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Chapter 92

Symptomatology of Cluster Headaches

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DEFINITION OF CLUSTER HEADACHE

IHS Code and Diagnosis

3.1 Cluster headache
3.1.1. Episodic cluster headache
3.1.2. Chronic cluster headache

WHO Code and Diagnosis

G44.0 Cluster headache syndrome

Short Description

According to the International Classification of Headache Disorders II (ICHD-II) (22), cluster headaches are attacks of severe, strictly unilateral pain that is orbital, supraorbital, temporal, or any combination of these sites lasting 15 to 180 minutes and occurring from once every other day to eight times a day. The attacks are associated with one or more of the following, all of which are ipsilateral: conjunctival injection, lacrimation, nasal congestion, rhinorrhea, forehead and facial sweating, miosis, ptosis, and eyelid edema. Most patients are restless or agitated during an attack.

Attacks occur in series lasting for weeks or months (*cluster periods*) separated by remission periods, usually lasting months or years. Cluster headache is most often episodic, but about 10 to 15% of cases are chronic wherein patients suffer attacks recurrently for at least a year with remissions lasting less than 1 month (14). The symptomatology of the chronic and episodic form is otherwise almost identical.

Previously Used Terms

Erythroprosopalgia of Bing
Ciliary or migrainous neuralgia (of Harris)
Erythromelalgia of the head
Horton headache
Histaminic cephalalgia
Petrosal neuralgia (of Gardner)
Sphenopalatine
Vidian and Sluder neuralgia
Hemicrania periodica neuralgiformis

The IHS diagnostic criteria for cluster headache according to ICHD-II are as follows (22):

A. At least five attacks fulfilling B through D.
B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15 to 180 minutes if untreated.
C. Headache is accompanied by at least one of the following:
  1. ipsilateral conjunctival injection and/or lacrimation;
  2. ipsilateral nasal congestion and/or rhinorrhea;
  3. ipsilateral eyelid edema;
  4. ipsilateral forehead and facial sweating;
  5. ipsilateral miosis and/or ptosis; or
  6. a sense of restlessness or agitation.
D. Attacks have a frequency from one every other day to eight per day.
E. Not attributed to another disorder.

PREMONITORY SYMPTOMS

Nonpainful symptoms may occur minutes to weeks before the pain of a cluster headache. Some authors refer to the symptoms occurring days to weeks before a cluster period as *premonitory* and symptoms occurring minutes to hours before an individual attack *prodromal* (5,48). These symptoms may include lethargy, elation, irritability, paresthesia, nausea, and strange sensations throughout the body. Patients also may experience sensations in the area of subsequent pain, including awareness, twinges, pressure, tingling, or pulsations (5). The line between *prodrome* and *premonitory* can be indistinct and

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the ICHD-II has discouraged the use of *prodrome* to avoid confusion.

CHARACTERISTICS OF INDIVIDUAL ATTACKS

Cluster headache attacks include recurrent bouts of extremely severe pain in association with prominent signs of cranial autonomic activation, both of which typically occur in a cyclical, or periodic, fashion. Wilfred Harris' and Bayard Horton's observations from 1926 and 1939, respectively were key in making the clinical phenotype known to the medical world (21,25).

CLINICAL MANIFESTATIONS OF PAIN

In the majority of cases, pain starts in the retro-orbital, supraorbital, or temporal regions, but it may radiate to the forehead, upper or lower jaw, nostril, ear, half of the head, and, in some cases, the ipsilateral neck or shoulder (Fig. 92-1. Attacks of infraorbital as opposed to only supraorbital pain are sometimes distinguished as *lower* and *upper cluster headache* with higher propensity for autonomic symptoms in the former (6). In the great majority of patients, the pain of cluster headache always affects the same side of the head; however, up to 14% of patients may experience a side shift with the pain during a cluster period, whereas 18% may have side shifts from one cluster period to the next (3). During attacks and more rarely between attacks, patients may be supersensitive to touch in the symptomatic area.

