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LETTERS TO THE EDITOR

Could CGRP mAbs for migraine trigger rheumatoid arthritis? Insights from a case report

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Dear Editor,

Monoclonal antibodies (mAbs) targeting Calcitonin gene-related peptide (CGRP) have recently shown promising clinical outcomes as migraine prevention therapies[1]. Fremanezumab, a CGRP mAb, is recommended for adults with migraines who experience four or more migraine days per month or have not responded to at least three preventive drug treatments[2]. These therapies exhibit high specificity, with minimal interaction with the immune system, and musculoskeletal adverse events (AEs) are uncommon[3]. However, an Australian case series suggest that CGRP mAbs may trigger inflammatory flares in patients with pre-existing autoimmune diseases[4].

We report the case of a 56-year-old woman with a history of severe migraines, hypertension, and depression. Her neurological evaluation and head CT scan showed no abnormalities. She initiated treatment with fremanezumab 225 mg/monthly, which led to decrease

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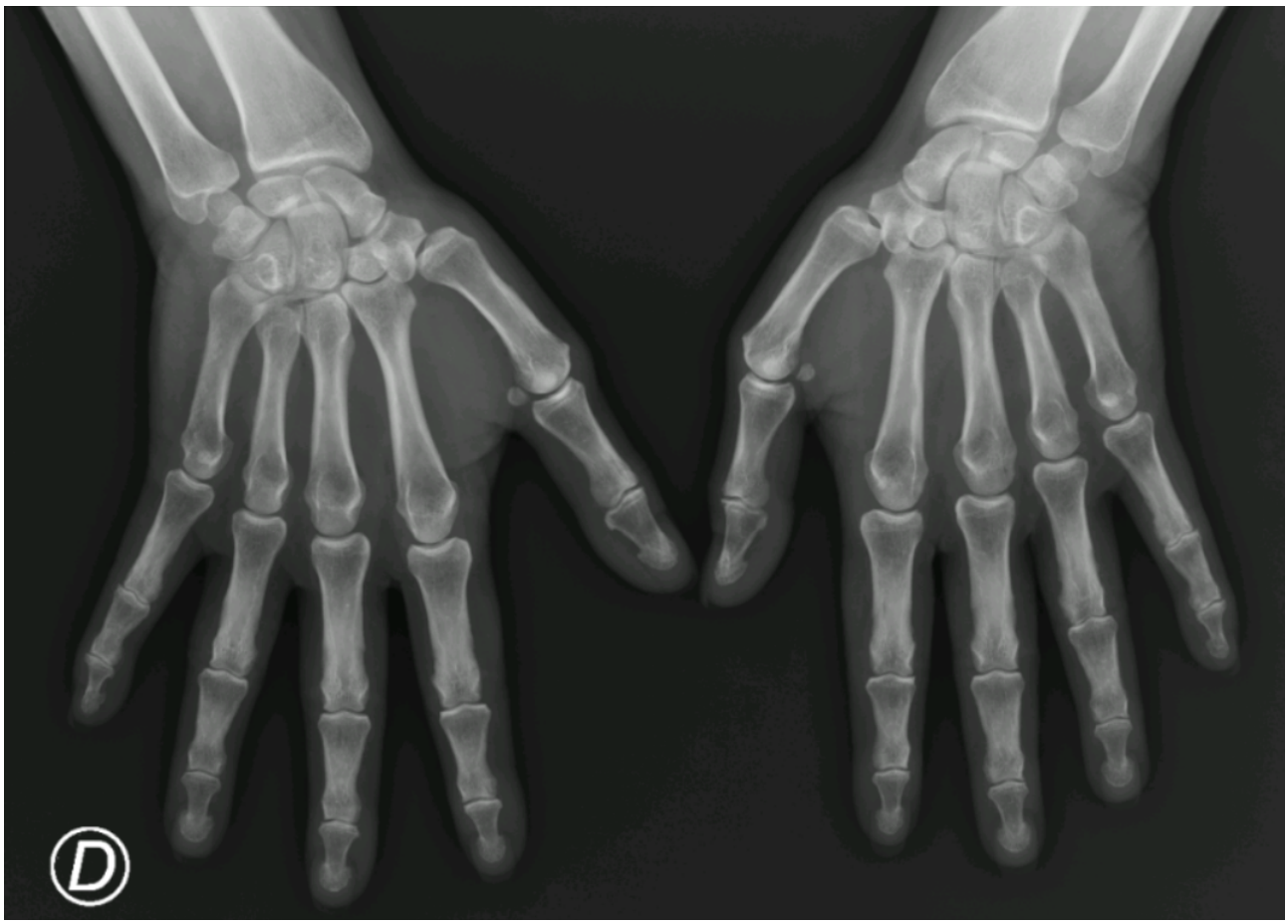

Figure 1. Hand radiograph: Baseline radiograph of the hands showing no abnormalities. The letter "D" indicates the right side.

in her migraine intensity and frequency. However, after three months of treatment, the patient reported symmetric polyarthritis affecting the wrists, hands, shoulders, knees, and feet. Physical examination revealed polyarthritis in the wrists, metacarpophalangeal, proximal interphalangeal, and knee joints. Further investigations revealed elevated C-reactive protein levels (0.95 mg/dL) and an erythrocyte sedimentation rate of 46 mm/hour. Additionally, she had positive for anti-cyclic citrullinated peptide antibodies (28 U/mL), and exhibited low-titer (< 1/160) anti-nuclear antibodies. Hand, feet and knees radiographs that showed no abnormalities (Figure 1). A diagnosis of rheumatoid arthritis was presumed, leading to the initiation of treatment with prednisolone 12.5 mg daily, methotrexate (MTX) 15 mg weekly, folic acid 5 mg weekly, calcium 1200 mg daily, and vitamin D 800 IU daily, resulted in clinical improvement and normalization of inflammatory markers. Her articular symptoms persisted after discontinuation of fremanezumab. Later, changed to leflunomide 20 mg due to gastrointestinal MTX intolerance and is currently in remission.

Conclusions: CGRP mAbs represent promising therapeutic strategies for migraines, with common side effects including inflammation at the injection site, constipation, and nausea[3]. While there are documented cases of immune-mediated disease flares, such as in psoriatic arthritis, psoriasis, and granulomatosis with polyangiitis, triggered by CGRP mAbs, this case represents the first report suggesting a possible association between fremanezumab and the onset of RA[4]. This unique case underscores the need for vigilance when prescribing CGRP mAbs to patients with underlying or potential autoimmune diseases. Further research is essential to fully comprehend the impact of CGRP modulation in rheumatic and autoimmune diseases.

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