

## Migraine and Cluster Headache: Coexistence, Laterality, and Gender

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### CLINICAL HISTORY

A 38-year-old woman reported a history of headache since aged 11 years, occurring about once a month. Triggers included stress and missing a meal, and she described a severe left or right hemicranial throbbing pain with associated nausea, vomiting, photophobia, and phonophobia, but no aura. Attacks lasted up to 3 days. An acetaminophen/aspirin/caffeine combination “dulled” the pain.

For the last year, she had a second type of headache involving severe right or left retro-orbital pressure with ipsilateral tearing and nasal congestion. The headache would awaken her from sleep and occurred only around 3:30 AM. Headache duration was 60 to 90 minutes, and the frequency had decreased from daily to once a week over several weeks preceding her presentation.

**Questions.**—How often do migraine and cluster-type headache occur in the same individual? How often does unilateral migraine change sides, and how often is the headache side-locked? How often does cluster headache change sides within cluster periods, and how often does cluster headache change sides from one period to the next? What is the female to male ratio of cluster headache?

### EXPERT COMMENTARY

The prevalence of cluster headache has been estimated to be between 0.02% and 0.4%.<sup>1-3</sup> Based purely on the prevalence of migraine, one might expect at least 15% of those with cluster headache to have both.<sup>4</sup> The reported occurrence of migraine in patients with cluster headache has varied considerably ranging from 0% to 65%.<sup>3,5-11</sup> The discrepancies can be attributed to a combination of factors including different sample sizes, diagnostic criteria, and methods of data collection. The age of onset of cluster headache is reported to be later than for migraine, and studies which have addressed the temporal relationship of the 2 disorders in the same individual have shown that most attacks of migraine cease following the onset of cluster headache.<sup>12-14</sup> Even so, the active coexistence of migraine and cluster headache does occur. One report of 10 patients so affected stated that a “migraine crisis” did not occur during the cluster period in any patient and, moreover, the attacks of migraine and cluster headache did not present near one another.<sup>15</sup> Other authors, however, have witnessed occasional migraine attacks during and often limited to the cluster period, with migraine attacks witnessed in some male and female patients with no clear antecedent history of migraine.<sup>12,16</sup>

The distribution of pain in migraine and cluster headache is predominantly in the first division of the trigeminal nerve.<sup>11,17</sup> The pain of migraine is unilateral in about two thirds of patients, but may be bilateral at onset (40%) or start unilaterally and become generalized. The side may change within the same attack.<sup>18</sup>

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The pain is side-locked (always on the same side in all attacks) in 17% of migraineurs.<sup>19</sup> The pain of cluster headache is almost invariably unilateral and usually experienced consistently on the same side. More patients experience right- than left-sided attacks, and 9% to 16% have experienced attacks on both the right and left side during different attacks. This is more common in different cycles, but can occur during the same cycle.<sup>3,8-11,20</sup> In one study involving 230 patients with cluster headache, of those patients with episodic cluster headache, 14% had experienced a side shift only within the same cycle, while 18% had experienced attacks on one side during one cycle and a side shift in a subsequent cycle. Only 3% had experienced side changes within a given cycle and symptoms exclusively on one side during one cycle and the other side during a subsequent cycle.<sup>11</sup> Pain occurring simultaneously on both sides during an attack has been reported, but is rare.<sup>21,22</sup> A change of side within the same attack is even more rare.<sup>10,11,23</sup>

Cluster headache has been reported more commonly in men than in women. The observed ratio has varied between 2.5 to 7.1:1.<sup>3,11,14,24-27</sup> More recent and larger studies suggest the ratio most likely ranges from 3 to 4:1.<sup>11,25,28</sup>

Individuals with cluster headache have been described to have "leonine facies" and women to have a masculine appearance, but there is no evidence of alteration in the male or female sex hormones to account for the difference in sex distribution.<sup>6,29,30</sup> In fact, low serum testosterone levels have been reported in men during an active cycle compared with the remission period, and in and out of the cycle compared with controls.<sup>3,31-34</sup> In females, there seems to be no association with menarche, menstruation, oral contraceptives, or menopause.<sup>24,35,36</sup> It has been reported that most females experience remission during pregnancy, although this is not a consistent finding.<sup>35</sup>

Three large series have addressed the male to female ratio by decade of onset. Manzoni reported a gradual reduction in the male to female ratio from 6.2:1 before 1960 to 2.1:1 for those individuals with onset between 1990 and 1995. This was attributed to significant changes in life-style, such as smoking and employment rate, which have shown a similar fall in the male to female ratio for the corresponding decades.<sup>25</sup>

Ekbom et al reported similar findings which again were attributed to environmental influences and life-style changes.<sup>28</sup> Bahra et al reported that the ratio has been remarkably consistent through the decades (2 to 3.5:1) and attributed this to the study of a mainly nonclinic-based group of individuals. It was suggested that the reason for the difference in ratio trends by decade of onset could be attributed to patient referral bias, with some studies examining populations referred to secondary and tertiary centers. Coupled with the increasing number of working women contributing to household incomes, it would seem more plausible that women now are more likely to seek treatment.<sup>11</sup>

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