Dear editor,

Gleich Syndrome is a rare clinical entity, first described by Gerald Gleich in 1984.[1] It is characterized by episodic angioedema with hyper‑eosinophilia along with fever, periodic weight gain, and urticaria.

A 32‑year‑old female with a BMI of 21 kg/m^2 presented with low‑grade fever and pruritic, pinkish swellings on her back and face for 3 days [Figure 1]. She also complained of bilateral swelling around her eyes on day 1, which was absent on presentation. These symptoms had been recurring at 4‑6 week intervals since last 5 months, and each episode resolved with over‑the‑counter antihistamines without any sequel. There was no travel history or unusual exposure to any allergen, food, or drug prior to the onset of symptoms. There was no history of symptoms due to physical triggers such as pressure and temperature variations, or any history of weight loss, abdominal pain, wheezing, dyspnea, palpitations, or paresthesia. Personal and family history were unremarkable. Her general and systemic examinations were non‑contributory except for the presence of fever (oral temperature of 99.8 F). Dermatological examination revealed multiple, faintly erythematous wheals of varying sizes on the upper back and forehead. Test for dermographism was negative. Her general and systemic examinations were non‑contributory except for the presence of fever (oral temperature of 99.8 F). Dermatological examination revealed multiple, faintly erythematous wheals of varying sizes on the upper back and forehead. Test for dermographism was negative. She provided a history of angioedema which had resolved. A provisional diagnosis of recurrent episodic chronic spontaneous urticaria with angioedema was made, and the patient was started on oral antihistamines. Her hemogram was within normal limits except for eosinophilia (Hb: 7.95 mmole/L, platelets: 300 × 10^9/L, TLC: 12.4 × 10^9/L, and absolute eosinophil count: 11 × 10^9 cells/L). A peripheral blood smear (PBS) also demonstrated two eosinophils (spectacle‑shaped bi‑lobed nucleus with central orange granules) along with red blood cells and platelets in adequate numbers, without any atypical cells, thus ruling out malignancy [Figure 2]. We failed to conduct a bone‑marrow biopsy to confirm the absence of malignancy as the patient denied consent. ANA profile, C1 esterase, C3, C4, Serum IgE, Chest X‑ray, and stool examination were unremarkable. Skin biopsy was within normal limits ruling out urticarial vasculitis. Based on clinical findings, underlying hypereosinophilia, and lack of any end‑organ manifestations, malignancy, or vasculitic disorders, we considered the differentials of urticarial vasculitis, parasitic infestation, and hypereosinophilia syndrome (HES). Skin biopsy ruled out urticarial vasculitis, while normal stool examination and transient symptom with an absolute eosinophil count of <15 × 10^9 cells/L ruled out parasitic infestation and HES, respectively. Thus, we made a diagnosis of Gleich Syndrome and initiated low‑dose oral prednisolone along with symptomatic antihistamines. Rapid resolution of symptoms was noted, and repeat eosinophil count following therapy was within normal limit.(cf. HES – persistent eosinophilia for at least 6 months)

Gleich syndrome is a rare and lesser‑known entity, with about 50 cases reported globally, mostly from Japan, Europe, and the United States. The pathophysiology is attributed to secretion of IL‑5 and IL‑6 by helper T cells which stimulate eosinophils. These eosinophils secrete eosinophilic cationic protein to cause a vascular leak, subsequently resulting in angioedema and weight gain.[3] Interestingly, Khori et al.[3] have regarded this syndrome as a multilineage cell‑cycle disorder. Patients typically present with recurrent, episodic non‑allergic

Figure 1: (a) Urticarial wheal on back, (b) Urticarial wheal on forehead

Figure 2: PBS showing two eosinophils (solid arrows) along with adequate RBCs (linear arrows) and platelets (solid arrowheads) [Leishman Giemsa, 100×]
Letter to the Editor

1. Episodic angioedema with eosinophilia (Gleich syndrome) is a multilineage cell cycling disorder. Haematologica 2015;100:300‑7.

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If angioedema and urticaria are episodic, associated with additional features such as fever, weight gain, and oliguria, Gleich syndrome should be considered as a differential, along with other causes of hyper-eosinophilia and constitutional symptoms such as parasitic infections, drugs, neoplasms, eosinophilic granulomatous polyangiitis (EGPA), hypeeosinophilic syndrome (HES), eosinophilia-myalgia syndrome, and cyclical hypeeosinophilia.9,10

Another important differential is capillary leak syndrome, which may be associated with episodic edema, weight gain, renal failure, and normal serum eosinophil count, while Gleich syndrome is characterized by transient eosinophilia with systemic involvement.11

A cytokine profile showing high serum IL-5 concentration skews the diagnosis toward Gleich syndrome, but this investigation was not available at our set-up. Although Gleich syndrome is a diagnosis of exclusion, one must remain aware about this condition. This case has been reported to generate awareness about this yet unexplored and under-reported entity in the present set-up.

Declararion of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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