



## Kounis Syndrome Accompanying Diffuse Alveolar Hemorrhage due to Pinaverium Bromide: A Case Report

Pinaverium Bromide Bağlı Diffüz Alveoler Hemorajiye Eşlik Eden Kounis Sendromu: Olgu Sunumu

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## Kounis Syndrome Accompanying Diffuse Alveolar Hemorrhage due to Pinaverium Bromide: A Case Report

### ABSTRACT

Kounis syndrome is defined as a coronary artery distortion due to hypersensitivity to various reasons such as drugs, environmental exposure, nutrients, coronary stents, etc. Diffuse alveolar hemorrhage is a life-threatening condition that clinically presents with hypoxemic respiratory distress, low hematocrit level, hemoptysis, and extensive pulmonary infiltration. Drugs involving pinaverium bromide as an active ingredient is frequently used for relieving gastrointestinal complaints. In this report, we present a case of a young female patient with Kounis syndrome accompanying diffuse alveolar hemorrhage admitted to our emergency department due to allergic reaction following Pinaverium Bromide intake.

**Keywords:** Anaphylaxis, diffuse alveolar hemorrhage, Kounis Syndrome, Pinaverium Bromide

### ÖZET

Kounis sendromu, çeşitli nedenlere bağlı olarak koroner arter bozulması olarak tanımlanır. Bu nedenler arasında ilaçlar, çevresel maruziyetler, besinler, koroner stentler vb. yer alabilir. Diffüz alveoler hemoraji hipoksemik solunum sıkıntısı, düşük hematokrit seviyesi, hemoptizi ve geniş pulmoner infiltrasyon ile klinik olarak kendini gösteren hayatı tehdit eden bir durumdur. Pinaverium bromid etken maddesi içeren ilaçlar sıklıkla gastrointestinal şikayetlerin hafifletilmesi için kullanılır. Bu raporda, Pinaverium bromid alımını takiben alerjik reaksiyon nedeniyle Acil Servisimize başvuran ve Kounis sendromu ile birlikte diffüz alveoler hemorajiye sahip genç bir kadın hastayı sunuyoruz.

**Anahtar Sözcükler:** Anafilaksi, diffüz alveoler hemoraji, Kounis Sendromu, Pinaverium Bromid

## Introduction

Kounis syndrome (KS) is defined as a coronary artery distortion due to hypersensitivity to various reasons such as drugs, environmental exposure, nutrients, coronary stents, etc (1). The disease involves three variants as vasospastic allergic angina, allergic myocardial infarction, and stent thrombus consisting of obstructing thrombus formed by eosinophil and/or mast cell infiltration (1). The variant developing due to vasospasm after drug use is type 1, and there are many examples reported in the literature (2, 3). Diffuse alveolar hemorrhage (DAH) is a life-threatening condition that clinically presents with hypoxemic respiratory distress, low hematocrit level, hemoptysis, and extensive pulmonary infiltration (4, 5). Pulmonary-renal syndromes, connective tissue disorders, infections, and medication are the main reasons for DAH. Treatment of DAH mainly depends on treatment of the underlying cause and corticosteroid is the mainstay of the treatment in many cases. Cessation of medication is recommended in drug-related and other exposure-related DAH cases (4). Drugs involving Pinaverium bromide (PB) as an active ingredient is frequently used for relieving gastrointestinal complaints (6). In this report, we present a case of a young female patient with KS accompanying DAH admitted to our emergency department (ED) due to allergic reaction following PB intake.

## Case report

A 26-year-old female patient with abdominal pain was admitted to family physician and a medication involving PB as an active ingredient was administered. After medication, the patient developed tongue swelling, itching on the body, chest pain, and shortness of breath. In her medical history, any chronic disease or smoking was not determined. Her vital signs were as follows: Blood pressure: 89/60 mmHg, heart rate: 86 beats/minute, temperature: 36,1°C, oxygen saturation: 98%. On physical examination, an uvula edema was determined.

