Chapter 136

Headache in Patients with Coexisting Other Pain Disorder

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GENERAL CONSIDERATIONS

When considering the association of headache and other pain disorders, several questions arise: do migraine, other headaches, and other pain disorders share biologic mechanisms? Do coexisting pain disorders activate or facilitate activity of primary headache conditions? Do the underlying mechanisms of migraine and clinical consequences of these mechanisms instigate or influence activity of other pain disorders? Do medications prescribed to treat one pain disorder influence activity of another coexistent pain disorder? Could one type of chronic pain disorder cause functional or structural changes in central pain pathways that will influence the threshold to develop or lead to exacerbation of another pain disorder?

In pediatric and adolescent pain studies, headache has been associated with greater prevalence of other pain complaints such as neck and back pain (7,21,27). Antilla et al. found that 8- to 9-year-old children with migraine reported neck–shoulder pain, abdominal pain, back pain, and otalgia significantly more often than children with nonmigraine headache (3). Of those children with migraine, a second pain complaint was most frequently reported in the migraine with aura group. Among children with nonmigraine headache, the report of a second pain complaint was positively correlated with the frequency of headache attacks.

Similarities in the transmission, facilitation, and inhibition of pain signaling among all pain disorders might be expected to allow for the interaction of one pain disorder with another and the influence of one on the other. Despite this seemingly reasonable assumption, a 25-year follow-up study of patients in a general medical practice demonstrated that an episodic pain disorder tended to evolve into a chronic pain disorder remaining in the original region affected and did not evolve into a generalized chronic pain disorder (13). For example, in this study, a prior history of migraine increased the risk to develop chronic head pain (Odds ratio [OR] 1.9, 95% Confidence interval [CI]: 1.6–2.3) and chronic neck pain (OR 1.4, 95% CI: 1.1–1.7) but not other chronic pain disorders. Only a previous episode of mental illness was a significant predictor for developing a chronic pain disorder regardless of eventual location. This association was most specific for depression or nonpsychotic anxiety, which are common psychiatric comorbidities of migraine.

Limitations in evaluating the evidence regarding the associations of headache and other pain disorders include recruitment bias (community vs. clinic-based or primary care vs. specialty pain program), subject reporting errors (self-reported diagnoses, retrospective reporting, recall errors), inadequate study design (questionnaire-based history gathering, questioning bias, general medicine practitioner vs. pain specialist, retrospective analysis, lack of confirmatory diagnostic tests), inconsistent use of standardized diagnostic criteria within or across studies, and the effect of psychiatric comorbidities such as somatization leading to high health care utilization, ultimately resulting in more clinical diagnoses for that individual and biasing the presence in favor of finding comorbid disorders.

It is reasonable to assume that the experience of pain, in particular the comorbidity of multiple pain disorders, is a complex interaction of genetic, biologic, neurogenic, psychologic, and environmental influences that give rise to a wide variety of clinical presentations, interactions, and treatment considerations.

TREATMENT CONSIDERATIONS

Medications prescribed to treat a pain disorder can have an important adverse effect on patients who experience or have a genetic predisposition for migraine. The concept of analgesic rebound or medication-overuse headache is well

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established in the field of migraine studies (36). Bahra et al. reported that the regular use of analgesic medications such as opioid analgesics, nonsteroidal antiinflammatory drugs, and acetaminophen for rheumatologic conditions contributed to de novo chronic daily headache (CDH) in patients with a previous history of International Headache Society (IHS)-defined migraine but not in patients with no previous history of headache (4). Also notable is that the high baseline prevalence of migraine (41%) and CDH (11%) in arthritis patients might suggest common pathophysiologic mechanisms or other influences that promote coexistence of the two conditions. Wilkinson et al. similarly reported that patients with a history of migraine developed de novo CDH after taking daily opioids that were prescribed to control bowel hypermotility after colectomy for ulcerative colitis (41). Can we assume that the frequent use of analgesics for any pain condition increases the risk for developing a chronic pain disorder over time? Zwart et al. followed more than 32,000 subjects over a period of 11 years and found that subjects using daily or weekly analgesics at baseline had a greater likelihood of experiencing chronic pain at follow-up (45). Although the risk was seen for all pain disorders studied (neck pain, low back pain, and migraine and nonmigraine headache), the risk was greatest for subjects with migraine (RR 13.3, 95% CI: 9.3–19.1) when compared to those with nonmigraine headache (RR 6.2, 95% CI: 5.0–7.7), neck pain (RR 2.4, 95% CI: 2.0–2.8), and low back pain (RR 2.3, 95% CI: 2.0–2.8). The frequent use of opioid analgesics for the treatment of chronic noncancer pain other than migraine has been implicated in the development of progressive pain escalation, a phenomenon that has been called "opioid-induced hyperalgesia" (23,24), but patients with migraine appear to have a greater vulnerability for this consequence.

