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FeiXiang Ling, Meng Wu, GuoYu, RiMei Zhou, LiKun Han, Jia Wang, LiBing Ma & Aijun Jia

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Postoperative Adrenal Crisis and Atrial Tachycardia Associated with an Ectopic ACTH-Secreting Thymic Neuroendocrine Tumor: A Case Report and Literature Review

1 FeiXiang Ling¹, Meng Wu², GuoYu¹, RiMei Zhou¹, LiKun Han¹,Jia Wang³,LiBing
2 Ma^{4*†}and Aijun Jia^{1*†}

3 ¹Intensive Care Unit, The First Affiliated Hospital of Guilin Medical University,
4 Guilin, Guangxi Zhuang Autonomous Region, China

5 ²Spinal Surgery, The First Affiliated Hospital of Guilin Medical University,
6 Guilin, Guangxi Zhuang Autonomous Region, China

7 ³ Endocrinology Department, The First Affiliated Hospital of Guilin Medical
8 University, Guilin, Guangxi Zhuang Autonomous Region, China

9 ⁴Respiratory and Critical Care Medicine Department, The First Affiliated
10 Hospital of Guilin Medical University, Guilin, Guangxi Zhuang Autonomous
11 Region, China

12 * Correspondence:

13 LiBing Ma

malibing1984@163.com

Aijun Jia

jiaaijunps@163.com

†These authors have contributed equally to this work.

Abstract

Background: Thymic neuroendocrine tumors associated with ectopic adrenocorticotrophic hormone (ACTH) syndrome are rare, and postoperative adrenal crisis presenting with atrial tachycardia as the initial manifestation is even more uncommon. As a result, evidence to guide early recognition and management remains limited.

Case presentation: This article reports a case of an ectopic ACTH-secreting thymic neuroendocrine tumor, complicated by postoperative adrenal crisis, with recurrent atrial tachycardia. Following tumor resection, the patient developed profound shock accompanied by recurrent atrial tachycardia, which improved significantly after prompt initiation of glucocorticoid administration and ventricular rate control.

Conclusions: Adrenal crisis often presents with nonspecific clinical symptoms, predisposing it to delayed or missed diagnosis. However, during the perioperative management of ectopic ACTH-secreting neuroendocrine tumors, failure to administer glucocorticoids promptly and adequately can trigger an adrenal crisis that may rapidly progress to life-threatening complications,

including atrial tachycardia, shock, and acute respiratory failure. Therefore, clinicians should aim to recognize this risk at the earliest possible stage. A multidisciplinary approach during the perioperative period remains essential to ensure timely and individualized glucocorticoid replacement therapy, thereby optimizing patient outcomes.

Keywords: ectopic ACTH; thymic neuroendocrine tumor; atrial tachycardia; adrenal crisis; glucocorticoid

1 Background

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms that arise from neuroendocrine cells and peptidergic neurons. Although relatively uncommon, they account for approximately 2% of all malignancies, occurring most frequently in the gastrointestinal tract and respiratory system^[1] Thymic neuroendocrine tumors (TNETs) represent the rarest and most heterogeneous subtype within this group. Classified as mediastinal epithelial tumors, they constitute only 2%–5% of thymic tumors and 0.5% of all NETs ^[2, 3]. TNETs typically affect older men and are characterized by aggressive biological behavior and poor prognoses ^[4].

Ectopic adrenocorticotrophic hormone syndrome (EAS) is a distinct form of Cushing syndrome (CS) that belongs to the adrenocorticotrophic hormone (ACTH)-dependent subtype. This condition results from the excessive secretion of biologically active ACTH or ACTH analogs by non-pituitary tumors. This ectopic hormone production persistently stimulates adrenal cortex hyperplasia,

59 leading to hypersecretion of cortisol and subsequent debilitating clinical
60 symptoms. Among adult patients with CS, EAS accounts for 12% to 17% of
61 cases, thymic neuroendocrine are exceptionally rare and represent only 2% to
62 4% cases [5, 6].

63 Adrenal crisis (AC) is a life-threatening condition that occurs in patients with
64 primary or secondary adrenal cortical insufficiency. Precipitating factors
65 include surgery, stress, infection, or abrupt withdrawal of hormones, all of
66 which can lead to a critical deficiency in adrenal hormone secretion.

67 Glucocorticoid replacement therapy, correction of electrolyte imbalances, and
68 symptomatic management are effective interventions for alleviating distressing
69 symptoms. However, AC often presents acutely, with nonspecific features. This
70 diagnostic challenge is further heightened under general anesthesia, where
71 anesthetic agents can mask key symptoms such as nausea and abdominal pain.
72 In addition, limited physician awareness and intraoperative complications—
73 such as massive bleeding, hemorrhagic shock, or septic shock—frequently
74 contribute to delayed diagnosis and treatment. Such delays can result in
75 devastating outcomes, including atrial tachycardia, profound shock, and death.
76 This article reports a critical case of a patient with an ectopic ACTH-secreting
77 thymic neuroendocrine tumor who developed postoperative AC complicated by
78 recurrent atrial tachycardia. Given the complexity of the case and the patient's
79 unstable condition, timely diagnosis and aggressive management were crucial,
80 as failure to intervene carried a grave prognosis. To the best of our knowledge,
81 this is the first reported case where postoperative AC following the resection of
82 an ectopic ACTH-secreting thymic NET manifested as recurrent atrial

tachycardia, distinguishing it from previously reported cases that primarily presented with shock or respiratory failure.

