Physiological signs

False localising signs

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Neurological signs have been described as “false localising” if they reflect dysfunction distant or remote from the expected anatomical locus of pathology, hence challenging the traditional clinicanoanatomical correlation paradigm on which neurological examination is based. False localising signs occur in two major contexts: as a consequence of raised intracranial pressure, and with spinal cord lesions. Cranial nerve palsies (especially sixth nerve palsy), hemiparesis, sensory features (such as truncal sensory levels), and muscle atrophy, may all occur as false localising signs. Awareness that signs may be false localising has implications for diagnostic investigation.

The clinical examination of the nervous system is based on the premise of clinicanoanatomical correlation, with a particular neurological sign indicating pathology at a specific locus or pathway within the nervous system. Occasionally, however, this semiology “breaks down”, in that neurological signs may reflect pathology distant from the expected anatomical locus.

The notion of “false localising signs” was first elucidated by James Collier in 1904: on the basis of clinical examination during life and subsequent postmortem studies, he noted false localising signs in 20 of 161 consecutive cases of intracranial tumour examined pathologically, most occurring in patients with supratentorial lesions. Despite this high frequency (12.4%), Collier felt false localising signs were being observed less frequently because of the earlier diagnosis of tumours, a theme reiterated by later authors, implying that such signs are a late feature in the natural history of tumours. Gassel noted false localising signs to be more common in patients with raised intracranial pressure.

As there have been few previous reviews of false localising signs, this article attempts a brief overview of these phenomena and their possible pathophysiology. It does not aim to provide an exhaustive review of publications on the subject, most of which are case reports or small case series rather than systematic studies. Rather, it selects illustrative examples, particularly where these elucidate possible pathophysiological mechanisms.

Structural brain imaging, particularly magnetic resonance imaging (MRI), affording as it does the opportunity to study pathological anatomy contemporaneous with clinical examination, has provided some new insights into the causes of these signs.

False localising signs associated with intracranial lesions

Sixth nerve palsy

Sixth nerve palsy, either unilateral or bilateral, is the classic example of a false localising sign. It occurs in the context of raised intracranial pressure of whatever cause (supratentorial or infratentorial space occupying lesion, idiopathic intracranial hypertension, cerebral venous sinus thrombosis). It was the most common of the false localising signs observed by Collier (12/20) in cases of intracranial tumour. In a retrospective review of 101 cases of idiopathic intracranial hypertension (IIH), Round and Keane noted 14 cases (11 unilateral, three bilateral). IIH with sixth nerve palsy in the absence of papilloedema has also been reported.

The pathophysiological mechanism of sixth nerve palsy with increased intracranial pressure has traditionally been said to be stretching of the nerve in its long intracranial course, or compression against the petrous ligament or the ridge of the petrous temporal bone. Collier, however, was “unable to accept this explanation”, his view being that since the sixth nerve emerges straight forward from the brain stem, whereas other cranial nerves emerge obliquely or transversely, it is more liable to the mechanical effects of backward brain stem displacement by intracranial space occupying lesions.

Fifth and seventh nerve false localising signs

Dysfunction of the fifth and seventh cranial nerves has also been reported with raised intracranial pressure. This dysfunction may be hypoactive or hyperactive, manifesting with negative or positive Jacksonian symptoms, respectively; hence there may be trigeminal neuropathy or trigeminal neuralgia. Facial palsy of lower motor neurone type, or hemifacial spasm. Fifth and seventh nerve involvement has been recorded in the context of posterior fossa neoplasms or more diffuse neoplastic disease, and with IIH. Reports of false localising seventh nerve palsies suggest they most often occur at the same time as, or after, the development of sixth nerve palsies. Brain stem distortion resulting in traction on cranial nerves has been suggested as the pathophysiological mechanism in tumour associated cases, but this seems a less compelling explanation for IIH cases.

Collier suggested that motor involvement preceded sensory features in fifth nerve palsy, but the clinical features reported in subsequent cases.

Abbreviations: IIH, intracranial hypertension; MRI, magnetic resonance imaging.
suggest sensory findings are more prominent.\textsuperscript{7-10} Gassel found motor involvement in only two of eight patients with false localising third nerve involvement.\textsuperscript{11,12} Aranha et al reported both clinical and electrophysiological evidence of left trigeminal neuropathy in a patient with IH: 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.\textsuperscript{13}

Unlike fifth and seventh nerve palsies, trigeminal neuralgia and hemifacial spasm have only been reported in the context of posterior fossa mass lesions, most usually tumours,\textsuperscript{14,15} but also chronic calcified subdural haematoma. As with the idiopathic condition, there has been debate about the pathophysiology of trigeminal neuralgia associated with contralateral tumours. Some favour vascular compression of the nerve root as the proximate cause of paroxysmal ephaptic transmission,\textsuperscript{16} whereas others implicate angulation 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.\textsuperscript{17,18} In favour of the latter explanation, two cases have been reported in which trigeminal neuropathy was “converted” to trigeminal neuralgia (hence, a lesser degree of dysfunction) following removal of a contralateral posterior fossa tumour.\textsuperscript{11,12} However, other cases have been presented in which trigeminal neuralgia did not resolve after tumour removal alone.\textsuperscript{19} Matsurura and Kondo implicate adherence of arachnoid membrane to the nerve as a contributory factor and advocate its resection in order to straighten the nerve axis.\textsuperscript{17}