On electrocardiogram (ECG); ST elevations on DI, aVL leads and ST depression on V1, V2, V3, V4, V5, and V6 leads were observed, and the patient was diagnosed with KS (Figure I). The chest radiograph showed a reticulonodular pattern that could be

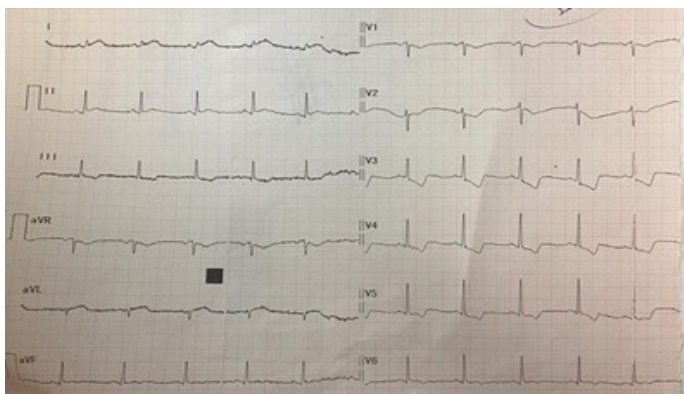
consistent with diffuse alveolar hemorrhage (Figure II). On thorax computed tomography (CT), findings of DAH were determined in lung parenchyma without any findings of pulmonary embolus (Figure III). On blood analysis White blood cell (WBC) count was  $20.3 \times 10^9/L$  with neutrophil dominance, troponin was 585 ng/L, pH was 7.29 and lactate was 3.16 mmol/L (Table I).

**Table I.** Laboratory findings of the patient on admission

Parameter	On Admission	Second Day of Hospitalization	Reference Range
Leukocyte ( $10^9/L$ )	20.30	14.69	4.49-12.68
Hemoglobin (g/dL)	16	15.8	11.9-14.6
Hematocrit (%)	46.9	46.1	36.6-44
Platelet ( $10^9/L$ )	244	282	154-400
RDW (%)	38.5	39.4	38.2-49.2
INR	1.15	1.17	0.8-1.2
PT (sec)	13.4	13.7	10-14
Troponin (ng/L)	585	424	0-300
D-dimer (mg/dL)	0.12	0.19	0-0.55
Creatinine (mg/dL)	0.6	0.7	0.5-1.1
LDH (U/L)	225	263	5-248
Total bilirubin (mg/dL)	0.52	0.42	0.3-1.2
Direct bilirubin (mg/dL)	0.11	0.08	0-0.2
CRP (mg/dL)	3.34	6.1	0-5
pH	7.29	7.37	7.35-7.45
pCO <sub>2</sub> (mmHg)	43	44	41-51
pO <sub>2</sub> (mmHg)	34.5	36.2	35-45
Lactate (mmol/L)	3.16	1.31	0.5-2
Bicarbonate	20.4	24.4	20-24

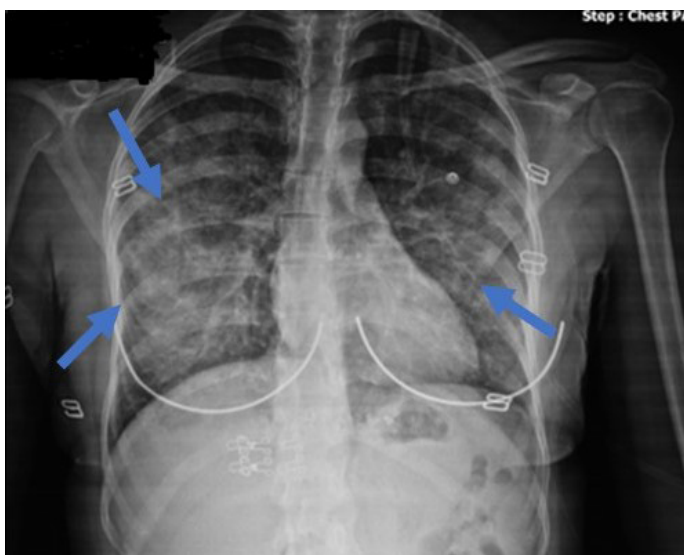
Based on these findings, supportive care was initiated for the diagnoses of KS and DAH, and to address the underlying anaphylaxis, 0.5 mg of intramuscular adrenaline was administered. Additionally, 4 mg dexamethasone intravenous was administered.

The patient was consulted with a cardiologist, chest diseases specialist, anesthesiologist, and dermatologist. The cardiologist recommended observation with medical support. The patient was hospitalized in the intensive care unit (ICU) by the anesthesiologist. The patient left with written consent on the second day of hospitalization.