The potential exacerbation of headache frequency and intensity in patients with migraine is a very important consideration when prescribing pain relievers for comorbid pain disorders.

LOW BACK PAIN

Duckro et al. examined the occurrence of headache as a sequela to or consequence of chronic low back pain (LBP) (16). Of patients with chronic LBP, 52.2% developed de novo headache and 15.2% experienced a significant exacerbation of an existing headache following the onset of LBP. The total prevalence of headache in the LBP group was very high at 82.6% but the greatest association was with migraine in particular. The prevalence of migraine before the onset of chronic LBP was 3.4% for men and 23.5% for women compared to 6.9% and 35.3%, respectively, after the onset of chronic LBP. Ahern et al. found that 61.4% of patients referred to a multidisciplinary pain clinic with chronic LBP also reported headache (2). In this group, 75.2% reported that their headaches began with or subsequent to the onset of LBP. In another study, Fishbain et al. reported on the prevalence of headache among 1466 patients admitted to a multidisciplinary pain management center for chronic neck and low back pain (17). Overall, 10.5% experienced headaches severe enough to interfere with daily functioning. Of this group, 55.8% reported that their headache was associated with the injury for which they sought treatment and 83.7% also had neck pain. IHS-defined migraine headache represented the most common headache diagnosis (90.3%) followed by cervicogenic headache (33.8%). Of all subjects with headache, 44.2% had more than one headache diagnosis and 74.6% had cervical muscle tender points when examined. There was a substantial overlap of patients having diagnostic features of both migraine and cervicogenic headache.

Chronic low back pain and migraine individually have been associated with a large socioeconomic impact. Dartigues et al. found that each condition had a similar impact on the number of lost workdays over 4 years: 31.8 days for migraine and 38.4 days for LBP; however, the group experiencing both conditions together demonstrated a statistically greater absenteeism of 58.1 days (14).

Although the mechanisms by which headache, migraine, and LBP coexist are unknown, there are potential concerns that treatment of LBP might influence the activity of migraine, chronic LBP might exacerbate existing headaches or contribute to the de novo onset of headache, and the coexistence of migraine and LBP can contribute to a greater degree of physical impairment than either condition alone.

NECK PAIN

The association of neck pain and headache can be explained by neuroanatomic connections in the head and neck region. A functional convergence of upper cervical and trigeminal nociceptive pathways potentially allows the referral of pain from the neck to trigeminal sensory receptive fields of the face and head (6). This interaction is believed to be bidirectional, thereby explaining the frequent presence of neck pain during acute episodes of primary headache. Pronounced levels of muscle tenderness, as well as postural and mechanical abnormalities, have been reported in tension-type (TTH) and migraine headache (5,22,25,38). Differences in neck posture and the presence of myofascial trigger points were observed in subjects with migraine, TTH, or both when compared to a control group of nonheadache subjects, and there were no significant differences observed in the headache groups (25). Neck pain is recognized as a common and prominent symptom of migraine (5,15,20,40) and is also a prodromal symptom of migraine (40). In a study of 50 patients with migraine, 64% reported neck pain or stiffness

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associated with their migraine attack. Of those migraine patients, 31% had neck symptoms as a prodrome, 93% during the headache phase and 31% during the recovery phase (5). In this study, seven patients also reported pain referred into the ipsilateral shoulder and one patient reported that his pain extended from the neck into the low back region. Kaniecki reported that 75% of the 144 patients with the diagnosis of IHS migraine reported neck pain associated with migraine attacks (20). Of these patients, 69% described the pain as "tightness," 17% as "stiffness," and 5% as "throbbing," and other terms were used by the remaining patients. The neck pain was unilateral in 57% of respondents, 98% of whom reported it to be ipsilateral to the headache. The neck pain presented as a prodrome in 61%, during the migraine attack in 92%, and as part of the recovery phase in 41%. In case reports, recurrent, unilateral neck pain without headache has been described as a variant of migraine since further history gathering in these cases uncovered previously overlooked migraine symptoms (15).

Concerns associated with the coexistence of headache and LBP such as medication-induced exacerbation of migraine is also of concern in the association of head and neck pain. More specific to the neck association is the exacerbation of headache by physical treatments used to treat a coexisting neck disorder, which is commonly observed in cases of cervical zygapophyseal joint injury or arthritis. On the other hand, migraine, a neurogenic condition that is believed to result in a lower threshold for neuronal activation, might be inappropriately activated by excessive nonnociceptive sensory signals traveling from tight muscles into a "sensitized" trigeminal–cervical nuclear complex via cervical spinal nerves. In this case, physical treatments might provide headache relief for patients who experience an exacerbation of migraine after neck injury or neck muscle spasm. Cervical spine arthritis might be linked to an exacerbation or de novo initiation of headache through these trigeminocervical pathways (26).