The attack often begins as a vague discomfort and rapidly increases to excruciating pain, reaching maximal intensity within 9 minutes of onset in 86% of sufferers (66). Cluster headache has often been described as the most painful primary headache syndrome. Patients have been known to commit suicide during attacks, justifying the moniker of "suicide headache." The quality of pain is constant, boring, pressing, or burning when reaching its peak. At times subjects report a feeling of a "hot poker" in the eye or an extremely severe pressure within or behind the eye. A minority (30%) describe the pain as throbbing or pulsating. However, sometimes it cannot be described or classified, and in some other cases it may have a mixed

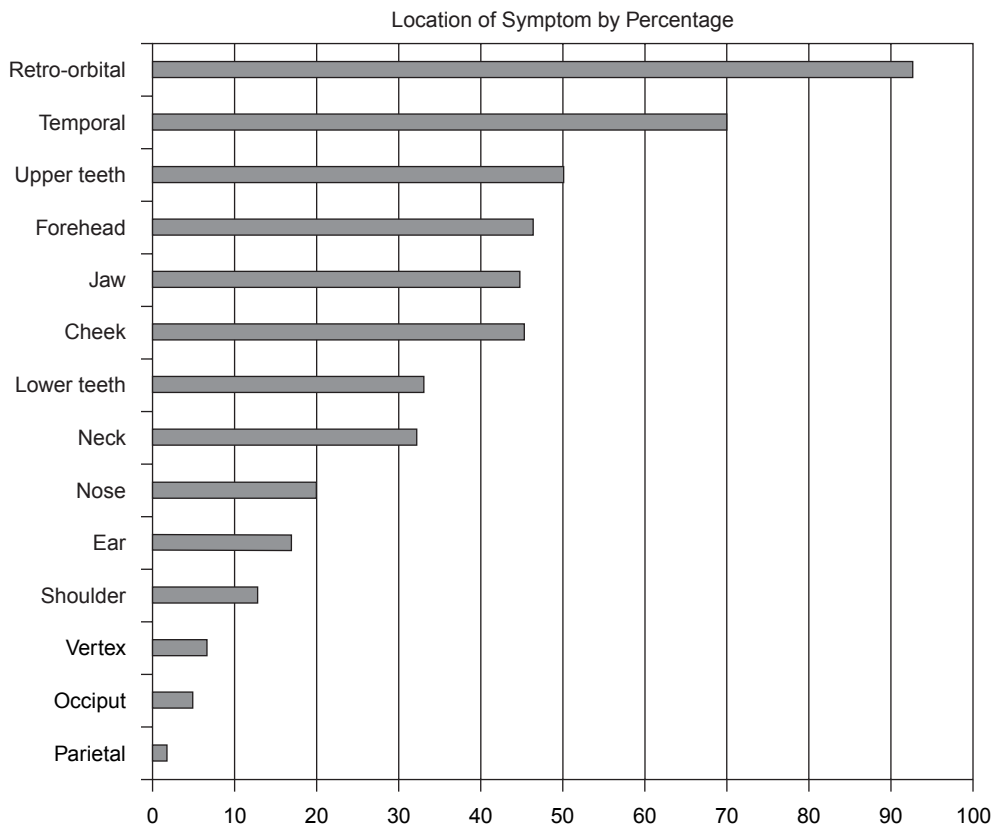

FIGURE 92-1. Location of pain during cluster headache attacks by percentage ($N = 230$ patients). Adapted from Bahra et al. (3).

Retro-orbital 92; Temporal 70; Upper Teeth 50; Forehead 46; Jaw 45; Cheek 45; Lower teeth 32; Neck 31; Nose 20; Ear 17; Shoulder 13; Vertex 7; Occiput 6; Parietal 1.

quality (throbbing and "neuralgic"). Sudden jabs of intense pain lasting 1 to 2 seconds also may be experienced in the symptomatic area during the attack.