Hemifacial spasm as a false localising sign of posterior fossa tumour seems altogether rarer than trigeminal neuralgia, indeed exceptional.\textsuperscript{16,20} As with trigeminal neuralgia, the question of whether the false localising sign follows neurovascular compression or mechanical distortion remains open.

Third nerve palsy and Kernohan’s notch phenomenon

Transtentorial herniation of the medial temporal lobe (uncus), as a consequence of shift of intracranial contents secondary to raised intracranial pressure, may be associated with third nerve palsy. Perhaps because of the intra-axial fascicular arrangement of fibres within the third nerve, the peripherally located pupilloc Jonckerian fibres are most vulnerable, such that unilateral mydriasis (“Hutchinson’s pupil”) may be the earliest sign. That the consequent fixed dilated pupil is ipsilateral to the lesion may be the earliest consistent sign of herniation.\textsuperscript{1}

Unilateral papilloedema may be described as false localising when associated with contralateral visual loss and optic atrophy due to subfrontal or middle cranial fossa en plaque meningioma (Foster-Kennedy syndrome).\textsuperscript{21} Papilloedema resulting from high CSF protein concentration may initiate an inappropriate search for an intracranial mass lesion.

Frontal ataxia, a cerebellar type of ataxia resulting from lesions of the contralateral frontal cortex in which fibres of the corticopontocerebellar pathway are said to be interrupted, is also a false localising sign, but its frequency is uncertain. Round and Keane reported four patients in their series of 101 with IH to have “ataxia”, meaning a transient postural giddiness with unsteadiness when beginning to walk; whether this was “frontal ataxia” is not clear. Although functional imaging studies have shown reduced metabolism in the cerebellar hemisphere contralateral to a middle cerebral artery territory infarct (“crossed cerebellar diaschisis”),\textsuperscript{22} this is not generally accompanied by clinical signs. Cerebellar ataxia contralateral to a posterior fossa mass lesion has been reported.\textsuperscript{23}

Exceptionally, false localising ninth and tenth nerve palsies have been described with posterior fossa tumour.\textsuperscript{24} All such reports predate modern structural brain imaging.

FALSE LOCALISING SIGNS ASSOCIATED WITH SPINAL CORD LESIONS

Foramen magnum and upper cervical cord lesions

Lesions at the level of the foramen magnum may produce, in addition to suboccipital and neck pain and upper motor neurone (long tract) signs, false localising signs: paraesthesia in the hands and lower motor neurone signs in the upper limbs.\textsuperscript{25} The wasting (“remote atrophy”), weakness, and areflexia may suggest the involvement of cervical cord segments well below the level of the foramen magnum lesion, hence are false localising. Similarly, a syndrome of “numb and clumsy hands” has been described with midline cervical disc protrusions at the C3/C4 level; concurrent with numbness of fingertips and palms, there may be a tightening sensation at mid-thoracic level.\textsuperscript{26} Cervical spinal cord lesions (cervical spondylosis, herniated disc) at or above the level of C4 in which finger and hand dysesthesia with hand muscle atrophy preceded limb spasticity or gait disturbance have also been reported.\textsuperscript{27}

There is currently no compelling pathophysiological explanation for these false localising signs, but three principal mechanisms have been invoked: arterial, venous, and mechanical.\textsuperscript{28} The arterial hypothesis postulates that tumour in some way compromises descending anterior spinal artery blood supply to the lower cervical cord with resultant focal ischaemia. However, this would also seem to require insufficiency of
radicular spinal arteries entering intervertebral foramina to join anterior spinal artery. Moreover, there is some evidence that blood flows rostrally rather than caudally in the anterior spinal artery; the low pressure venous system would seem inherently more vulnerable to the effects of compression than the arterial system, with resultant tissue stasis and hypoxia perhaps causing the clinically observed neurological dysfunction. Mechanical stresses within the spinal cord, consequent perhaps on the conjunction of extrinsic compression with the anchoring of the spinal cord by the dentate ligaments, have also been suggested to account for remote signs. The paucity of pathological material has made it difficult to obtain direct evidence in support of any of these hypotheses. In all cases, the differential decussation of corticospinal tract fibres to fore and hind limbs and the lamination of sensory tracts may be prerequisites for the clinical features. 2