FIBROMYALGIA

Fibromyalgia is defined as a nonarticular pain disorder predominantly involving muscles and other soft tissues and recognized as the most common cause of chronic, widespread musculoskeletal pain. In 1990, The American College of Rheumatology (ACR) proposed diagnostic criteria to standardize the study of patients with this condition (42). The diagnostic criteria include the presence of widespread pain (defined as pain in the left and right sides of the body as well as both above and below the waist) for at least 3 months. Axial skeletal pain, defined as pain of the cervical spine, anterior chest, or thoracic or lumbosacral spine, and pain in at least 11 of 18 specifically defined tender point sites must also be present. The estimated prevalence of fibromyalgia in the general population is 2% –3.4% in women and 0.5% in men. Its prevalence increases with age, reaching 7% in women of age 60 to 80 years (10). Its prevalence is reported to be 5.7% in a general medical clinic (18) and between 14% (44) and 20% (43) in rheumatology clinics.

Fibromyalgia can be associated with both migraine and tension-type headache. Headache is a common complaint of fibromyalgia patients (35), and fibromyalgia is more prevalent in the population of migraine patients (1,31).

Nicolodi et al. (28) studied 89 fibromyalgia patients and stated "fibromyalgia sufferers are headache sufferers" since all patients had met criteria for a primary headache diagnosis (84 migraine, 5 tension-type headache). Burg (8) studied 25 patients with fibromyalgia, the majority of whom were women. Approximately 80% of these patients experienced depression, anxiety, and a sleep disorder. Most of the patients had this condition for greater than 6 months, and all but a few had headaches. Other pain complaints such as back pain, diffuse tender trigger points, irritable colon symptoms, and dysmenorrhea were also common.

Hudson et al. (19) evaluated 33 women with fibromyalgia for concomitant medical and psychiatric disorders. These patients were found to have high lifetime rates of migraine, irritable bowel syndrome, chronic fatigue syndrome, major depression, and panic disorder. They also exhibited high rates of familial major mood disorder.

Paiva et al. (29) studied 25 patients with various headache diagnoses but having a common clinical feature; all patients reported morning or nocturnal headaches. Fibromyalgia was diagnosed in 24% of patients based on the presence of α:δ patterns during slow wave sleep by polysomnographic recordings, and then confirmed by a rheumatologist applying the ACR diagnostic criteria for fibromyalgia. In another study Nicolodi et al. (28) evaluated 205 severe headache sufferers (164 migraine, 41 TTH). Forty-eight percent (69 migraine, 30 TTH) of patients were given a diagnosis of fibromyalgia. The symptoms of fibromyalgia were observed to improve with headache treatment.

Peres et al. (27) studied 101 chronic migraine patients and were able to make a diagnosis of fibromyalgia in 35% of these patients using the ACR diagnostic criteria. Patients with fibromyalgia had more problems with insomnia, were older, and experienced headaches that were more incapacitating than experienced by patients without fibromyalgia. Insomnia and depression predicted the coexistence of fibromyalgia among chronic migraine patients. A subtype of chronic migraine patients comprising 25% of the sample had concomitant symptoms of migraine, fibromyalgia, depression, and insomnia.

Proposed pathophysiologic mechanisms involved in the clinical presentation of fibromyalgia are altered neurotransmitters and pain-modulating neuropeptides