The severity of attacks usually increases (together with the frequency) in the first few days or weeks and is most severe in the middle phase of the cluster period, but even then patients may occasionally experience milder attacks (52). In some patients a slight discomfort or ache persists in the symptomatic area between attacks.

AUTONOMIC FEATURES

During cluster headache attacks, subjects may experience either local or systemic features of autonomic nervous system activation to a degree commensurate with the severity of the pain. Among the local signs of autonomic involvement, lacrimation is the most common, being reported in 82 to 91% of cases, followed by ipsilateral injection of the conjunctiva (58 to 84%). A partial Horner syndrome, with a slight ipsilateral ptosis or miosis, and/or eyelid edema is often present during attacks (57 to 69%) and may persist between attacks in later stages of the disease in some patients. Nasal stuffiness or rhinorrhea experienced by most patients during attacks (68 to 76%) is usually ipsilateral to the headache, but rarely may be bilateral. Nasal stuffiness in some cases may precede the onset of pain, later in the attack being replaced by rhinorrhea (53). Increased forehead sweating can be measured during severe attacks, especially on the symptomatic side. This sign can be clinically observed, however, in only a minority of patients (62). A few patients report generalized sweating during attacks. Cardiovascular findings accompanying cluster attacks include the following heart rate changes: increase in heart rate at the onset of attacks, decrease in heart rate after attacks, and rhythm disturbances (54). These consist of frequent premature ventricular beats, transient episodes of atrial fibrillation, and first-degree atrioventricular block or sinoatrial block. Moreover, both diastolic and systolic blood pressures may be increased (55). Gastrointestinal symptoms are not typical of cluster headache attacks.

In a large series of consecutive patients, Ekbom (13) found that in 3% of cases the diagnostic criteria were not fulfilled because of the absence of local autonomic signs during cluster attacks. In the series described by Nappi et al. (46), 3% never experienced autonomic symptoms during cluster headache, although these attacks were not personally observed. It may be assumed that the impairment of autonomic functions in these cases was present to a mild degree that was not clinically manifest but would have required advanced laboratory studies for sheer detection. Conversely, patients may, either spontaneously or after trigeminal nerve sectioning, endure periodic attacks of autonomic symptoms resembling cluster headache without the pain (35,36).

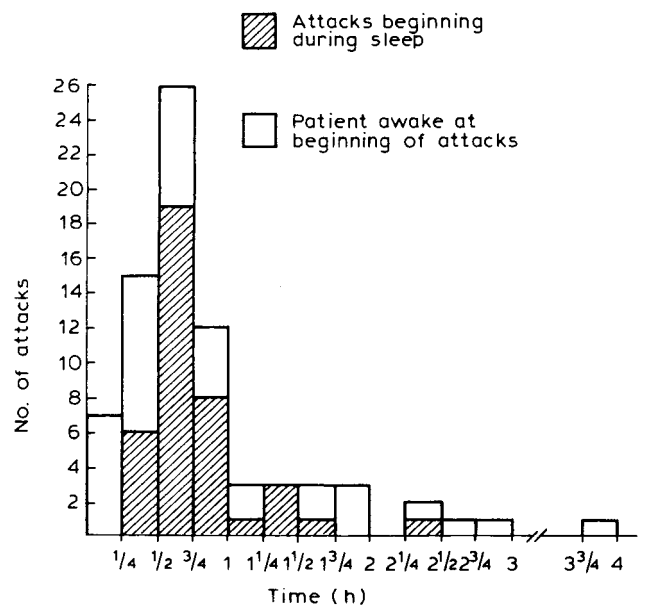

FIGURE 92-2. Duration of cluster headache attacks. Reproduced from Russell (52).

DURATION AND FREQUENCY OF INDIVIDUAL ATTACKS

Attacks typically last between 15 minutes and 3 hours, generally being shorter at the beginning and end of each cluster period. In a prospective study of 77 attacks (52), total duration was less than 30 minutes in 29%, less than 45 minutes in 62%, and less than 1 hour in 78% of patients (Fig. 92-2. A different prospective study of 230 patients found an average minimum attack duration of 72 minutes versus an average maximum duration of 159 minutes (3). The severity and duration of nocturnal and daytime attacks are similar.

