LETTER TO THE EDITOR

Silent or non-clinical infarct-like lesions in the posterior circulation territory in migraine: brain hypoperfusion or hyperperfusion?

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Kruit et al. (2005) described infratentorial predominantly cerebellar silent or non-clinical infarct-like lesions in a cohort of migraine patients with or without aura; these authors concluded that such discrete lesions represent the effects of episodic focal brain hypoperfusion coupled to embolic damage and elaborated upon a specific pathophysiological role for the cerebellum. While Kruit et al. (2005) attributed brain hypoperfusion to cortical spreading depression (CSD) there is a significant unbridged conceptual gap between CSD and cerebral oligoamia (Pearce, 1985; Blau, 1992; Vijayan, 1995). Conversely, a large, increasing body of evidence suggests that CSD has a neuronal protective influence (Thompson and Hakim, 2005; Yanamoto et al., 2005). The case for a primary pathogenetic role for the cerebellum in migraine is far weaker than that for the occipital cortex. Nevertheless, several lines of pharmacological evidence do not support a central brain neuronal origin for migraine (Gupta, 2005a).

In contrast to the relatively transient hypoperfusion that occurs in migraine, as reviewed by Kruit et al. (2005), a pronounced, sustained diffuse brain hyperperfusion appears to be a consistent feature of migraine attacks, both with and without aura (Kobari et al., 1989). In the elucidation of small brain ‘arteriolar’ lesions including deep white matter lesions (DWML) and lacunar infarcts, a crucial anatomic difference between deep arterioles embedded in brain tissue and more superficial cortical arterioles needs to be considered (Gupta, 2005b). In states of sudden profound cerebral hyperperfusion, lenticular or other deeper arterioles with limited distensibility are likely to be more susceptible to rheological barotraumas and undergo segmental arteriolar wall disorganization (lipohyalinosis or fibrinoid necrosis). Disruption of the blood–brain barrier (BBB) by hypoperfusion-induced necrosis or hyperperfusion-induced pressure diapedesis at the arteriolar or capillary levels probably produces discrete but identical MRI lesions; detection of changes by functional neuroimaging during primary headaches offers no clue as to the nature of the underlying physiological process. A cross-sectional study such as that of Kruit et al. (2005) using a single brain MRI cannot distinguish between persistent (permanent) DWML induced by hypoperfusion (infarcts) and transient lesions induced by hyperperfusion (infarct-like). In contrast to brain infarcts—ischaeamic or embolic—hyperperfusion-associated DWML are likely to be reversible, a feature which can be studied only through serial neuroimaging.

The particular propensity of the brain posterior circulation territory to manifest infarcts as well as infarct-like lesions in migraine remains unexplained. Neuroanatomically, two features appear relevant: (i) the posterior cerebral artery is especially labile at its origin and (ii) the occipital visual cortex has a dense innervation by the intrinsic (ascending) autonomic nervous system—noradrenergic and serotoninergic (Lance, 1990). The tonic vasoconstriction maintained in the posterior circulation territory probably explains the occurrence of ischaemic infarcts in this region in migraine. Paradoxically, the same neuroanatomical feature might maximally predispose the deeper embedded arteries of the posterior circulation territory to pressure diapedesis—non-ischaemic infarct-like lesions—during the profuse and sustained vasodilatation that characterizes migraine attacks. Secondly, a focal ischaemic-embolic aetiology is quite unlikely to explain a shower or cluster of MRI lesions as observed by Kruit et al. (2005); in contrast, a diffuse hyperperfusion likely disrupts the BBB at multiple sites and can generate several infarct-like lesions. Thirdly, non-selective beta-blockers are well known to increase peripheral resistance, including Raynaud’s phenomenon. Propranolol, the gold standard migraine prophylactic agent, would enhance vasoconstriction in the brain.
circulation. In the context of the putative role for embolic damage in migraine patients (Kruit et al., 2005), propranolol itself stimulates platelet aggregation (Joseph et al., 1988). The platelet-related pro-thrombotic tendency during propranolol therapy also does not appear to be clinically relevant in migraine. Fourthly, it is not known whether silent infarct-like lesions predispose to or are associated with the development of clinically significant infarct-lesions. Finally, migraine patients with posterior circulation infarct-like lesions tend to have a higher attack frequency and are more likely to have consulted a physician (Kruit et al., 2005). Since such patients are also more likely to be receiving migraine prophylactic therapy, the absence of a drug history is possibly the most important confounding feature of the index study. While beta-blockers generally maintain or enhance brain vasoconstriction, calcium-channel antagonists are potent vasodilators that lessen the likelihood of infarcts but might increase the tendency to develop infarct-like DWML. If drugs that either decrease or increase brain perfusion can prevent migraine, it appears reasonable to conclude that regional cerebral blood flow anomalies are unlikely to be primarily involved in its pathogenesis. Similar to CSD and regional changes in cerebral circulation, neither the aura nor the headache signals the true beginning of the migraine attack; onset of migraine lies in the prodromal and the ‘pre-prodromal’ phases.

Pathophysiological similarity between brain infarct-like lesions and infarcts, as suggested by Kruit et al. (2005), is debatable. Theoretically as well as practically, it is important to underscore the differences between infarcts and infarct-like lesions in migraine. To acquire biological significance and to deepen our understanding of causal mechanisms, epidemiological data must be integrated into relevant clinical evidences and basic sciences tenets.

References