

# Hypovolemic shock caused by intestinal angioedema induced by Angiotensin-Converting Enzyme inhibitors in postpartum period – A case series

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## Abstract

**Background:** Angiotensin converting enzyme inhibitors (ACEIs) are commonly used in the treatment of hypertension. We describe the first cases of angiotensin-converting enzyme inhibitor (ACEI) -induced intestinal angioedema in the postpartum period.

**Case presentation:** Both patients presented with hypovolemic shock and acute abdominal complaints. The first patient underwent laparotomy because of the suspicion of internal bleeding. Only large amount of ascites was found. After exclusion of other causes, the diagnosis of ACEI-induced intestinal angioedema was made. Pattern recognition in our second patient prevented invasive examinations. Both patients made full recovery after discontinuation of angiotensin converting enzyme inhibitor and with supportive therapy.

**Conclusion:** Identification of ACEI-induced intestinal angioedema as a cause of abdominal complaints and hypovolemic shock may avoid unnecessary invasive examinations. ACEIs should not be first choice in the treatment of hypertension in the postpartum period.

## Background

The National Institute for Health and Care Excellence (NICE) indicate ACEIs as first line treatment of hypertension before the age of fifty. Therefore, in the Netherlands, ACEIs are also used in women with hypertension in the postpartum period.

ACEI-induced angioedema is a known rare side effect of ACEIs. Angioedema is a condition caused by an increase in capillary permeability. ACEI-induced facial edema is a well-known possible life-threatening identity [1,2]. However, ACEI-induced intestinal angioedema is rarely reported. Intestinal angioedema may lead to acute and chronic abdominal complaints but can also mimic acute abdomen and cause hypovolemic shock [3,4].

We present here, as far as we know, the first two cases of ACEI-induced intestinal angioedema in the postpartum period. Both patients presented with signs of hypovolemic shock and abdominal complaints.

Quick identification of ACEI-induced intestinal angioedema as a rare cause of abdominal complaints and even hypovolemic shock may avoid unnecessary invasive examinations. Discontinuation of the ACEI and supportive therapy for their symptoms can resolve the condition.

## Case presentation

### Case one

Our first patient was rushed in the emergency department by ambulance with severe abdominal pain, vomiting and signs of hypovolemic shock. She was a gravida four para three abortus one with no significant medical or surgical history besides a cesarean section due to breech presentation in the second pregnancy. The latest delivery of a healthy daughter was vaginally 36 hours before presentation. This

delivery was induced at 38 week's gestation because of pregnancy induced hypertension. Postpartum methyldopa was changed in enalapril according to the local protocol. Twenty-four hours later she was dismissed with normal blood pressure and no complaints. On the emergency department an acute abdomen was diagnosed. At arrival she had a clammy skin, an altered level of consciousness and a blood pressure of 60/30 mmHg. Bedside abdominal ultrasonography, immediately available at our department, showed a large amount of free fluid.

After initial stabilization and before the results of the lab were known she was rushed in the operation room because of high suspicion of hypovolemic shock due to intra-abdominal bleeding. After vertical laparotomy they found 1100 cc of ascites and no signs of intra-abdominal bleeding or other intra-abdominal abnormalities. The analysis of the fluid described this as an exudate and not urine. Her hemoglobin level during surgery was 10.2 mmol/L. A drain was left in place for the case there was new fluid accumulation.

The patient was post-operative admitted to the critical care unit for monitoring. The next day after receiving enalapril here symptoms recurred, and she developed an itching rash on her thorax and arms. An allergic reaction was suspected and after a search in literature we

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discovered the possibility of ACEI-induced intestinal angioedema. Enalapril was discontinued and the patient received supportive therapy. She recovered completely and was discharged five days after admission.

## Case two

This primiparous, with no significant medical or surgical history, presented with abdominal pain, vomiting and diarrhea. Five days before she had labor induction at 35 weeks' gestation for severe Hemolysis Elevated Liver enzymes and Low Platelets syndrome. An abdominal ultrasound was performed at day of delivery because of severe pain in the upper abdomen. This ultrasound showed no signs of liver pathology or free fluid. During delivery intravenous admission of magnesium sulfate and nicardipine was started to prevent eclampsia and treat severe hypertension. A healthy premature girl was delivered spontaneously. Postpartum enalapril was started and the infusion of magnesium sulfate and nicardipine reduced and eventually stopped. At day four postpartum she collapsed in her room at the maternity ward. The patient had tachycardia and was hypotensive. A blood sample was taken and a second intravenous line was placed. She received fluids and medication. A bedside abdominal ultrasound was made bedside by the obstetrician. This ultrasound showed massive free fluid in the abdomen. A hypovolemic shock because of intra-abdominal bleeding was suspected. However, quick results of the blood sample showed her hemoglobin level to be elevated (7.8 mmol/L) compared with her previous results the day before (4.4 mmol/L), which made an intra-abdominal bleeding very unlikely. Symptom recognition of the previous case helped to suggest the possibility of a second case of ACEI-induced intestinal angioedema causing hypovolemic shock. The patient was stabilized after quick infusion of 1000cc heated crystalloids (Ringer's lactate solution). A second abdominal ultrasound by a radiologist showed a large amount of free fluid in the patient's abdomen and edema of the small intestines (Figure 1). The diagnosis of ACEI-induced intestinal angioedema was made. The patient was admitted to the intensive care for monitoring and supportive therapy with intravenous fluids. The admission of enalapril was immediately stopped. Her clinical condition improved quickly as the effect of enalapril worn off. She fully recovered after two days and was discharged.

