recognized statistical method to report odds and risk relationships in large nationally representative data sets. Finally, as an additional precaution, we made clear in our Discussion section that cross-sectional survey data cannot be used to make causal statements but only highlight potential areas for future research. We thank Dr. Woldeamanuel for reinforcing these important points and the need for more research.

References
1. Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: Figures and trends from government health studies. Headache 2018;58(4):496–505.
2. Smitherman TA, Burch R, Sheikh H, Loder E. The prevalence, impact, and treatment of migraine and severe headaches in the United States: A review of statistics from national surveillance studies. Headache 2013;53(3):427–36.
3. Lisa M. Sullivan. Essentials of Biostatistics in Public Health. 2nd ed. Sudbury, MA: Jones & Bartlett Learning; 2012.
4. McHugh ML. Multiple comparison analysis testing in ANOVA. Biochem Med (Zagreb) 2011;21(3):203–9.

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Epicrania Fugax with a Novel Sign: Pain Paroxysms with Parallel Forward or Backward Trajectories

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Dear Editor,

Epicrania fugax (EF) manifests as ultrabrief electric or stabbing pain paroxysms on the cranial surface of moderate or severe intensity. Sometimes, patients with EF also experience ocular or nasal autonomic accompaniments and interictal mild pain or hyperesthesia [1]. The frequency of these paroxysms varies greatly, from a few attacks per year to numerous attacks per day. Mostly, the paroxysms occur spontaneously, but they can also be triggered by touch or palpation. First reported by Pareja et al. in 2008 [2], EF has since been listed in the Appendix of the 3rd edition of the International Classification of Headache Disorders (ICHD-3) (Table 1) [3].

EF patients display various pain features that stem from posterior cranial areas moving to the ipsilateral anterior scalp, or from the frontal areas, eye, or nose toward the parietal or occipital region along lineal or zigzag trajectories [4, 5]. We performed a retrospective study on the clinical course of 960 patients attending a headache specialist clinic from January 2016 to December 2017 in our hospital. Among these patients, the three cases meeting diagnostic criteria for EF with a specific pain radiating pattern were reviewed.

The first patient was a 62-year-old woman who complained of headache paroxysms for three months. The pain was described as electric, with an intensity of 5 out of 10 on a visual analog scale (VAS; 0 = no pain, 10 = the worst imaginable pain). The paroxysms began in the right eye and spread posteriorly and caudally along two parallel backward zigzag trajectories to reach the ipsilateral suboccipital region and lasted for three seconds every time (Figure 1A). These attacks happened around twice per month and showed no apparent triggers. Physical or neurological examinations, routine blood tests, and a magnetic resonance imaging (MRI) scan of the brain detected
no abnormalities, but paresthesia along the spreading route of the pain was obvious. The patient rejected any preventive therapy and maintained similar pain quality, intensity, and frequency during the one-year follow-up. The second patient was a 42-year-old man who was referred to our clinic due to headache paroxysms for three years. The pain had a stabbing quality, an intensity of 6 out of 10 on the VAS, and started in the right occipital area, moving anteriorly in two parallel lineal trajectories to the right temporal scalp (Figure 1B). Attacks occurred two to three times per week and lasted about 10 seconds. Touching the scalp triggered the pain paroxysms, but they also occurred spontaneously. Moreover, a mild interictal pain at the starting site was mentioned. Physical and neurological examinations, routine blood tests, and brain MRI were normal. After treatment with carbamazepine (100 mg, bid) for one month, the attacks stopped, and treatment was discontinued. During the one-year follow-up after discharge, no relapse was reported.

The third patient was a 56-year-old woman who consulted us for intermittent headache paroxysms of five months’ duration. The pain was described as electric, starting from the left eye and moving caudally in two parallel zigzag trajectories to the ipsilateral suboccipital area (Figure 1C), lasting five seconds each time. The pain intensity was rated as 5 out of 10 on the VAS, and the episodes occurred three times per week. The patient showed no symptoms between paroxysms, although a history of migraine without aura was declared. Physical and neurological examinations, routine blood tests, and brain MRI were all normal, as in patients 1 and 2. We treated the patient with carbamazepine (100 mg, bid) for one month, the attacks stopped, and treatment was discontinued. During the one-year follow-up after discharge, no relapse was reported.