The attack frequency is usually one or two per 24 hours, although the IHS diagnostic criteria suggest a minimum of one attack every other day and a maximum of eight per day. It is noteworthy that, in the evaluation of the outcome of the disease made by Manzoni et al. (40), the frequency of attacks showed a dichotomous evolution in primary episodic and primary chronic cluster headache patients. In the former condition, the attacks tended to increase in frequency, whereas in the latter they tended to decrease during the course of the disease. The duration of each attack tended to lengthen in all groups.

BEHAVIOR DURING AN ATTACK

The typical patient behavior has been described in detail (4) and has been incorporated into the ICHD-II diagnostic criteria. Subjects prefer to isolate themselves; they appear

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agitated, restless, and feel an impulse to move around or go outside in an attempt to cope with the torment of excruciating pain (66). Subjects may rub or compress their head, pace, apply cold substances to the site of pain, or seek a dark room. The awareness of these typical patterns of walking, sitting, kneeling, lying, and standing during attacks helps the patient to realize that bizarre behavioral responses are not the mark of insanity. Violent behavior is rare, but subjects may strike their heads on the wall or with their hands. This behavior appears depend on the severity of the pain during attacks (52).

ACTIVE PHASES AND REMISSIONS

Periodicity is the hallmark of cluster headache. Episodic cluster headache often manifests with both a circadian (certain times of day) and circannual (certain seasons of the year) periodicity. Various attack patterns have been documented with peaks around 1 to 2 AM, 1 to 3 PM, and 9 PM (41).

Circadian Periodicity

In Russell's study (52), 51% of attacks began when patients were asleep, the peak frequency being from 4 AM to 10 AM (Fig. 92-3. The average time asleep per 24 hours for patients during the study did not exceed 6.9 hours, so that the relative frequency of attacks was increased during sleep. There is also a tendency for daytime attacks to begin during naps or periods of physical activity.

Cluster headache patients often develop attacks about 90 minutes after going to sleep, indicating a relationship with REM phase sleep (42). Nocturnal attacks can occur during periods of oxygen desaturation with obstructive sleep apnea (OSA) associated with REM sleep and 31 to 80% of cluster headache sufferers may have evidence of OSA during polysomnography (18,47).

Circannual Periodicity

Attacks also cluster in series or bouts termed *cluster periods* that last weeks or months perhaps once or twice a year during which patients suffers 1 to 8 daily attacks (37). Although most subjects have one cluster period per year, up to 27% of sufferers may have only one cluster period ever and rarely patients may go as long as 25 years between periods (3,24,63). Remissions usually last between 6 months and 2 years. Although they are often relatively constant in individual patients, there are considerable interpatient variations. In the series of 428 patients described by Kudrow (30), remissions lasted 1 year or less in 67% and 2 years or less in 81% of patients. Female patients during pregnancy sometimes experience a remission period, with the attacks often returning shortly after delivery (15). Occasionally patients report the occurrence of a few mild attacks during a period when they are otherwise asymptomatic. A seasonal occurrence of cluster periods has been

