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at 5.4 and Anti-C1q antibody was negative. His angioedema episodes were triggered by trauma and occurred about once a month. Symptoms improved with the use of recombinant C1 esterase inhibitors. However, his angioedema episodes worsened over the past year, occurring every 2-3 days without a trigger. His attacks were often accompanied by significant abdominal pain. The patient was referred for further management of his HAE. Interestingly, his past SERPING1 gene sequencing was negative, making HAE less likely. Repeat C4 was low (<4 mg/dL) and C1q was low-normal at 5.1. Given concern for possible AAE, serum protein electrophoresis with immunofixation was obtained, which showed mild IgM gammapathy. He was started on lanadelumab-filyo with successful control of his angioedema.

Conclusion: C1q is normal in 30% of AAE, and many cases cannot be distinguished from HAE from complement levels alone. Therefore, in patients without strong family history and relatively late age-of-onset, AAE should be strongly suspected despite normal C1q level. Lymphoproliferative disorder should be screened in patients suspected of AAE.

M100
PROPHYLACTIC PLASMA-DERIVED C1-ESTERASE-INHIBITOR REPLACEMENT IN A PATIENT WITH ACQUIRED ANGIOEDEMA AND POSSIBLE PRE-CLL CLONE
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Introduction: Acquired Angioedema (AAE) represents an extremely rare disorder with an estimated prevalence of 1:500,000. AAE pathogenesis involves decreased C1-esterase-inhibitor (C1-INH) function, leading to excess bradykinin. C1-INH deficiency may be attributed to consumption or C1-INH auto-antibody, sometimes with concomitant lymphoproliferative neoplasm or autoimmune disease.

Case Description: A 62 year-old woman presented with recurrent facial, extremity, and/or severe bowel angioedema with profound hypotension and unresponsiveness. Prior history was notable for idiopathic abdominal pain and diarrhea. Family history included chronic lymphocytic leukemia (CLL). AAE diagnosis was confirmed: C4 (<2 mg/dL), C1-INH-function (10%), C1q (<3.6 mg/dL). Decreased total IgG (393 mg/dL) was detected, prompting evaluation for hypo-gammaglobulinemia etiology which was unrevealing. Autoimmune and gastro-intestinal workups were unremarkable. Lymphocytosis or lymphadenopathy were not evident. Peripheral flow cytometry revealed an aberrant population (2.8%) of CD5(partial+),CD10(-),CD23(partial+) kalla-restricted B lymphocytes, suggesting a pre-CLL clone. Although angioedema abated with on-demand icatibant, angioedema frequency and severity increased. Plasma-derived C1-INH (pdC1-INH) was initiated weekly without angioedema recurrence. While receiving pdC1-INH, C1-INH-function increased (71%) and IgG improved (526 mg/dL).

Discussion: We describe a case of AAE with possible pre-CLL clone that favorably responded to prophylactic pdC1-INH. Since evidence is limited, AAE lacks specific approved therapies. Recommended prophylactics including danazol or tranexamic acid, though generally tolerated, carry a variable response rate and thrombosis risk, respectively. Prophylactic pdC1-INH may be considered in severe cases. Prophylaxis remains controversial, given unpredicttable response to on-demand pdC1-INH use in the presence of C1-INH auto-antibody and theoretical risk of resistance over time. Close monitoring for clinical CLL in this patient remains imperative.

M101
JOINT PAIN: A RARE SYMPTOM IN PATIENTS WITH HEREDITARY ANGIOEDEMA WITH NORMAL C1-INH
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Introduction: Hereditary angioedema (HAE) is an uncommon genetic disorder, with patients experiencing unpredictable episodes of angioedema. Subtypes include HAE with a deficiency of C1 esterase inhibitor levels (HAE-C1INH) and HAE with normal serum and functional levels of C1-INH (HAE-nl-C1INH). The etiology, pathophysiology, and prevalence of HAE-nl-C1INH are not well understood. We present a case series of an unusual clinical symptom in patients with HAE-nl-C1INH.