Here we introduce three cases of EF with pain spreading along two parallel trajectories, a pattern never before reported. EF was originally regarded as a pain paroxysm spreading from posterior cranial areas to the ipsilateral anterior scalp in a single linear or zigzag trajectory [2], after which EF with backward radiation was proposed in 2010, 2011, and 2013 [4, 6, 7]. Recently, four EF patients with pain spreading both forward and backward in the same person were reported [5]. In addition, pain traversing the midline to the contralateral side [2, 7], radiating coronally [8], or moving in multiple directions [9] has been described. But our cases are the first reported in Asian patients. The diverse pattern of pain radiation 

| Table 1. Diagnostic criteria for epicrania fugax (ICHD-3) |
|----------------------------------------------------------|
| **A4.11 Epicrania fugax** |
| **Description:** Brief paroxysmal head pain, with stabbing quality, describing a linear or zig-zag trajectory across the surface of one hemicranium |
| **Diagnostic criteria:** |
| A. Recurrent stabbing head pain attacks lasting 1–10 seconds, fulfilling criterion B |
| B. The pain is felt to move across the surface of one hemicranium in a linear or zig-zag trajectory, commencing and terminating in the territories of different nerves |
| C. Not better accounted for by another ICHD-3 diagnosis |

ICHD-3 = 3rd edition of the International Classification of Headache Disorders.
indicates the potentially complex mechanisms underlying the pathogenesis of EF.

Mechanisms underlying the etiology of EF include aberrant ephaptic transmission connecting different nerve fibers, transdiploic conductance of signals through pain fibers, and functional convergence of different afferents within the central nervous system [10]. Furthermore, central mechanisms could explain the advent of autonomic symptoms. The patterns of paroxysms in our three cases are consistent with the potential contribution of the supraorbital nerve in ophthalmic division of the trigeminal nerve (V-1) and the greater occipital nerve in the second cervical root (C2).

In conclusion, we reported three cases fulfilling the diagnostic criteria of EF but with pain spreading in a distinctive manner, which might represent a new variant of EF. Our description might help enrich the diverse clinical phenotypes of EF and reinforce the differential diagnosis between EF and other primary headaches.

References

1. Guerrero AL, Cuadrado ML, Porta-Etessam J. Epicraniafugax: Ten new cases and therapeutic results. Headache 2010;50(3):451–8.
2. Pareja JA, Cuadrado ML, Fernandez-de-las-Penas C, et al. Epicraniafugax: An ultrabrief paroxysmal epi-cranial pain. Cephalalgia 2008;28(3):257–63.
3. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1–211.
4. Cuadrado ML, Gómez-Vicente L, Porta-Etessam J, Marcos-de-Vega MA, Parejo-Carbonell B, Matías-Guiu J. Paroxysmal head pain with backward radiation: Will epicraniafugax go in the opposite direction? J Headache Pain 2010;11(1):75–8.
5. Barón-Sánchez J, Gutiérrez-Viedma Á, Ruiz-Piñero M, Pérez-Pérez A, Guerrero A, Cuadrado M. Epicraniafugax combining forward and backward paroxysms in the same patient: The first four cases. J Pain Res 2017;10:1453–6.
6. Herrero-Velázquez S, Guerrero-Peral ÁL, Mulero P, et al. Epicraniafugax: The clinical characteristics of a series of 18 patients. Rev Neurol 2011;53(9):531–7.
7. Cuadrado ML, Ordás CM, Sánchez-Lizcano M, et al. Epicraniafugax: 19 cases of an emerging headache. Headache 2013;53(5):764–74.
8. Casas-Limón J, Cuadrado ML, Ruiz M, et al. Pain paroxysms with coronal radiation: Case series and proposal of a new variant of epicraniafugax. Headache 2016;56(6):1040–4.
9. Cuadrado ML, Aledo-Serrano A, Di Capua D, Pareja JA. A multidirectional epicraniafugax. Cephalalgia 2015;35(9):835–6.
10. Devor M. Pathophysiological response of nerves to injury. In: McMahon SB, Koltzenburg M, Tracey I, Turk D, eds. Wall and Melzack’s Textbook of Pain. 5th ed. Philadelphia, PA: Elsevier Saunders; 2013:861–88.