Sex Differences in Migraines

Date Created:
Author: Melissa Usoz, MS, BS
Editors: Jennica Siddle, MD, MPH, and Janice Werbinski, MD, FACOG, FAMWA

Case Overview

Migraines remain one of the top ten causes of disability worldwide, with little improvement from 2010 to 20213. Its continued burden, especially among women, calls for a sex-specific approach to research, diagnosis, and treatment.

History of Present Illness

A 51-year-old G4P1122 post menopausal female presented to the ED with a headache that woke her from sleep and new neurologic symptoms. The headache began a few days prior, described as diffuse and throbbing across her forehead, partially relieved by Tylenol, and rated 6/10 in intensity. She denied visual changes or GI symptoms but reported transient anomia, left facial numbness, and left arm tingling. She also described chest pressure like “an elephant sitting on my chest.” Her history includes hypotension (on midodrine), anxiety, and a maternal history of heart attack. She is a former smoker, works in healthcare, and lives with her husband and son. She denied alcohol and drug use. In addition she takes klonopin three times a week as needed for anxiety, but has not taken this in over a week.

Past Medical History

- Anxiety
- Depression
- Hyperlipidemia
- GERD
- OSA
- Urge Incontinence
- Headache

Surgical History

- Cholecystectomy

Medications

- Klonopin 2mg PRN
- Midodrine 10mg three times daily
- Lamitical 25mg twice daily
- Protonix 40mg daily
- Mirabegron 25 mg daily
- Pristiq 100mg daily
- Ubrelvy 100mg PRN

Vital Signs

- Temp: 97.9F
- BP: 159/91
- HR: 105 bpm
- RR: 16
- O2 Sat %: 98%

Physical Exam

- General Appearance: Patient appeared anxious but not in any acute distress, pleasant demeanor
- Eyes: EOM intact, PERRL
- Cardiovascular: Regular rate and rhythm, no murmurs, rubs, or gallops
- Pulmonary: Normal WOB, no wheezes, rales, or rhonchi
- Abdominal: Flat, soft, non-tender, non-distended
- Neurologic: Neurologic: A&Ox3, no focal deficits, strength 5/5 in all extremities, decreased sharp sensation in left arm/hand with normal sensation in left forearm, right arm, and bilateral lower extremities; no ataxia or pronator drift. Sensory deficit in LUE resolved on repeat exam.

ED Course

Initial differentials included TIA, atypical migraine, ACS, anxiety, electrolyte abnormality, and medication side effect. NIHSS was 1 for a transient left arm sensory deficit. EKG and troponins were normal, lowering concern for cardiac causes. She denied any aura's associated with her migraine and had no red-flag features on exam; therefore, neuroimaging was deferred as the likelihood of a stroke or hemorrhage was low. CBC, BMP, and chest X-ray were unremarkable. The patient received a 1L normal saline bolus, Compazine 5 mg IV, Benadryl 12.5 mg IV, and magnesium 2 g IV. On reassessment, her blood pressure improved to 118/81 with heart rate of 68, and her headache and neurologic symptoms resolved. She was discharged the same day with return precautions and a final diagnosis of migraine without status migrainosus.

Discussion

Migraines exhibit a strong sex difference in both prevalence and clinical presentation. Prevalence follows a bimodal distribution for both sexes, peaking at ages 35 and 50, then decreasing with age.[1] In adult women after puberty, migraines are 3–4 times more frequent than in men.[2] Female sex hormones such as estrogen and progesterone affect brain signaling and blood vessel function involved in migraine attacks. Estrogen, in particular, influences neurotransmitters like serotonin and glutamate, which may explain the higher frequency and severity of migraines in women.[6] Hormonal fluctuations around menstruation, pregnancy, and menopause are closely linked to changes in migraine patterns. In addition to considering hormonal changes, it is important to review medications as well. In this particular case, she is prescribed midodrine which works by signaling blood vessel constriction in order to increase blood pressure which can also lead to headaches.

Beyond patient-level factors, population data shows that sex strongly shapes the migraine impact in women. A large European cohort study found females had a higher frequency of migraine attacks but fewer non-migraine headaches than males. Attacks lasted longer, were more intense, and more often unilateral, pulsatile, and exacerbated by activity in females.[4] US and European studies reported greater headache-related disability in females, who carry 79% of the migraine disease burden.[4,5] One study found 34% of women versus 25% of men missed school or work due to migraine.[7] Women also experience longer recovery times, sometimes 3–6 days, compared to men's typical two days.[13] Among disadvantaged women, those reporting headache as a chronic health condition were twice as likely to have lost a job in the prior year due to health.[11] Workplace productivity loss from migraine results in an estimated $375.40 USD loss per person annually (MIDAS).[12] These findings highlight the need for targeted strategies to improve migraine management, reduce productivity losses, and lower related costs— a burden falling disproportionately on women.

Evidence increasingly supports migraines as a risk factor for major cardiovascular disease. A recent metaanalysis found a twofold increased risk of ischemic stroke for women with migraine, driven by aura.[14] Age modifies this risk, with women ≤45 years old who have migraine with aura at higher risk.[15] Similarly, the risk of venous thrombus is sex- and age-dependent, with women at increased risk compared to men when associated with aura.[15] Data on migraine and myocardial infarction remain conflicting and require further study. These findings emphasize the importance of recognizing migraine with aura as a sex- and age-specific cardiovascular risk factor, particularly for younger women.

Sex differences in migraine treatment are increasingly recognized. An Italian survey found women were more likely than men to use prescription medications and preventive therapies for migraines. Men were also less likely to seek medical care for migraines.[7] This may reflect the stigma of migraines as a "woman's disease," discouraging men from seeking help. A meta-analysis of triptan use found no sex difference in 2-hour pain-free response rates, but men had a 36% lower risk of recurrence and fewer adverse events.[8] Clinical trials of migraine treatments heavily favor female participants (~17% male), limiting insights into sex-specific responses.[9,10] These findings underscore the need for inclusive research addressing sex-specific differences in migraine treatment and prevention.

In conclusion, addressing sex differences in migraine prevalence, presentation, and treatment is essential to reduce disability, medical risk factors, and improve outcomes for both women and men.

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