Chapter 87

Anatomy and Pathology of Cluster Headaches

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The location of maximal pain in cluster headache (CH) is strikingly similar in almost every sufferer: it is felt deep in or behind the orbit on one side. The signs of disturbed autonomic function in the eye, nose, and facial skin are also closely linked to the pain, both spatially and temporally. This points to deep orbital or retro-orbital structures as being affected in the disease. The tendency to develop CH on the other half of the face is 200 times higher than for an individual to develop the disease at all (33). This indicates that a structure with anatomic connections over the midline is involved.

CH persists, and may also arise, after ipsilateral enucleation (18). Likewise, CH may even arise after ipsilateral orbital exenteration (6,23). This demonstrates that CH may arise after an operation in this area but that the pain of CH does not originate in the eye and that intact structures in the orbit are not necessary for the formation of attacks. Thus, pain appears to originate from retro-orbital structures, except in cases with referred pain (see below).

PATHOLOGY OF IDIOPATHIC CASES

Epidemiologic studies reveal a marked correlation between CH and prior head trauma (5,6). Narrow nasal passages, such as a deviated nasal septum, are often found on the painful side in CH sufferers (7,8). Surgical resections in this area, to eliminate narrow conditions, are sometimes beneficial (7). Craniometric measures in CH suggest narrowness of the cavernous sinus/hypophyseal fossa region (8). These findings may represent constitutional predisposing factors for CH. Investigations with magnetic resonance imaging (MRI) of the cavernous sinus region outside of CH attacks has not revealed any pathologic changes (9).

By the aid of voxel-based morphometric analysis of MRI scans, an increase in tissue volume within the posterior hypothalamic area has been found in CH sufferers (10). This finding was bilateral, remained outside periods of attacks, and was interpreted as an increase in neuronal density. The area is similar or identical to local findings during attacks of an ipsilateral increase in blood flow (see neuroimaging of cluster headache), as a cause or a consequence of pain.

PATHOLOGY OF SYMPTOMATIC CASES

Several symptomatic cases have been described in which CH-like attacks have evolved secondary to the growth of an intracranial expansive process, ipsilaterally, or in the midline: orbitosphenoidal aspergillus infection (11), parasellar meningioma (12), adenoma of the pituitary gland (12,13), calcified lesion in the region of the third ventricle (14), aneurysm of the anterior or posterior communicating artery (15,16), dilated ipsilateral and aneurysmatic contralateral internal carotid artery (ICA) intracranially (15), granulomatous tissue in the cavernous sinus (17) epidermoid tumor in the clivus expanding rostrally to the suprasellar cistern (18), large arteriovenous malformations in the ipsilateral frontal, temporal, parietotemporal, or occipital lobes (19–22), meningioma or inflammatory myofibroblastic tumor on the undersurface of the tentorium cerebelli (23,24), and upper cervical meningioma (2).

Thus, when restricted to a small area, most of these processes are located near the midline in the middle fossa of the skull base, where the hypophysis is surrounded by the cavernous sinus region. The cases from the posterior brain and cervical regions (innervated by pain fibers from C1–C3 levels) may be explained as referred pain.

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THE CAVERNOUS SINUS/HYPOPHYSEAL REGION: ANATOMIC CONSIDERATIONS

Knowledge about the local anatomy, including pathways of autonomic and sensory pain fibers, is important to understand why a process in the cavernous sinus/hypophyseal region can contribute to CH pain as well as accompanying symptoms indicative of sympathetic hypofunction and parasympathetic hyperfunction.

Hypofunction of Sympathetic Nerves

Pharmacologic tests have shown that most CH sufferers, throughout the period of attacks, have a partial lesion of the sympathetic fibers to the eye and forehead skin, ipsilateral to pain and sometimes bilateral. The majority of studies locate this lesion to the peripheral (third) neuron. These sympathetic fibers run along the surface of the ICA through the carotid canal. Branches form a delicate plexus to innervate the ICA wall and its branches as the artery becomes intracranial, whereas a further branching takes place after the ICA has entered the cavernous sinus region. Here branches are issued to (a) the ophthalmic nerve to reach the eye and forehead skin (25), (b) the oculomotor nerve to reach the smooth muscle portion of the levator palpebrae muscle, and (c) the tentorial nerve to reach the epiphysis and the dural sinuses and veins (26).

ICA dissection as well as carotid thromboendarterectomy often causes lesions of these sympathetic fibers in the ICA wall. CH can start in connection with an ICA dissection (27,28). CH-like attacks are sometimes present during the first few weeks after carotid thromboendarterectomy (29). CH can reappear after several years in silence following carotid thromboendarterectomy (30). All of these observations indicate that a disturbed local sympathetic nerve function is of crucial importance for developing CH.

Hyperactivity of Parasympathetic Nerves

Conjunctival injection, lacrimation, rhinorrhea, and nasal congestion on the painful side during attacks may indicate parasympathetic hyperfunction. Sphenopalatine ganglion blockade is sometimes beneficial in CH (31). Parasympathetic fibers to the intracranial ICA and its branches reach the ICA wall through (a) the deep petrosal nerve from a ganglion along the greater superficial petrosal nerve and (b) rami orbitales from the sphenopalatine ganglion that run through the supraorbital fissure to the cavernous region (32–34).

Hyperactivity of Sensory Nerves

Pain is intense in CH and usually located within the distribution area of the ophthalmic division of the trigeminal nerve. The pain threshold is reduced within this area during CH periods (35). Sensory fibers to the intracranial ICA and its branches in humans are mainly derived from the ophthalmic trigeminal division, leaving the ophthalmic trunk shortly distal to the ganglion and running a short course through the cavernous sinus region (33). Some of the fibers join and follow the abducent nerve to innervate the basilar artery and branches (32,33). The greater superficial petrosal nerve also contributes with sensory fibers to the ICA tree (33,34).

It is highly likely that the trigeminal and facial sensory fibers also innervate the walls of the cavernous sinus. Other dural sinuses are densely innervated by pain fibers from the tentorial nerve (36,37). The sympathetic, parasympathetic, and sensory fibers gather as a plexus in the connective tissue of the cavernous sinus/hypophyseal region before they follow each other to the various destinations (26,32–34). Thus, nerves in this region appear to be of importance to produce the major symptoms of CH.

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