1. **Cover Letter**

Dauren S. Tashenov

RSE “Medical Center Hospital of the President’s affairs Administration of the Republic of Kazakhstan”

E495 street, building No.2, Yessil region, Astana, Kazakhstan

Postal code: 010000

Dauren.tashenov@gmail.com

+7(708)310-68-21

We present a clinical case "Chronic Spontaneous Urticaria and Autoimmunity: Association of Chronic Autoimmune Gastritis with Autoimmune Urticaria"

Our case underscores the lack of scientific information regarding the connection between chronic spontaneous urticaria and autoimmune gastritis. The presented case may contribute to further study of this association and understanding the pathogenesis of chronic urticaria.

The case description includes the patient's medical history, research findings, and treatment outcomes. We hope for the interest of your Journal Club.

2. **Title page**
   1. **Title**

Chronic Spontaneous Urticaria and Autoimmunity: Association of Chronic Autoimmune Gastritis with Autoimmune Urticaria. Case report.

   2. **Authors**

Galiya M. Tusupbekova, PhD, Chief of the Allergy Center

RSE “Medical Center Hospital of the President’s affairs Administration of the Republic of Kazakhstan”

Dauren S. Tashenov, Allergist

RSE “Medical Center Hospital of the President’s affairs Administration of the Republic of Kazakhstan”

3. Conflict of Interest: none

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5. Keywords

Chronic spontaneous urticaria, autoimmune gastritis, biological therapy, omalizumab.

6. Abbreviations/Acronyms

CSU – Chronic spontaneous urticaria

AH – Antihistamines

CRP – C-reactive protein

AAG - Autoimmune atrophic gastritis

ECL – Enterochromaffin-like

3. Manuscript Text File

Despite thorough clinical and laboratory investigations, a clear cause of chronic spontaneous urticaria (CSU) remains unidentified in approximately 75% of patients, with treatments proving ineffective. [2] Inflammatory conditions of the upper gastrointestinal tract, independent of H. pylori, are considered potential triggers for the development of CSU. Symptoms such as anemia, decreased vitamin B12 levels, recurrent urticaria without other etiology, positive antibodies to parietal cells, and elevated gastrin levels suggest autoimmune atrophic gastritis (Fig. 1) as a possible cause of chronic urticaria. [2]

Autoimmune atrophic gastritis (AAG) is an organ-specific autoimmune disease affecting the gastric body and fundus mucosa. Although the exact mechanisms remain unclear, in both adult and pediatric patients described in the literature, changes lead to proliferation of gastric neuroendocrine-like (ECL) cells and paracrine histamine release. Several pathogenesis mechanisms of CSU have been proposed, with evidence suggesting reactions involving AAG and ECL cells as potential factors contributing to its development. Excessive histamine production/release into the bloodstream may trigger or exacerbate CSU in AAG, independent of Helicobacter pylori, thus indicating histamine release from ECL cells as a primary modulator. [1]

Patient: Male, 39 years old. Since late 2023, he experienced generalized urticarial rashes with periorbital angioedema and lip swelling. These symptoms occurred for the first time alongside catarrhal symptoms in the nasopharynx and asthenic manifestations (body ache, weakness). No causative factors related to acute allergies from medications, food, physical factors, or stress were identified. Upon

admission, during initial rest, laboratory tests showed an inflammatory response with moderate leukocytosis and segmented neutrophilia in the complete blood count. CRP was elevated, and ASLo was moderately elevated. The patient was urgently hospitalized at the Central Clinical Hospital of the Republic of Kazakhstan. Despite therapy, urticaria showed no clear improvement. CRP and D-dimer levels were high. IL-6 levels were elevated. COVID-19 IgG antibodies were detected in serologic testing. Further examination revealed moderate elevations in liver transaminases, bilirubins, and IgE levels (up to 250 IU/mL). Therapy with glucocorticosteroids (GCS), antihistamines (AH), and proton pump inhibitors (PPI) led to regression of symptoms within 48 hours. The attending therapist decided to independently perform endoscopic washing of the intestines, which resulted in a sudden deterioration of the patient's condition with a recurrence of generalized urticaria, body temperature rising to 38.6°C, and sharp stomach pain. CRP levels sharply increased to 114 mg/L (0-5), and D-dimer levels increased to 10.70 mg/L (0-0.5). IL-6 levels were high. Over 7 days, therapy with oral prednisolone 60 mg, dexamethasone 4 mg intramuscularly at night, chlorpheniramine 1 ml intramuscularly twice daily, and levocetirizine 5 mg tablet 2-4 times daily did not yield positive dynamics in urticaria symptoms. After obtaining results of autoimmune markers with positive antibodies to parietal cells and presence of atrophic gastritis without H. pylori, the condition was assessed as the debut of severe CSU associated with AAG. UAS7 score was 42 points. UCT score was ≤ 11 points. The patient was recommended biological therapy with omalizumab at an initial dose of 300 mg subcutaneously. On the same day, GCS and PPI were discontinued. Within 12 hours of omalizumab administration, urticaria regressed. Over the following 4 weeks, UAS7 score was 0 points. UCT score was 16 points. Omalizumab 150 mg subcutaneously was subsequently administered every 4 weeks for 4 months. During this period, UAS7 score remained 0 points with omalizumab therapy. Biological therapy with omalizumab was suspended in April 2024.

