Raynaud's phenomenon secondary to erenumab in a patient with chronic migraine

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Introduction

Chronic migraine (CM) is a debilitating neurological disorder with a prevalence of 0.5% to 5% in the general population [(1)]. It is associated with significant negative impact on quality of life (QOL) and mental health [(2)]. Monoclonal antibodies targeting the CGRP pathway have been shown to be effective in episodic and chronic migraine. These molecular treatments work by binding either to the CGRP receptor or the CGRP ligand [(3)]. Raynaud's phenomenon (RP) is characterized by brief reduction of blood flow to the extremities due to vasoconstriction [(4,5)]. The relationship of RP and migraine is previously documented. Zahavi et al. reported RP in association with migraine in 26% (29/111) of patients [(4)]. RP secondary to administration of migraine specific therapies, such as CGRP monoclonal antibodies, has been recently reported in a few cases.

Case History

- A 45 year old right-handed lady who developed chronic daily headache (CDH) with migraine features in 2018 after a viral infection.
- She had migraine in her teens, often associated with her menstrual cycle. There is no history of migraine aura. The headaches progressively increased in frequency and severity in her 30s. The pain is usually holocranial. She also has bilateral facial pain. With worsenings, there is associated phonophobia, aggravation by physical activity and severe fatigue.
- The patient denied photophobia, nausea, vomiting and cranial autonomic symptoms. Poor sleep and physical activity worsen the headaches. The patient has a previous history of varicose vein surgery and panic attacks. There is no history of rheumatological disease. She had sinus surgery in 2009, with no improvement in her headache and associated migraine symptoms.

Clinical Examination & Treatment

- The clinical examination was normal, including fundoscopy. Her routine blood tests including full blood count, biochemical profile, renal, liver, thyroid function, vitamin B12 and folate were within the normal limits. MRI brain and MR venogram (MRV) of the intracranial vessels were unremarkable.
- Her other medication consists of 30mg daily, paracetamol PRN and naproxen PRN.
- She had failed five migraine prophylactic drugs due to side effects and/or lack of efficacy: propranolol, amitriptyline, topiramate, flunarizine and venlafaxine.
- Therefore, as per national and international guidelines, she was started on erenumab 70mg, monthly subcutaneous injection.

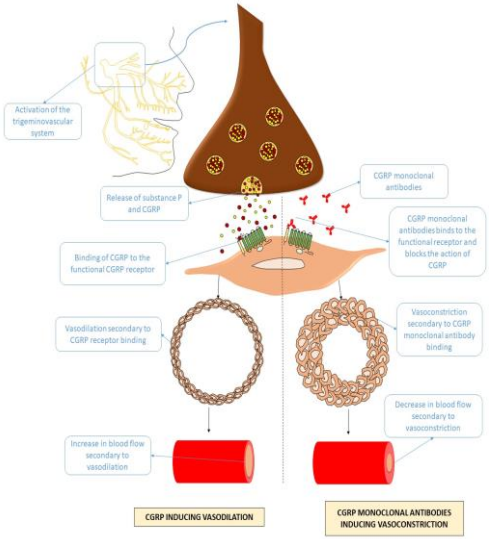
Observation

- The patient reported 40% improvement in headache severity and overall migraine symptoms, but with no crystal clear days.
- Two weeks later she developed intermittent blue discoloration of both hands, which worsened over a period of 7-8 months on Erenumab treatment (figure)
- The symptoms were worse in cold weather and improved in the summer time. Hand movements also improved the symptoms.

- The patient had never experienced such symptoms prior to erenumab administration. A diagnosis of RP secondary to erenumab was made.
- Discontinued treatment after 8 months voluntarily and on medical advice. RP symptoms have improved by approximately 70% and she is now off erenumab for more than 1 year.
- Currently having Botox treatment with improvement of approximately 40-50% in terms of headache and migraine severity

Discussion

- Vasoconstriction is believed to be a major feature of RP and can be triggered by external stimuli, including cold water or weather.
- Targeting the CGRP receptor with monoclonal antibodies is effective in the management of migraine [(3,7)]
- The most likely mechanism by which CGRP monoclonal antibodies cause RP is primarily due to vasoconstriction, but this can only occur in conjunction with several other factors, including genetic and hormonal influences
- CGRP monoclonal antibodies therefore antagonise CGRP's role as a potent vasodilator in this context [(2, 3)]. When administered, erenumab binds to the functional receptor, subsequently blocking its function [(3, 4)].
- This prevents the cascade of reactions within the cell responsible for vasodilation, presumably leading to the development of RP in a small number of cases [(3, 4)].



Conclusion

- This side effect information did not emerge from clinical trials. The presence of significant or debilitating RP in a small proportion of patients with migraine who are treated with CGRP monoclonal antibodies has clinical implications, including the necessity for cessation of treatment in some patients. Furthermore, this class of drugs could exacerbate the symptoms of RP in patients with a previous history of this condition. A previous background history of RP secondary to connective tissue disease might prevent patients from initiating these new class of migraine preventative medications.

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