Case Description: Eight females (median age, 37.5 years; range, 24-65 years) with HAE-nl-C1INH were identified. Their HAE attacks were properly managed with prophylactic and on-demand treatment, but they presented with bilateral joint pain in the hands and/or feet and pain in prominent joint areas (eg, knees/elbows) that was not associated with swelling during HAE attacks. Medical history included chronic sinusitis (n=8), polycystic ovary syndrome/endometriosis (n=6), and alopecia (n=8). All patients were being treated by an endocrinologist for hypothyroidism and had a standard immunophenotyping panel done, which included lymphocyte phenotyping and T and B cell panels. All patients were previously referred to a rheumatologist. None were antinuclear antibody positive, and other arthritis-related blood tests were normal. All patients had been diagnosed with rheumatoid arthritis, based on clinical symptoms, with no response to methotrexate (n=1), certolizumab/efalizumab (n=1), or hydroxychloroquine (n=1). One patient received intravenous immunoglobulin after being diagnosed with comorbid immunodeficiency (antibody deficiency); this also helped to resolve the joint pain.

Discussion: We propose that joint pain, not associated with an angioedema attack, may present in patients with HAE-nl-C1INH. Furthermore, comorbid endocrine or immune dysregulation may be present.

M102
A CASE OF DELAYED UVULAR ANGIOEDEMA AFTER ADMINISTRATION OF THE COVID-19 VACCINE
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Introduction: Serious adverse allergic reactions to the mRNA COVID-19 vaccines are rare. This is an unusual case of delayed angioedema following administration of the Pfizer-BioNTech COVID-19 vaccine.

Case Description: A 33-year-old male with type I diabetes, eosinophilic esophagitis, peanut allergy, and asthma received the first dose of his Pfizer-BioNTech COVID-19 vaccine without immediate adverse reactions. About 25 hours later, he woke up with severe uvular swelling with associated nausea, emesis, and dyspnea. He had no prior history of angioedema. He denied tongue or lip swelling, pruritus, or hives. Review of other additional triggers was unrevealing. He self-administered IM epinephrine at home without significant improvement. He presented to the emergency department, where he was found to be hypertensive and tachycardic. Physical exam was notable for drooling and tripodding, and flexible laryngoscopy showed grape-sized uvular swelling. Intubation was deferred due to his ability to protect his airway. He received diphenhydramine, systemic corticosteroids, IM epinephrine, and remained on an epinephrine drip for several hours. The angioedema gradually improved over 24 hours. Tryptase and C4 levels returned normal. He was advised to defer his second dose of the vaccine due to the severity of his reaction.
Discussion: This case most likely represents delayed angioedema to the COVID-19 vaccine. Other differentials for uvular swelling, such as infection, trauma, and drug exposure were ruled out. The absence of personal or familial history of angioedema made chronic spontaneous angioedema unlikely. Clinicians should be aware of the possibility of delayed angioedema following administration of the COVID-19 vaccine.

M103
UNDER THE MASQUERADE OF ANGIOEDEMA, CHELIITIS GRANULOMATOSA AN IMPORTANT CLINICAL CONSIDERATION
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Introduction: Cheilitis granulomatosa (CG) is a rare benign infiltrative disorder characterized by firm asymmetric painless swelling of the lip, with diagnosis possible by clinical history alone.

Case Description: A 25F with history of Crohn’s disease presented with one month of painless lip swelling. She started tofacitinib two months earlier due to poorly controlled Crohn’s and prior adverse reaction to other medications. She did not improve with diphenhydramine, prednisone, or tofacitinib discontinuation. Exam revealed asymmetric swelling of the left lip, with gum edema. Biopsy demonstrated CG, attributed to Crohn’s disease. She was treated with intraleisional triamcinolone, and safely resumed tofacitinib.

