To the Editor: In 2016, a 35-year-old Chinese man was admitted to our hospital who had experienced multiple thromboses for 9 years, severe fatigue, and oliguria for a total of 3 weeks. The patient had been diagnosed with pulmonary embolism and multiple deep vein thromboses at a local hospital 9 years ago. The patient was prescribed warfarin, and the international normalized ratio (INR) was maintained between 2.42 and 3.18. While laboratory findings revealed a prolonged case (77.8 s) of activated partial thromboplastin time (APTT) at that time, no further investigations were carried out and anticoagulation therapy for the patient was terminated after 3 months.

In March of 2016, the patient was admitted to a local hospital for acute cholecystitis and cholelithiasis. Laboratory tests revealed significantly prolonged APTT (74.5 s). Fatigue and oliguria were observed in the patient following laparoscopic cholecystectomy and amoxicillin administration. Urine output was observed to increase to 1000 ml/d following the withdrawal of antibiotics, while fatigue was exacerbated with a low-grade fever and a loss of appetite.

This patient was transferred to our hospital with a fever of 39.5°C and low blood pressure (BP, 86/48 mmHg, 1 mmHg = 0.133 kPa). In addition, urinary tract infection (UTI), and hyperhomocysteinemia. The blood vessels ultrasound and nuclear medicine ventilation-perfusion (V/Q) scan revealed thromboses in the left popliteal vein and pulmonary arteries. A computed tomography scan revealed high-density masses in bilateral adrenal glands that were highly suggestive of bilateral adrenal gland hematomas [Figure 1]. The clinical picture of abnormal electrolytes results and hyperpigmentation of the skin and mucosa elicited investigation into Addison’s disease due to bilateral adrenal hemorrhage, which was then confirmed by the detection of low plasma cortisol levels (3.8–11.0 μg/dL) and high adrenocorticotropin levels (524–888 pg/ml), leaving the function of adrenal reticular zone and adrenal medulla normal.

Hydrocortisone replacement therapy was immediately started. Because of the thrombosis, the patient was given subcutaneous low-molecular-weight heparin, and then switched to a long-term
Adrenal involvement in the antiphospholipid syndrome:
density masses indicating bilateral hematomas in adrenal glands. glands showing bilateral adrenal hemorrhage. Arrow: Slightly high
histological structures help to explain the bilateral pattern associated
onset of microthrombosis.
proteinases, which activates endothelial cells and leads to the
antibodies promote apoptosis and the release of lysosomal
target of antiphospholipid antibodies, could play a role. These
lysobisphosphatidic acid contained in the zona fasciculata, a
thrombosis and subsequent postinfarction hemorrhage. The second
the abrupt transition of artery‑capillary plexus promotes venous
between a rich arterial supply and limited venous drainage. It is
Two pathogenic mechanisms of adrenal hemorrhage in APS
have been proposed. The first mechanism claims that the special
vascularization of adrenal glands is responsible for the imbalance
between a rich arterial supply and limited venous drainage. It is
the abrupt transition of artery‑capillary plexus promotes venous
thrombosis and subsequent postinfarction hemorrhage. The second
proposed mechanism suggests that a large amount of membrane
lysobisphosphatidic acid contained in the zona fasciculata, a
target of antiphospholipid antibodies, could play a role. These
antibodies promote apoptosis and the release of lysosomal
proteinases, which activates endothelial cells and leads to the
onset of microthrombosis.\(^1\) The symmetrical anatomical and
histological structures help to explain the bilateral pattern associated
with adrenal hemorrhage. APS causes hemorrhagic infarction of
the adrenal glands and is typically associated with stress factors,
including surgery, infection, or hemorrhagic diathesis associated
with anticoagulation therapy.\(^2\) The formation of thrombi as a
result of insufficient anticoagulation could also result in adrenal
insufficiency.\(^4\)

Anticoagulation therapy remains the standard therapy despite its
association with the formation of hematomas. The target INR range
for this therapy remains controversial. In a single series study, it
was found that 80% of physicians chose to maintain INR between
3 and 3.5 in APS patients with adrenal hemorrhage‑infarction in
an effort to reduce thrombotic recurrences. However, other reports
suggest that an INR below 3 should be maintained. With intensive
anticoagulation treatment, the bleeding rate has been documented
to be approximately 3.9% per patient per year.\(^5\) In the absence of
recommendations, we prefer to take a more conservative approach
in an effort to prevent further hemorrhage and we set the INR target
between 2 and 3.

The majority of patients with adrenal involvement in APS have been
shown to develop an irreversible cortisol deficiency and atrophy
of the adrenal glands. However, few patients have demonstrated
an adequate cortisol response to Synacthen during the follow‑up
period.\(^6\) Hypothalamus‑pituitaria‑adrenal axis function monitoring
was carried out for the patient in the case of recovery.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient
consent forms. In the form, the patient(s) has/have given his/her/
their consent for his/her/their images and other clinical information
to be reported in the journal. The patients understand that their
names and initials will not be published and due efforts will be
made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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