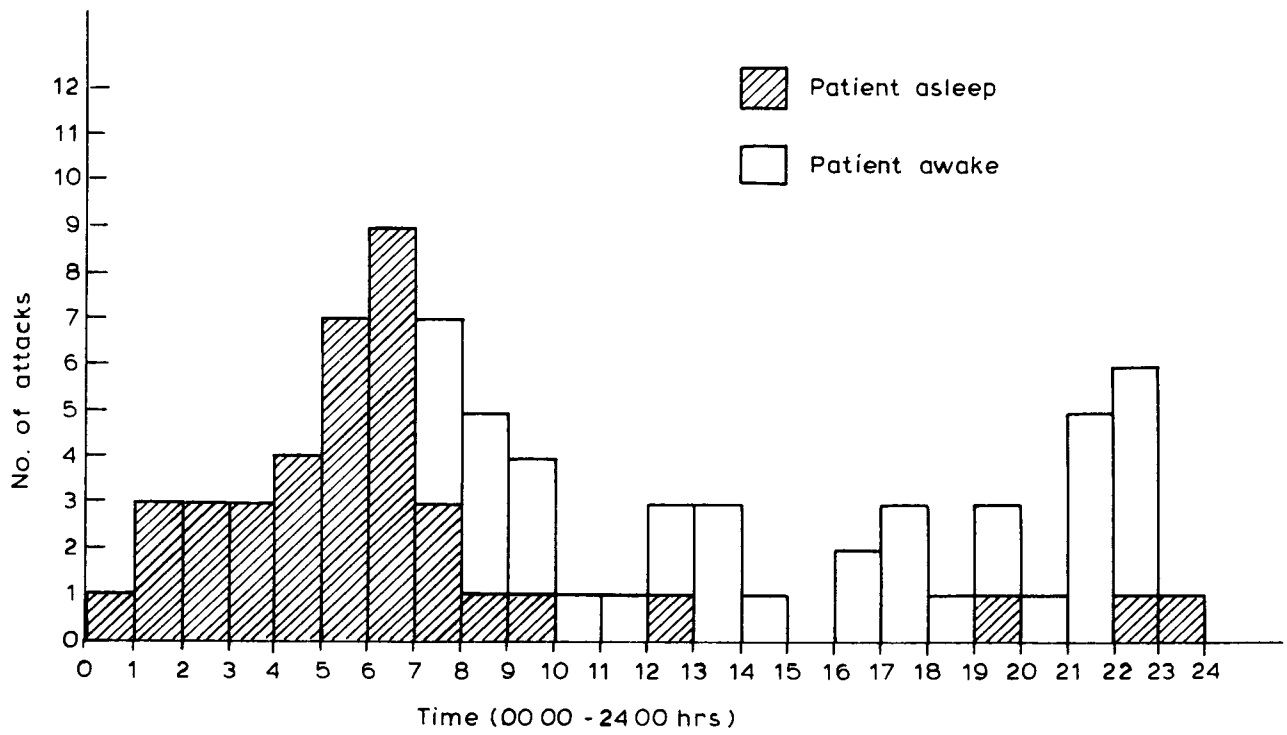

FIGURE 92-3. Time of onset of cluster headache attacks. Reproduced from Russell (52).

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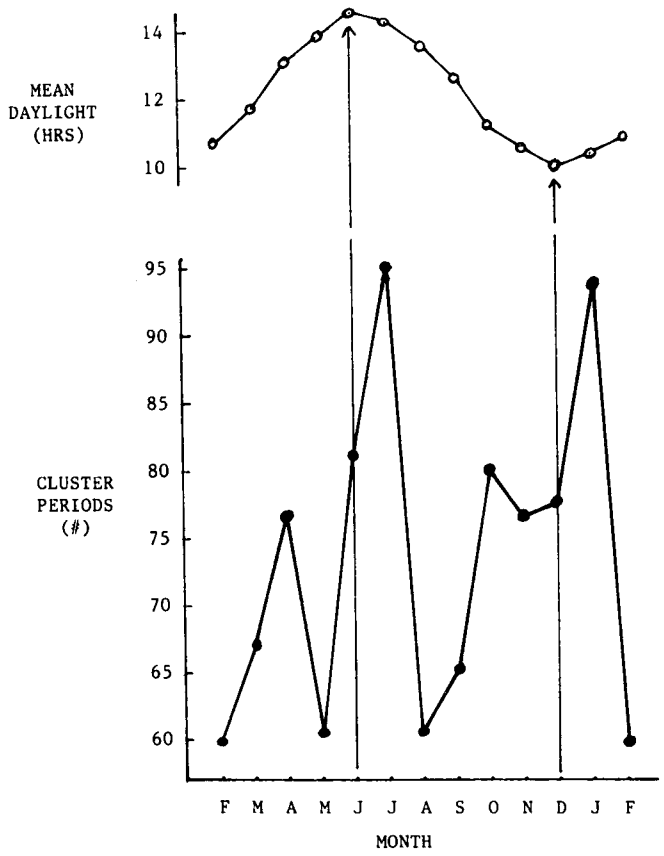