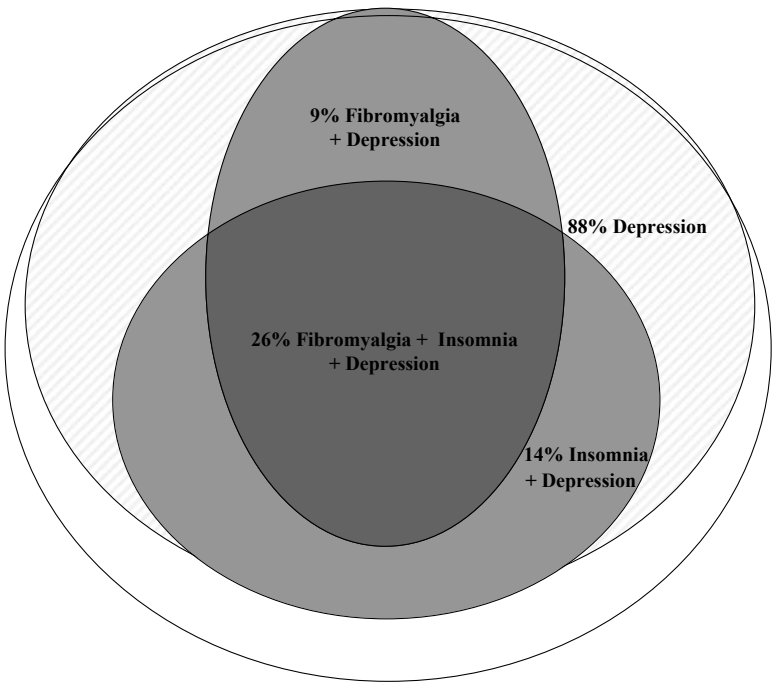

FIGURE 136-1. Chronic migraine comorbidity with fibromyalgia, depression, and insomnia.

(serotonin, substance P), neuroendocrine changes (melatonin, hypothalamic–pituitary–adrenal axis), and defective functioning of the descending noxious inhibition systems. Central sensitization has been implicated in both fibromyalgia (37) and migraine (9). Peres et al. (33) found greater glutamate levels in subjects with chronic migraine compared to controls, and even greater levels were demonstrated in patients with fibromyalgia when compared to those without fibromyalgia. Therefore, central sensitization mediated by the glutamatergic system could theoretically be a mechanism linking migraine and fibromyalgia. A complex association of genetic, immunologic, neurogenic, psychologic, and sleep physiology are likely involved in both conditions.

Treatment options for fibromyalgia and migraine patients include the use of tricyclic antidepressants, physical exercises, physical therapy, and psychotherapy. Other options for the treatment of both conditions are the antiepileptic drugs, sometimes referred to as neuronal stabilizers. Peres et al. have shown that topiramate is an effective treatment for the management of both fibromyalgia and chronic migraine (30). Since glutamate levels are increased in such patients, other medications modulating this system could be potentially beneficial. Melatonin has also demonstrated treatment efficacy in both conditions (12,32).

More studies on headache characteristics, diagnosis, impact, and management in fibromyalgia patients are necessary to derive any firm conclusions regarding shared mechanisms and the most effective approach to the management of these conditions, especially when occurring together.

TEMPOROMANDIBULAR DISORDER AND REGIONAL MYOFASCIAL PAIN

Temporomandibular disorders (TMDs) include a number of clinical problems that involve the masticatory muscles, the temporomandibular joint (TMJ), or both. Regional myofascial pain syndrome is characterized by the presence of taut muscle bands and myofascial trigger points that when stimulated radiate pain into local and distant reference zones. TMD and regional myofascial pain syndrome are closely associated conditions and often coexist with fibromyalgia and primary headache conditions.

Ciancaglini and Radaelli studied the relationship between headache and symptoms of TMD in 483 subjects. Headache was significantly more prevalent in subjects with TMD than in subjects without TMD symptoms (27.4% vs. 15.2%). Of TMD symptoms, temporomandibular pain, TMJ sounds, and pain on movements of the jaw were more commonly associated with headache using a univariate analysis (OR 1.83, 95% CI: 1.07–3.15) (3). Pettengill demonstrated that headaches were common in patients with TMD symptoms and that headache intensity was more severe in TMD patients when compared to non-TMD patients (3).

Vasquez-Delgado et al. studied psychologic and sleep profiles in 67 patients with chronic daily headache (CDH) and primarily chronic migraine, and compared them to 67 patients with myofascial pain (MP) and 67 patients with TMJ intracapsular pain (IC). The CDH and MP groups revealed higher levels of psychologic distress than the IC group on most psychologic domains. Sleep quality was

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significantly worse in the MP group than in the CDH and IC groups (39).

The association of headache, TMD, and regional myofascial pain is very complex. The chronic regional face that is a direct consequence of the TMD and myofascial pain disorder is often complicated by referred head and neck pain, analgesic overuse, depression, anxiety, and sleep disturbance. Any of these conditions alone or in association can incite the de novo activation or exacerbation of a coexisting primary headache disorder.

SUMMARY

Physiologic facilitation of pain transmission as a consequence of one pain disorder or its treatment might influence the de novo activation or exacerbation of another pain disorder. When specifically relating this concept to primary headache disorders, there appears to be bidirectional influences that not only contribute to the potential for headache exacerbation in patients who develop a second pain disorder but also an increased likelihood that patients with migraine will develop a second chronic pain disorder. Recognition of these associations will ultimately improve our understanding of pain mechanisms and provide an awareness of not only the beneficial effects of early and aggressive pain treatment but also its potential deleterious consequences in patients presenting with more than one pain disorder.

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