## Discussion

It is believed that approximately 0.1–0.5% of patients taking ACEIs will develop angioedema and that ACEIs account for 30% of all cases of angioedema.<sup>4</sup> However, ACEI-induced intestinal angioedema is rarely reported. In 2017 a literature review by Wilin, *et al.* noted only 25 cases

of this rare side-effect. They present one extra case themselves [5]. After this publication only few other case reports were published but none in the postpartum period.

Angioedema is the vascular leakage of serum from small vessels with accumulation of this serum in interstitial tissue space causing swelling. The possible explanation of this angioedema may include bradykinin accumulation. ACEI block the formation of angiotensin II, a deactivator of bradykinin. The increased levels of bradykinin increase the levels of endothelium derived relaxing factor and prostaglandin E<sub>2</sub> and I<sub>2</sub>. These vasoactive peptides lead to vasodilation and vascular permeability [2].

Scheirey, *et al.* suggest that estrogen may play a role in the pathogenesis because of the large number of obese women in their population and other case reports [6]. In general, risk factor to develop angioedema are female sex, African ethnicity, smoking and certain atopic diseases [7]. Both our patients were of female sex, Caucasian ethnicity, non-smoking and non-obese.

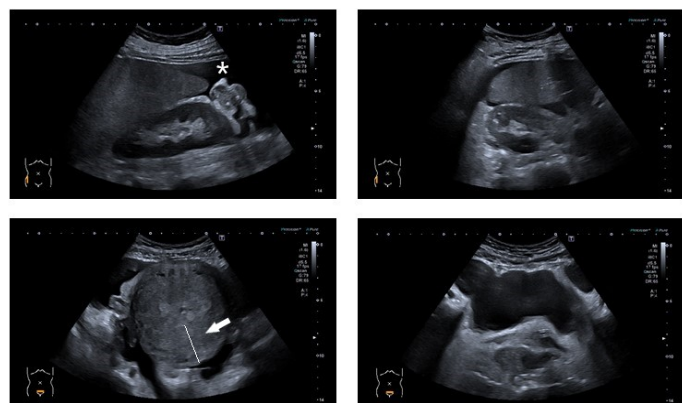
In this case report we have presented two cases of abdominal pain and hypovolemic shock caused by ACEI-induced intestinal angioedema in the postpartum period. After the first cases, which resulted in an unnecessary laparotomy pattern recognition helped us in the second case to obtain a diagnosis without the need of invasive procedures. The laboratory finding that suggested ACEI-induced intestinal angioedema was increased hemoglobin combined with free fluid on ultrasound.

Only Myslinksi, *et al.* described two cases of hypovolemic shock like our case [3]. The symptoms of ACEI-induced angioedema may develop at any time after the start of administration. The diagnosis of ACEI-induced intestinal angioedema remains one of exclusion to help diagnose the condition, specific CT findings are being described: preserved luminal transit with small-bowel wall thickening, dilatation and straightening and ascites. Edema of the wall of the stomach has also been reported. Laboratory findings may include a mild leukocytosis and increased hemoglobin levels due to the fluid shift [6]. Both of our patients had a mild leukocytosis and increased hemoglobin levels. As the combination of the symptoms with ascites and bowel wall thickening in patients taking ACEIs is highly suggestive a paracentesis is not required if this condition is suspected [8]. Discontinuation of the ACEI is the main treatment combined with supportive therapy for the symptoms. The adverse effect should be carefully noted in the patient's history to prevent recurrent episodes due to repeated exposure to ACEI.

Change of the Dutch protocol should be considered as there are many safer options such as calcium channel blockers and beta blockers for the treatment of postpartum hypertension [9].

## Learning points/take home messages

- Identification of ACEI-induced intestinal angioedema as a rare cause of abdominal complaints and even hypovolemic shock may avoid unnecessary invasive procedures in patients taking ACEI.
- Discontinuation of the ACEI is the main treatment combined with supportive therapy.
- The combination of the symptoms with ascites and bowel wall thickening on imaging is highly suggestive which makes a paracentesis unnecessary if this condition is suspected and other causes are excluded.



**Figure 1.** Ultrasound shows a large amount of free fluid (asterisk) in the abdomen and edema of the small intestines (arrow)

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