FIGURE 92-4. Daylight changes and cluster onset. Reproduced from Kudrow (31).

found by Ekbom in a series of patients examined in 1970 (9) and by Kudrow (30), who found an increased number of cluster periods in February and June, whereas August and November had the lowest number of cluster periods. Kudrow also found that the frequency of onset of cluster headache phases parallels the increase (and/or decrease) of light hours of daylight (Fig. 92-4; he identified two peaks of the cluster onset occurring 7 to 10 days before the longest and the shortest days of the year (31).

The influence of light and dark cycles (*zeitgebers*) on cluster headache helps to explain the predilection for attacks to occur with rhythmicity and this in turn suggests hypothalamic involvement. This relation was further solidified when functional imaging demonstrated activation of the posterior hypothalamus during a cluster headache and resolution of cluster headache after placement of stimulating electrode within the hypothalamus (34,43).

PRECIPITATING FACTORS

Alcohol intake during cluster periods (but not during remission) can promptly precipitate cluster attacks. However, according to Kudrow (30), Ekbom (12), and Klimek (27), only small quantities of alcohol trigger attacks, whereas larger amounts can have an opposite (or, in some cases, protective) effect on the daily occurrence of the painful crisis. Klimek reported that in some patients suffering from chronic cluster headache the attacks were reduced after the intake of a large amount of alcohol, the length of their remission being related to the quantity of alcohol consumed. Interestingly, drugs known to treat cluster periods successfully cannot prevent the attack induced by alcoholic drinks.

Among the precipitating factors of cluster headache crisis, some drugs should be cited, such as histamine, administered intravenously or subcutaneously, and sublingual nitroglycerin (8). Also, patients with cluster headache induced by Valsalva or television viewing have been reported (51). OSA is more common in cluster headache sufferers than in the general population and treatment with continuous positive airway pressure can resolve attacks in some individuals (47).

ALLEVIATING FACTORS

Factors and procedures alleviating headache symptomatology are reported only anecdotally by patients, and systematic studies are lacking. Ekbom (10) in 1975 found that the compression of the ipsilateral superficial temporal artery can reduce the pain of spontaneous or trinitrine-induced attacks. In some cases, digital compression of the common carotid artery may have the same effect. It is interesting to note that some patients alleviate the pain symptomatology through short-lasting, intense, physical activity.

ASSOCIATED SIGNS AND SYMPTOMS

Nausea may be experienced during severe attacks in 50% of patients along with at least one attack including photophobia (often unilateral) in 56% cases and phonophobia in 43%, although vomiting occurs in at least one instance in only 23% (3). A few patients have reported increased salivation or diarrhea during attacks. Contralateral carpal spasm, seizures, contralateral paresthesias, vertigo, and mild ataxia (26,33,53,60,64) have been reported during attacks in a few isolated cases. Occasionally, otherwise typical attacks of cluster headache may be accompanied by symptoms more typical of migraine such as aura or even hemiparesis (58,59). Premonitory symptoms should not be confused with the focal cerebral dysfunction termed *aura*. Aura before cluster headache is generally infrequent, although one study found that 33 of 230 (14%) patients suffered visual, motor, or sensory aura prior to a cluster attack (3,58).

Infrequently, patients may suffer cluster headache with coexistent trigeminal neuralgia (*cluster-tic syndrome*).

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These individuals may endure the two types of pain simultaneously, in separate attacks, or either may precede the other by up to years (67).

Vertigo is rarely an associated symptom during cluster attacks. This *cluster-vertigo syndrome* has yet to be substantiated as a distinct clinical entity. Speculation as to a common pathophysiology between cluster headache and cluster vertigo exists because attacks may have similar clustering, duration, onset, age group, and male preponderance, but phenotypic data are both lacking and marred by inconsistent application of various terms used to describe it (17).