A 19M with history of well-controlled Crohn’s disease’s presented with three months of fluctuating lip swelling. He had no response to antihistamines. Subsequent treatment with prednisone resulted in partial improvement over several days. Concurrent medications including ciprofloxacin and rifaximin were discontinued with no difference in swelling. On exam, he had asymmetric swelling of the lower lip. Labs revealed normal C4, C1 inhibitor level and function, and C1q. He was referred to dermatology and diagnosis of CG was confirmed clinically. Empiric treatment of CG with doxycycline and topical tacrolimus was initiated.

Neither patient had associated rash, pruritus, fissured tongue, dysphagia, abdominal pain, facial nerve paralysis, dyspnea, or family history of angioedema.

Discussion: An atypical pattern of symptom development and treatment response should prompt consideration of alternative etiologies of lip swelling. Early diagnosis of CG allows for targeted therapies and avoids unnecessary labeling of hypersensitivities that may negatively impact patient comorbidities.

M104
AN UNUSUAL PRESENTATION OF HEREDITARY ANGIOEDEMA
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Introduction: The presentation of hereditary angioedema (HAE) is diverse, from asymptomatic to severe asphyxia and death. Because of its potential for severe outcomes, it is important to recognize even asymptomatic cases.

Case Description: A 21-year-old female who suffered from recurrent urinary tract infections (UTI) with low complement was referred for immunology evaluation. She experienced five UTIs during the previous year. She did not suffer from other infections but did experience joint pains in her neck and back. She followed with rheumatology for an elevated ANA but had no definitive diagnosis. Family history was positive for Grave’s disease and intermittent, idiopathic abdominal pain in her father. Initial evaluation showed decreased CH50 (<13 U/ml) and C4 (7 ml/dL), and low C1 esterase inhibitor (24 ml/dL) and function (24%). Mannose binding lectin and AH50 were normal, as were cellular, humoral, and phagocyte evaluation. On further questioning, she denied any obvious angioedema but did report intermittent idiopathic episodes of abdominal bloating. Targeted immunodeficiency genetic panel showed that she was heterozygous for a pathogenic c.1397G>T (p.Arg466Leu) SERPING1 variant, consistent with HAE. She was not approved for lanadelumab prophylaxis, so was started on ecallantide.

Discussion: This patient’s personal history of abdominal bloating and paternal history of idiopathic abdominal pain were important red flags for possible HAE that were minimized by the patient. While these unusual presentations may be challenging to recognize, it is important to identify such patients in order to provide them with appropriate diagnosis, prophylaxis and acute treatment to minimize adverse outcomes.

M105
AQUAGENIC URTICARIA: AN INFREQUENT ALLERGIC REACTION TO WATER
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Introduction: Aquagenic urticaria (AU) is a rare type of inducible chronic urticaria. It occurs after exposure to water, regardless of its temperature. Due to the lack of scientific evidence regarding the pathophysiological mechanisms, there is no specific treatment for the disease, so it is based on avoiding the trigger and symptomatic control.

Case Description: A 15 year-old female patient presented a 6-month history of recurrent episodes of hives, erythema, and generalized pruritus 10 minutes after starting to bathe and with complete remission within 60 minutes. Skin lesions did not occur with exposures less than 10 minutes, a water provocation test was performed. The evaluation of the water-exposed surface was applied for 20 minutes, and it was observed that the patient presented a wheal of 1x1 cm, with erythema of 2x2 cm, in the upper and lower right quadrants. The patient presented lesions in the neck and on the face, areas where the water was in contact with the skin by contiguity, due to the prone position (Figure 1). The patient was diagnosed with AU and treatment was started with double dose oral cetirizine, responding adequately to treatment.

Discussion: The diagnosis of AU is based on the patient’s medical history and the results of a water provocation test. We must consider that exposure to water is constant throughout the day and is an important part of proper hygiene, so treatment with a dose of 10 mg of cetirizine twice a day was initiated to achieve an adequate therapeutic response.