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BACKGROUND

Hereditary angioedema (HAE) and Covid-19 can independently lead to an exaggerated inflammatory response. Pregnancy poses specific challenges for HAE patients, as elevated estrogen levels can influence disease severity. We describe two patients with HAE type 1 who developed Covid-19 while unvaccinated during pregnancy.

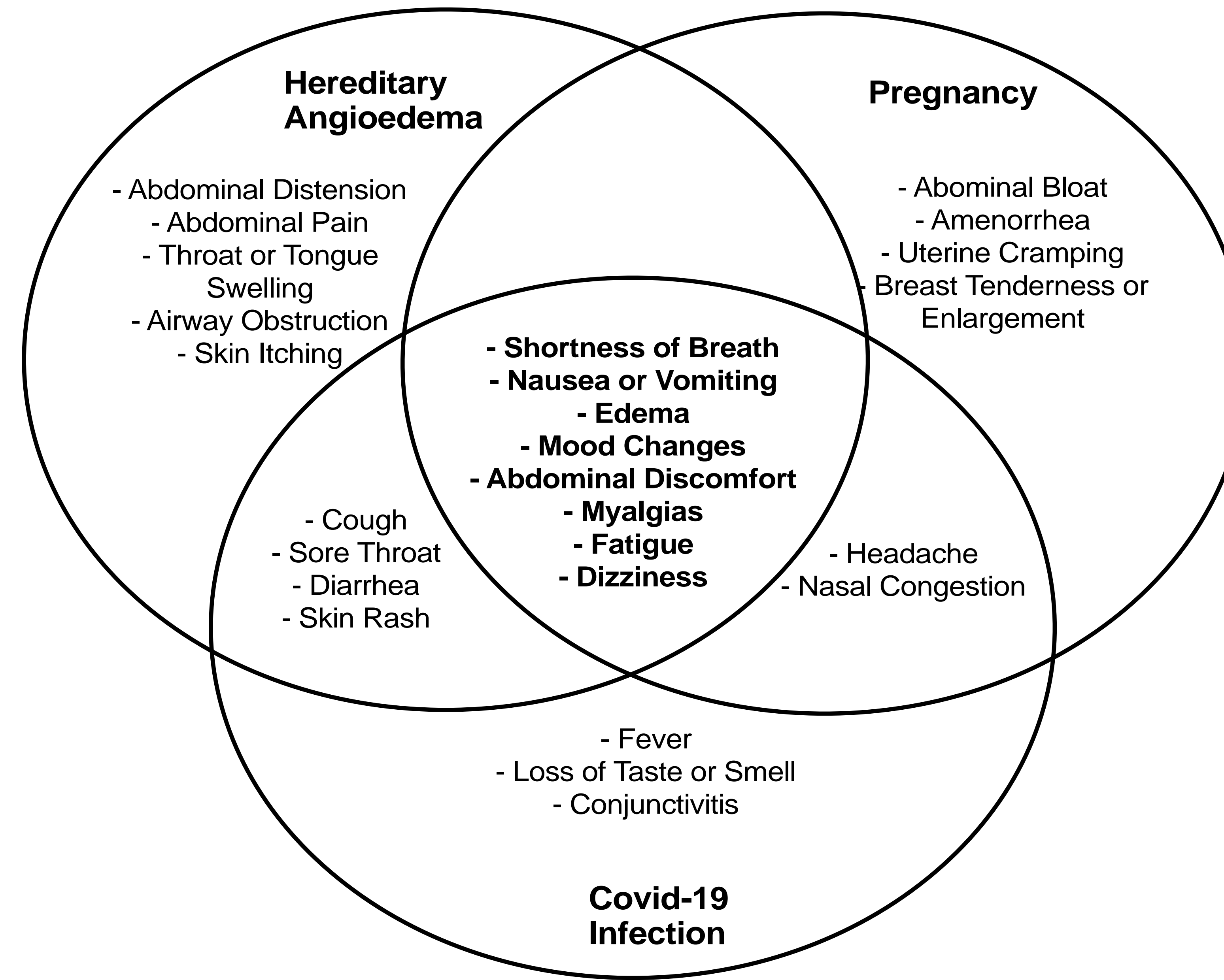
PRESENTATION

Patient 1	Patient 2
20-year-old Caucasian female with known HAE type 1. Maintained on Haegarda® 60 IU/kg with disease control prior to presentation.	24-year-old Hispanic female with history of obesity (BMI=40), seizure disorder, and HAE type 1. Maintained on Haegarda® 60 IU/kg with disease control prior to presentation.
Presented 22 weeks with abdominal pain and extremity swelling without respiratory symptoms. Later developed loss of taste and smell.	Presented with headache cough, congestion, nausea with vomiting at 27 weeks after contact with person with confirmed Covid-19. Initially hypoxic requiring 3 L/min oxygen via nasal cannula.

LABORATORY EVALUATION

<i>SERPING1</i> sanger sequencing by GeneDx - heterozygous mutation (c.707 T>C, p.F2365).	<i>SERPING1</i> sanger sequencing by GeneDx - heterozygous mutation (c.666_667delTC, p.Q223DfsX33).
SARS-CoV-2 diagnosed on routine nasal swab surveillance screening in the ER by PCR via Texas Children's Hospital Laboratory.	SARS-CoV-2 diagnosed by home antigen testing, confirmed by PCR via Texas Children's Hospital Laboratory.
CRP 2.2 mg/dL, C4 4 mg/dL.	Chest X-ray with hypoinflated lung volumes and multifocal basilar prominent consolidative opacities. CRP 16.1 mg/dL.

