about the pathophysiology of trigeminal neuralgia associated with contralateral tumors. Some favor vascular compression of the nerve root as the proximate cause of paroxysmal ephaptic transmission, whereas others implicate angulations and distortion of the nerve root entry/exit zone as a consequence of displacement of brain tissue caused by an expanding mass lesion in the posterior fossa. In favour of the latter explanation, two cases have been reported in which trigeminal neuralgia was ‘converted’ to trigeminal neuralgia (hence, a lesser degree of dysfunction) following removal of a contralateral posterior fossa tumor. However, other cases have been presented in which trigeminal neuralgia did not resolve after tumor removal alone. Matsuura and Kondo implicate adherence of arachnoid membrane to the nerve as a contributing factor and advocate its resection in order to straighten the nerve axis.

**Abducens Nerve**

Sixth nerve palsies are the most common false-localizing sign of raised ICP. In one series of 101 cases of IIH, 14 cases were noted, 11 unilateral and three bilateral. Stretching of the nerve in its long intracranial course or compression against the petrous ligament or ridge of the petrous temporal bone have been suggested as the mechanism for false-localizing sixth nerve palsy.

**Facial Nerve**

Lower motor neurone type facial weakness has been described in the context of IIH, sometimes occurring bilaterally to cause facial diplegia, usually with concurrent sixth nerve palsy or palsies. Hemifacial spasm has rarely been described with contralateral posterior fossa lesions.

**Vestibulo Cochlear Nerve**

Hearing loss has on occasion been reported as a complication of IIH.

**Multiple Lower Cranial Nerve involvement**

Concurrent false-localizing involvement of multiple cranial nerves has been noted on occasion, for
example, trigeminal, abducens and facial nerves with a contralateral acoustic neuroma, and trigeminal, glossopharyngeal and vagus nerves with a contralateral laterally-placed posterior fossa meningioma.

Motor System

Kernohan’s Notch Syndrome: False-localizing Hemiparesis

A supratentorial lesion, such as acute subdural hematoma, may cause transtentorial herniation of the temporal lobe, with compression of the ipsilateral cerebral peduncle against the tentorial edge; since this is above the pyramidal decussation, a contralateral hemiparesis results. Occasionally, however, the hemiparesis may be ipsilateral to the lesion, and hence false-localizing; this occurs when the contralateral cerebral peduncle is compressed by the free edge of the tentorium. This is the Kernohan-Woltman notch phenomenon, or Kernohan’s notch syndrome. There may be concurrent homolateral third nerve palsy, ipsilateral to the causative lesion.

Brainstem Compression: False-localizing Diaphragm Paralysis

Hemidiaphragmatic paralysis with ipsilateral brainstem (medullary) compression by an aberrant vertebral artery has been described, in the absence of pathology localized to the C3-C5 segments of the spinal cord where phrenic motor neurones originate, hence it a false-localizing sign. Foramen Magnum/Upper Cervical Cord

Paresthesia in the hands with intrinsic hand muscle wasting and distal upper limb areflexia, with or without long tract signs, suggestive of a lower cervical myelopathy may occur with lesions at the foramen magnum or upper cervical cord (‘remote atrophy’).

Lower Cervical/Upper Thoracic Cord

Compressive lower cervical or upper thoracic myelopathy may produce spastic paraplegia with a mid-thoracic sensory level (or ‘girdle sensation’). For example, in one case a spastic paraplegia with a sensory level at T10 was associated with cervical compression from a herniated disc at C5/C6. Radiculopathy

False-localizing radiculopathy may occur in the context of IIH and cerebral venous sinus thrombosis, manifesting as acral paresthesias, backache and radicular pain, and less often with motor deficits, which on occasion may be sufficiently extensive to mimic Guillain-Barré syndrome (flaccid-areflexic quadriplegia). The postulated mechanism for such radiculopathy is mechanical root compression due to elevated cerebrospinal fluid (CSF) pressure.

Cerebellar Syndrome

Frontocerebellar pathway damage, for example, as a result of infarction in the territory of the anterior cerebral artery, may result in incoordination of the contralateral limbs, mimicking cerebellar dysfunction. Suboccipital exploration to search for cerebellar tumors based on these clinical findings was known to occur before the advent of brain imaging.

Pseudo-internuclear Ophthalmoplegia

To describe internuclear ophthalmoplegia, usually indicative of medial longitudinal fasciculus dysfunction, in patients with myasthenia gravis, this ‘pseudo-internuclear ophthalmoplegia’ has also been observed in dermatomyositis.

Pseudoathetosis

Pseudoathetosis or abnormal writhing movements, usually of the fingers, caused by a failure of joint position sense (proprioception). They indicate disruption of the proprioceptive pathway, from peripheral nerve to parietal cortex. It may be mistaken for choreoathetosis. However, these abnormal movements are relatively constant irrespective of whether the eyes are open or closed and occur in the absence of proprioceptive loss.

Pseudosyringomyelia

Pseudosyringomyelia” has been used to describe a selective loss of pain and temperature sensation with relative preservation of vibration and position sense seen in amyloid polyneuropathy and Tangier disease, (a small fibre sensory neuropathy), in the absence of any spinal cord pathology, and hence false-localizing.

DISCUSSION

False localizing neurological signs have presented significant challenges to clinical neurologists. In the era before neuroimaging, operations were sometimes performed on, and treatments administered to, the wrong side based on these signs.