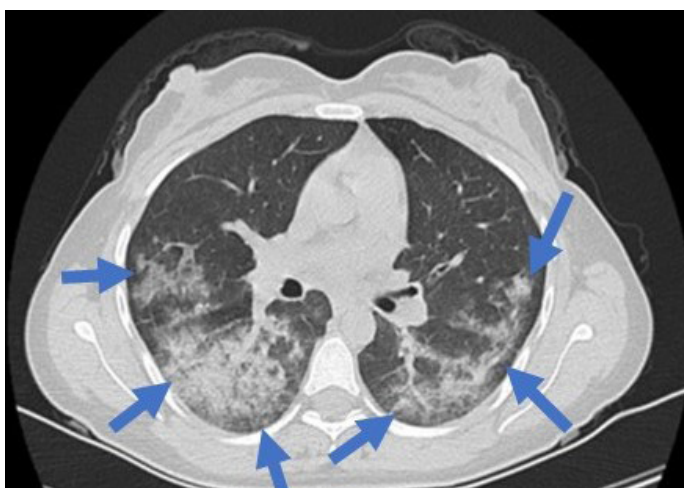


**Figure I.** The patient’s initial ECG shows ST depressions on leads V1, V2, V3, V4, V5, and V6, with ST elevations on leads DI and aVL.

Informed consent was obtained from the patient and their relatives for the use of medical data and images related to this study.



**Figure II.** Chest X-ray: Diffuse reticulonodular pattern



**Figure III.** Thorax Computed Tomography: Diffuse alveolar hemorrhage in lung parenchyma

### Discussion

The main clinical signs and symptoms of KS are associated with chronic allergic reactions accompanied by cardiac symptoms. Cardiac symptoms and findings are related to ECG changes such as ST segment elevation/depression, heart block in any grade, and cardiac arrhythmias mimicking digitalis intoxication (1). KS has 3 types. Type I represents coronary spasm due to endothelial dysfunction and microvascular angina. Type II involves patients with a history of occult atheromatous disease. Type III represents patients with aspirated coronary artery stent thrombus with eosinophil and mast cell involvement observed with hematoxylin eosin and Giemsa dye. KS is a complex form of acute coronary syndrome needs to be diagnosed and treated promptly. After surviving the acute event, a 12-derivation ECG, echocardiogram, and a complete cardiac assessment involving risk factor modifications must be performed (7). Although it is not a rare disease it is rarely diagnosed and may easily be misdiagnosed (1). Thus, it is important for EM physicians to obtain a 12-lead ECG and a detailed cardiac anamnesis. DAH should be kept in mind when a patient admits with hypoxemia, new-onset anemia, and alveolar infiltrations on chest X-ray. Nevertheless, in approximately 1/3 of the patients, hemoptysis cannot be determined (4). A detailed history involving exposure to drugs, physical examination, and laboratory findings should be evaluated in combination to establish a diagnosis (5). DAH is a medical emergency and immediate cessation of medication is recommended in DAH cases (4). PB is a calcium channel blocker agent generally used for irritable bowel syndrome (6). In the literature, we could not coincide a case of DAH due to PB. To our knowledge, this is the first case of KS accompanying DAH due to PB. In conclusion, PB is an easily available and frequently used medicine. Clinicians should be aware of lethal complications of PB such as KS and DAH.

## References

1. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med* 2016;54(10):1545-1559.
2. Raschi E, Fertonani Affini L, Antonazzo IC, Diemberger I, Poluzzi E, De Ponti F. Drug-induced Kounis syndrome: A matter of pharmacovigilance. *Int J Cardiol* 2019;274:381.
3. Ece Y, Erenler AK, Doğan T. Kounis Syndrome following metamizole infusion. *Sakarya Med J* 2016;6:170-174.
4. Newsome BR, Morales JE. Diffuse alveolar hemorrhage. *South Med J* 2011;104(4):269-274.
5. Ioachimescu OC, Stoller JK. Diffuse alveolar hemorrhage: diagnosing it and finding the cause. *Cleve Clin J Med* 2008;75(4):258-280.
6. Bor S, Lehert P, Chalbaud A, Tack J. Efficacy of pinaverium bromide in the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *Therap Adv Gastroenterol* 2021;14:17562848211033740.
7. Tsigkas G, Chouchoulis K, Theodoropoulos K, Kounis NG, Alexopoulos D. Allergic reaction reveals a non-lethal late stent thrombosis. A new subtype of Kounis syndrome?. *Int J Cardiol* 2011;149(2):281-282.