4. References

1.J. Bufka, J. Sýkora, L. Vaňková, V. Gutová, Š. Kačerová, O. Daum, J. Schwarz. Impact of autoimmune gastritis on chronic urticaria in pediatric patients – pathophysiological point of views. *European Journal of Pediatrics.* 2023

2.Pavel Kolkhir, Ekena Borzova, Clive Grattan, Riccardo Asero, Dmitry Pogorelov, Marcus Maurer. Autoimmune comorbidity in chronic spontaneous urticaria: A systematic review. *Autoimmunity Reviews.* 2017

5. Figure legend, if applicable

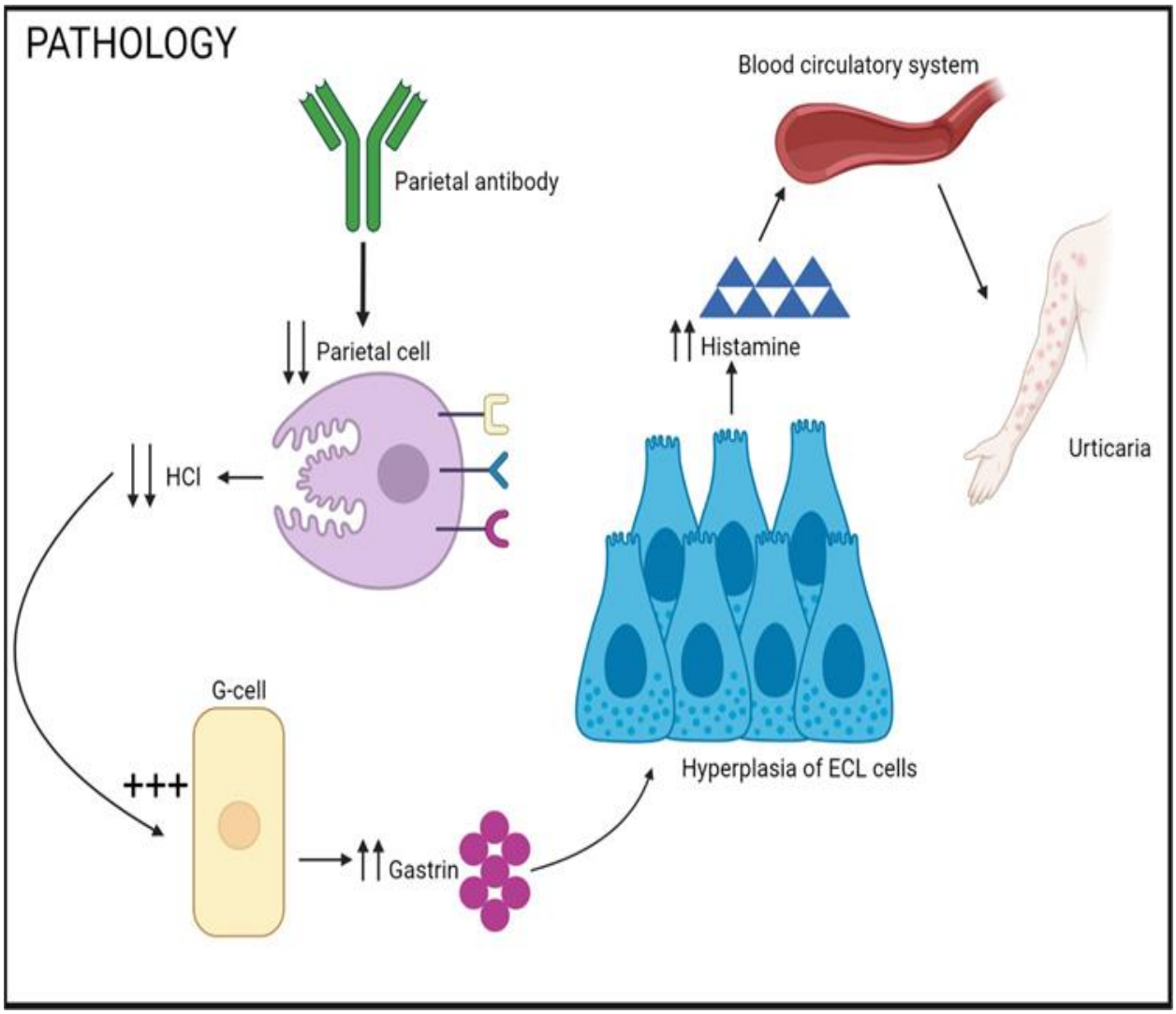

Fig. 1 The pathophysiology of chronic spontaneous urticaria in autoimmune atrophic gastritis is complex and involves alterations in acid secretion, enterochromaffin-like cell hyperplasia, leading to excessive histamine release into the bloodstream, which may trigger chronic urticaria.