For the practicing neurologist, an awareness of the possibility of false localizing signs, and knowledge of the situations in which they are most likely to occur, is necessary to heighten the index of clinical suspicion, so that the possible pathological import of false localizing signs is not missed. The pathophysiology of many false
localizing signs is still poorly, if at all, understood.\textsuperscript{1,33} The preponderant association with extrinsic mass lesions, such as intracranial tumors (especially meningioma), subdural hematoma, and intervertebral disc prolapse, has long been noted, although intrinsic lesions may certainly be responsible on occasion.\textsuperscript{10,14} Some of these pathologies exert their effects acutely, whereas for others (for example, meningiomas) it is their slow growth which is implicated. The possibility of multifactorial pathophysiology therefore seems likely.

Most importantly, since false localizing signs may be indicative of serious, even life threatening, pathology within neural pathways, awareness of them and the situations in which they occur, will facilitate appropriate and timely investigation and management.

REFERENCES

The Future is Predictable... ⏰

The Future is ALARMING!!!

DATE: 14TH NOV, 2030 A.D.
LOCATION: INDIA (THE DIABETIC CAPITAL OF THE WORLD)
POPULATION: 1,100 CRORES
DIABETIC POPULATION: 289 CRORES & STILL COUNTING...

Let’s challenge the future...
Let’s control the rising incidences of diabetes
With the comprehensive range of products...

GLYCIPHAGE®
(Metformin 250 mg Tablets, 500 mg & 850 mg Press Tablets)

GLYCIPHAGE® SR
(Metformin 500mg & 1gm Sustained Release Tablets)

GLYCIPHAGE® G
1mg
2mg
(Metformin SR 500mg + Glimepiride 1mg / 2mg Tablets)

GLYCIPHAGE® FORTE
(Metformin SR 1000mg + Glimepiride 1mg / 2mg Tablets)

GLYCIPHAGE® P
15mg
30mg
(Metformin SR 500mg + Pioglitazone 15mg / 30mg Tablets)

GLYCIPHAGE® PG
1mg
2mg
(Metformin 500 mg SR + Pioglitazone 15 mg + Glimepiride 1mg/2mg)

Voliphage™
(Voglibose 0.2 mg / 0.3 mg Tablets)

Voliphage-M™
1.2 mg / 1.3 mg
(Metformin S.R. 500 mg + Voglibose 0.2 mg / 0.3 mg Tablets)

DIABETIX
A Division of FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.

DIAVIT™ Plus
Subscribe to all Journals
YOU PAY ₹ 14,200/-

Yes, I am interested in subscribing to the *Institutional Combo Package for one year (Institutional) (Individual)

<table>
<thead>
<tr>
<th>JOURNALS</th>
<th>ISSUES/YEAR</th>
<th>INSTITUTIONAL (₹ Amount)</th>
<th>INDIVIDUAL (₹ Amount)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indian Journal of Clinical Practice</td>
<td>12</td>
<td>4,000/-</td>
<td>1,650/-</td>
</tr>
<tr>
<td>AOCC</td>
<td>12</td>
<td>4,000/-</td>
<td>1,650/-</td>
</tr>
<tr>
<td>The Asian Journal of Diabetology</td>
<td>4</td>
<td>1,200/-</td>
<td>550/-</td>
</tr>
<tr>
<td>Asian Journal of Obs &amp; Gynaec Practice</td>
<td>4</td>
<td>1,200/-</td>
<td>550/-</td>
</tr>
<tr>
<td>Asian Journal of Paediatric Practice</td>
<td>4</td>
<td>1,200/-</td>
<td>550/-</td>
</tr>
<tr>
<td>Asian Journal of Ear, Nose &amp; Throat</td>
<td>4</td>
<td>1,200/-</td>
<td>550/-</td>
</tr>
<tr>
<td>Journal of Applied Dentistry</td>
<td>4</td>
<td>1,200/-</td>
<td>550/-</td>
</tr>
</tbody>
</table>

Payment information:

Name: .......................................................... Pay Amount: ..........................................................
Speciality: ..........................................................
Address: ..........................................................
Country: .......................................................... State: ..........................................................
Pincode: ..........................................................
Telephone: ..........................................................
E-mail: ..........................................................

Dated (dd/mm/yyyy): ..........................................................
Cheque or DD No.: ..........................................................

Total ₹15,200/- for 1 Year

Cheques/DD should be drawn in favor of “M/s IJCP Publications Ltd.”
What Makes People Think and Behave Differently? Clues Provided by Brain Research

Differences in the physical connections of the brain are at the root of what make people think and behave differently from one another. Researchers reporting in the Cell Press journal Neuron shed new light on the details of this phenomenon, mapping the exact brain regions where individual differences occur. Their findings reveal that individuals' brain connectivity varies more in areas that relate to integrating information than in areas for initial perception of the world.

The researchers discovered that the brain regions devoted to control and attention displayed a greater difference in connectivity across individuals than the regions dedicated to our senses like touch and sight. When they looked at other published studies, the investigators found that brain regions previously shown to relate to individual differences in cognition and behavior overlap with the regions identified in this study to have high variability among individuals. The researchers were therefore able to pinpoint the areas of the brain where variable connectivity causes people to think and behave differently from one another. (Source: Science Daily)

FDA: Alzheimer Drugs must Show Clinical Benefit

In a long-awaited draft guidance document, the FDA said it would not accept biomarker or imaging-based outcomes as a primary endpoint in pivotal trials for Alzheimer’s disease drugs.

The primary efficacy measure for proposed disease-modifying therapies must reflect a benefit in patients’ cognition and/or ability to function, the agency indicated.

In fact, the FDA would prefer that sponsors of Alzheimer’s disease therapies include both types of clinical outcomes in their primary endpoints.

"Clinical trials in the dementia stage of AD (Alzheimer’s disease) should use a coprimary outcome measure approach in which a drug demonstrates efficacy on both a cognitive and a functional or global assessment scale,” the draft guidance said. (Source: MedPage Today)