**Lower cervical cord and upper thoracic cord lesions**

Because of the anatomical decussation of spinothalamic tract fibres two or three segments above the level at which they enter the spinal cord from their respective dermatomes, it is not unusual for sensory levels two or three segments distant from the level of cord pathology to be observed clinically. However, more distant sensory and motor signs may be observed with cord pathology, whose explanation is altogether more challenging. Compressive cervical myelopathy may produce a false localising thoracic sensory level, 3 sometimes called a mid thoracic girdle sensation, 4 in addition to lower limb weakness and hyperreflexia. Similarly, lumbar spinal disease may be simulated by more rostral pathology, for example, urinary retention, leg weakness, and lumbar sensory findings may be the presenting features of high thoracic cord compression, with anulcerodirectional discrepancy of as much as 11 segments. 5

As with foramen magnum and upper cervical cord lesions, opinion is divided as to the pathophysiological explanation for these observations. Comparing axial MR images of the cervical cord in 10 patients with compressive cervical myelopathy, five with girdle signs and five without, Ochiai et al noted that the midline ventral portion of the cervical cord was more markedly compressed in those with the false localising sensory level. This observation led them to suggest that ischaemia in the watershed zone of the anterior spinal artery, affecting the medial portion of the laminations of the spinothalamic tract, was the causative mechanism for the girdle sensation, rather than direct compression of spinothalamic fibres. 6 Jamieson et al, however, favoured venous obstruction with ensuing intramedullary stasis and hypoxia as the explanation for remote phenomena. 7 Of course, different cases may have different pathogenesis, and/or more than one mechanism may be operating in any one case.

**OTHER “FALSE LOCALISING” SIGNS**

The “false localising” terminology has also been used in other contexts, for example to describe interinuclear ophthalmoplegia, usually indicative of medial longitudinal fascicular dysfunction, in patients with myasthenia gravis; 8 this “pseudo-interinuclear ophthalmoplegia” has also been observed in dermatomyositis. Similarly, myasthenic nystagmus may suggest a brain stem lesion.

Other “pseudo-signs” are described which might be encompassed by the “false localising” rubric, 9 such as pseudo-(choreo)athetosis and pseudoastereognosis, which may occur with high cervical cord lesions rather than intracranial pathology. Signs traditionally thought to be of cortical origin, such as aphasia and inattention, may sometimes occur with exclusively subcortical pathology; conversely, exclusively cortical lesions may sometimes result in dysarthria. Sensory stimuli (tactile, visual) may be detected contralateral to the stigmated side (alloaesthesia, allochiria). “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 localising.

**DISCUSSION**

False localising 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. 2

Thankfully practice is now somewhat easier with the benefit of structural imaging, although confusion may still occur, and the appropriate part of the central nervous system may not be imaged. 3 For the practising neurologist, an awareness of the possibility of false localising 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 localising signs is not missed.

The pathophysiology of many false localising signs is still poorly, if at all, understood. 10 11 The preponderant association with extrinsic mass lesions, such as intracranial tumours (especially meningioma), subdural haematoma, and intervertebral disc prolapse, has long been noted, although intrinsic lesions may certainly be responsible on occasion. 10 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.

After almost one hundred years use, the term “false localising sign” is thoroughly ingrained in clinical teaching, although it is important to be aware that such signs are in no way “false”. The practical implication of the name is that such signs cannot be relied on when assessing clinical localisation, which challenges traditional clinicoanatomical correlation. “Diaschisis” is a technical term for dysfunction distant from pathology, particularly familiar in the field of functional imaging. 12 However, it is associated with the notion of “transneural depression”, which may not be relevant to the pathophysiology of these signs, besides being something of a mouthful for clinical practice. Perhaps “distant signs” or “remote signs” would fit the bill, though lacking any emotive resonance. Most importantly, since false localising 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.

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**REFERENCES**


Intracranial hypertension secondary to giant arachnoid granulations

We present a case of intracranial hypertension in a non-obese male in whom the only finding resulting from additional tests was the presence of giant arachnoid granulations in lateral sinuses. A 51 year old man presented episodes of transient obstructions of vision in the left eye lasting a few seconds. On general physical examination, the patient was not obese (170 cm height, 70 kg weight) and no relevant findings were detected. During neurologic examination a complete left papilledema was detected. The fundus had a normal pallor and papillomacular bundle. The optic disc was normal in appearance, and the left papillomacular bundle was not visible. The left macula was not visible at all, but a small patch of retina was visible just posterior to the fovea.

During neurologic examination a complete left papilledema was detected. The fundus had a normal pallor and papillomacular bundle. The optic disc was normal in appearance, and the left papillomacular bundle was not visible. The left macula was not visible at all, but a small patch of retina was visible just posterior to the fovea. The patient had no visual symptoms.

Arachnoid granulations are present in a variable percentage of the population (0.3-24%) and very rarely do they produce any symptoms. Their function is not wholly understood, although cerebrospinal fluid resorption seems to be the most likely. They increase in size with age so that the granulations may protrude into the lumen of the venous sinus and, in theory at least, dilate it and obstruct venous flow. If this occurred it could result in intracranial hypertension, as we suggest in our case.

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