FAMILY HISTORY

A family history for cluster headache is rare and was not present in more than 3 to 4% of patients (women 7 to 8%, men 2 to 5%) reported by Kudrow (30), although Bahra et al. (3) found that patients had a first-degree relative with cluster headache in 5% and migraine in 26% (1). Manzoni et al. found a positive family history in only 5 (0.8%) of 590 cases examined in the Headache Centers of Pavia and Parma (45).

Five monozygotic twin pairs with cluster headache have been reported (56) and Russell has shown that between 1947 and 1985, 47 first-degree relatives were affected in 1,182 families (57). Familial cases are more likely to involve women than sporadic cases, suggesting an autosomal gene influence with a dominant, recessive, or multifactorial inheritance.

GENDER

Cluster headache (along with short-lasting unilateral neuralgiform pain with conjunctival injection and tearing [SUNCT]) represents one of the few forms of primary headache that prevails among males, with women representing only 10 to 30% of those affected (39).

A gradually decreasing male:female ratio has been observed in some populations (from 6.2:1 in the 1960s to 2.1:1 in the 1990s in Parma, Italy) and may be caused by lifestyle patterns previously more common among men, including tobacco and alcohol use (38). The gender ratio does not appear to be different between episodic and chronic forms but in familial cases the male:female ratio may be as low as 1:2 (31).

PAST MEDICAL HISTORY

The past medical history of cluster headache patients is usually unremarkable. However, several researchers have reported an increased incidence of previous head trauma (16,33,41) and peptic ulcer (19,23,29). In the posttraumatic patients described by Manzoni et al. (41) who suffered from unilateral head injury with loss of consciousness, the traumatized cluster headache side was the one subsequently affected by cluster headache. A personal history of both cerebrovascular disease and hypertension has not been found to be statistically different from that of controls, whereas a higher incidence of coronary heart disease has been found in some reports among cluster headache patients (33).

There have been at least eight cases of cluster headache occurring ipsilaterally to an enucleated eye (49,50).

AGE OF ONSET

The mean age of onset was 28.0 years in the series of Friedman and Mikropoulos (16), 27.5 years in the series of Ekbom (11), 29.6 years in that of Kudrow (30), and 28.9 years in that of Manzoni et al. (41). Although cluster headache may appear at any age, its onset is usually later compared with that of migraine. Cluster headache is uncommon in children but can occur as early as age 6. Only 17.7% of the cases described by Zanferrari et al. had their onset prior to 18 years of age, and only 2.2% prior to 10 years (68). Unfortunately, mean time to diagnosis after onset ranges from 7 to 16 years (3).

LIFE HABITS AND PERSONALITY PROFILE

Cluster headache sufferers are more likely to have a significant history of cigarette smoking (85% men, 60% women) and alcohol consumption compared to the general population and other primary headache sufferers (11,30,38,41,65). However, no significant correlation was demonstrated between withdrawal from alcoholic drinks or smoking and changes in the course of cluster headache. It seems likely, however, that giving up drinking can favor the onset of a remission period in some cases (40). Moderate or severe stress may precede the onset of a cluster period, and an exaggerated life habit profile seems to characterize cluster headache patients (44).

Graham (19) first described male subjects with cluster headache as having a leonine appearance. He hypothesized that they were usually very insecure, were dependent on their wives' decisions, and had strong traits of hysteria (20). The deep furrows within the brow that produce the leonine facies may be secondary to tobacco use. According to other researchers (16,28), the typical patient suffering from cluster headache is ambitious, is hard working, and has obsessive personality traits, but also has feelings of inadequacy and dependency (50,61).

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In contrast, cluster headache patients did not differ essentially from other headache groups with regard to psychological status (6,7). Using the Minnesota Multiphasic Personality Inventory, cluster headache subjects had a personality profile similar to that observed in migraine (2,26,36).

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