Clinical Presentation



DIAGNOSIS

Patient 1	Patient 2
HAE flare in the setting of Covid-19 during pregnancy.	Covid-19 infection and pneumonia during pregnancy.

TREATMENT

2500 IU of IV human C1-INH for flare.	IM ceftriaxone, azithromycin. Therapy escalated to remdesivir, dexamethasone, baricitinib. No additional C1-INH.
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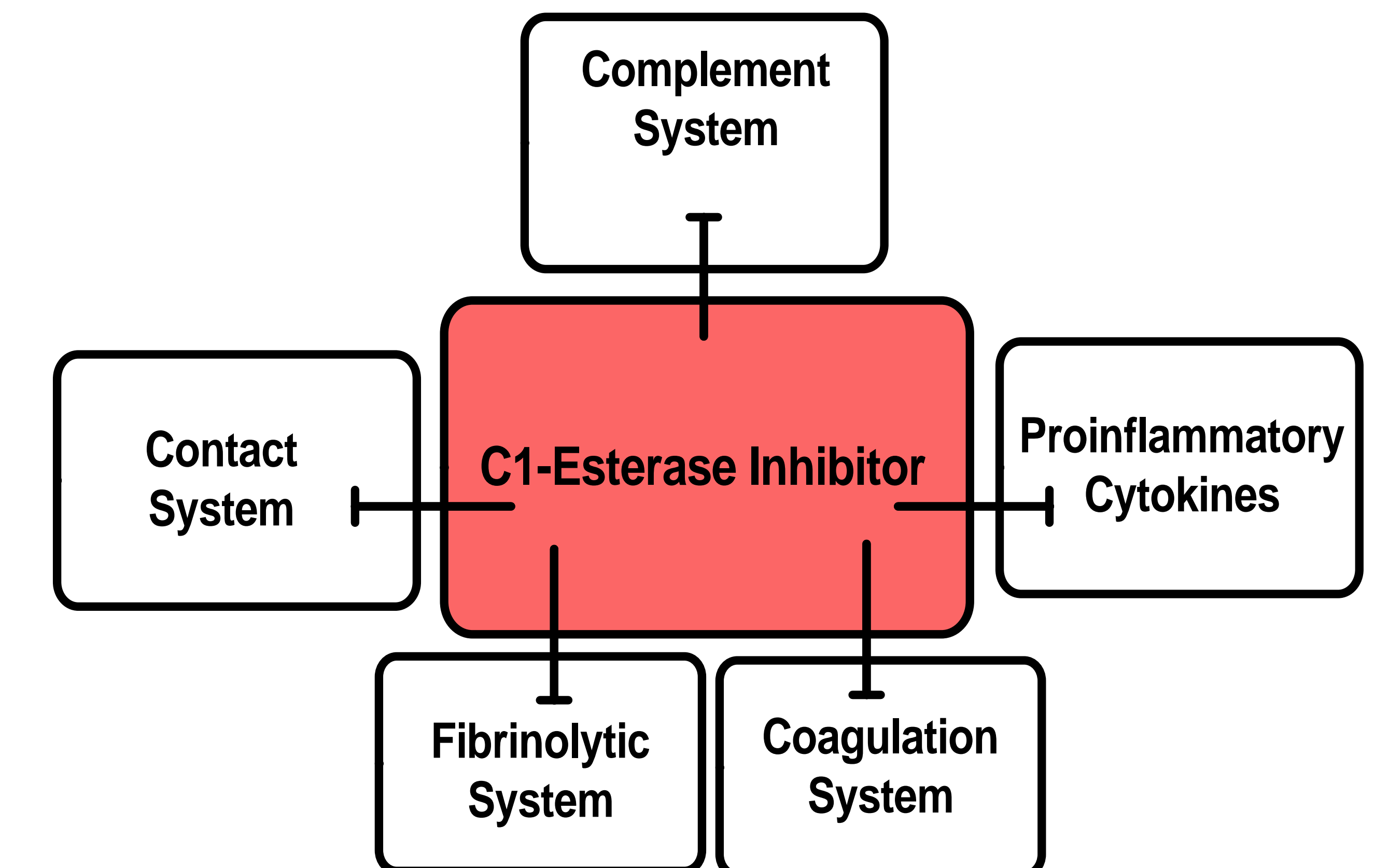
OUTCOME

Swelling and abdominal pain resolved after one day hospital observation. Pregnancy progressed, healthy newborn.	Notably without flare symptoms. Hospitalized for four days, discharged on room air at 29 weeks. Pregnancy progressed, healthy newborn.
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DISCUSSION

Hereditary angioedema (HAE) is a rare disorder typified by deficient or dysfunctional C1 esterase inhibitor (C1-INH). HAE and Covid-19 exhibit pathophysiologic overlap via the activation of complement, contact, and coagulation systems, and in the production of proinflammatory cytokines. Both HAE and Covid-19 can independently lead to an exaggerated inflammatory response. Elevated estrogen levels in the pregnancy state can result in a physiologic state that increases risk for both angioedema flares and exacerbate inflammation in Covid-19 infection. Common pathway blockade through C1-INH may dampen inflammation and improve outcomes.

Common Pathway Blockade



CONCLUSIONS

- Further studies regarding C1-INH impact on severe inflammation associated with Covid-19 needed.
- Case highlights the importance of maintaining adequate therapy in HAE patients, particularly during pregnancy.