2 Case presentation

Patient (male, 52 years old) was admitted to the Endocrinology Department of our hospital on March 17, 2025. The main symptom was weakness in both lower limbs for 2 months. His medical history included untreated hypokalemia diagnosed on February 24, 2025, alongside hypertension and diabetes for more than 2 months. Blood pressure was adequately controlled with daily medication, and the patient denied the use of exogenous hormones. On examination, vital signs were as follows: temperature 36.3 °C, pulse 67 beats per minute, respiration rate 20 breaths per minute, and blood pressure 132/79 mmHg. His weight was 74 kg, with a BMI of 25.6 kg/m². The remainder of the physical examination was unremarkable. Laboratory evaluation showed a glycated hemoglobin level of 6.4% at admission, 6.40 mmol/L fasting blood glucose, 2.67 mmol/L electrolyte potassium ion:, and 143 mmol/L electrolyte sodium ion. Endocrine test results are presented in Table 1.

Table 1. Preoperative Endocrine Profile Evaluation in Patients

Parameter	8:00	16:00	23:59	Reference value
Baseline cortisol	41.385	34.936	29.757	AM:4.26–24.85;4PM:2.9–17.3; 12PM:0–6.72 (µg/dL)

Baseline ACTH	278.641	226.924	181.962	7.2–63.4 (pg/mL)
Baseline 24-hour urine cortisol	960			50–437 µg/24h
Low-dose dexamethasone suppression test cortisol	50.259			AM:4.26–24.85; 4PM:2.9–17.3; 12PM:0–6.72 (µg/dL)
24-hour urine cortisol	1260.00			50–437 µg/24h
ACTH	195.017			7.2–63.4 pg/mL
High-dose dexamethasone suppression test cortisol	>60.000			AM:4.26–24.85; 4PM:2.9–17.3; 12PM:0–6.72 (µg/dL)
24-hour urine cortisol	1320.00			50–437 µg/24h
ACTH	249.933			7.2–63.4 (pg/mL)
Thyroid function				
FT3	4.34			3.1–6.8 (pmol/L)
FT4	20.6			12–22 (pmol/L)
TSH	0.164			0.27–4.2 (µIU/mL)

104 ACTH: adrenocorticotrophic hormone; FT3: free triiodothyronine; FT4: free thyroxine;

105 TSH: thyroid-stimulating hormone

106 Both low- and high-dose dexamethasone suppression tests failed to achieve
107 cortisol suppression. Routine blood tests, liver and kidney function tests,
108 cardiac echocardiography, electrocardiography, and pulmonary function
109 testing revealed no abnormalities. However, chest computed tomography (CT)
110 performed on March 29, 2025 (plain and contrast-enhanced) demonstrated a
111 space-occupying lesion in the anterior superior mediastinum, highly suggestive
112 of thymoma (Figures 1a, b). Cranial magnetic resonance imaging excluded the
113 presence of a pituitary tumor, thereby ruling out pituitary ACTH secretion as a
114 potential cause. Therefore, the endocrinology department diagnosed the
115 patient with ectopic ACTH and considered that the source of the thymus lesion

116 was likely to be the cause of the problem. On March 30th, the patient was
117 reluctant to undergo the thymus lesion surgery immediately owing to personal
118 reasons. On May 22nd, the patient went to the thoracic surgery department for
119 surgical treatment on his own. The patient underwent median thoracotomy for
120 resection of the mediastinal tumor under general anesthesia on May 26th. The
121 preoperative vital signs of the patient remained stable. Invasive arterial
122 pressure monitoring was established via radial artery puncture under local
123 anesthesia, and central venous access was obtained through right internal
124 jugular vein cannulation. Anesthesia was induced with intravenous midazolam,
125 fentanyl, rocuronium, etomidate, and oxycodone, followed by tracheal
126 intubation and mechanical ventilation. Anesthesia was maintained with
127 propofol, remifentanyl, and intermittent boluses of rocuronium. Following
128 standard disinfection and draping, the surgery was performed. The mediastinal
129 tumor, along with surrounding adipose tissue, was meticulously dissected and
130 completely excised. Intraoperatively, invasive blood pressure remained stable
131 within the range of 120–170/60–90 mmHg. Electrolyte analysis revealed a
132 potassium level of 2.90 mmol/L, while blood glucose and other biochemical
133 parameters showed no significant changes. Estimated blood loss was
134 approximately 100 mL. During the operation, no glucocorticoids were used for
135 the patient. Two hours postoperatively, intravenous hydrocortisone (100 mg)
136 was initiated, and electrolyte imbalances were actively corrected.
137 Subsequently, intravenous injection of hydrocortisone (100 mg) was
138 administered at 8 am daily. Pathological examination (Figures 2a, b) identified a
139 NET within the mediastinal fat, displaying histological features suggestive of an

140 atypical carcinoid. The tumor measured 10 cm × 7 cm × 5 cm.
 141 Immunohistochemistry showed the following profile: CK(+); CgA(+); Syn(+);
 142 CD56(+); CD117(+/-); TTF-1(-); CD5(-); P63(-); Ki67 (positive in 20% of tumor
 143 cells). On postoperative day two, the patient experienced three distinct
 144 episodes of atrial tachycardia, with heart rate surging to 200 beats per minute
 145 (electrocardiograms shown in Figures 3a, b). During the third episode, the
 146 heart rate again reached 200 bpm and was accompanied by an alarming fall in
 147 blood pressure to 60/48 mmHg. At the time, the patient's body temperature
 148 was 37°C, the random blood glucose was 8.1 mmol/L, the electrolyte levels
 149 were 130 mmol/L sodium, 3.69 mmol/L potassium, and 2.1 mmol/L lactate level
 150 Lac. No abnormalities were found in the related pathogen tests. The results of
 151 the infection indicators test for the patient at that time showed an elevated
 152 leukocyte count ($12.81 \times 10^9/L$) and an elevated high sensitivity C-reactive
 153 protein (57.18 mg/L) level, and a procalcitonin (2.96 ng/mL) level. Aggressive
 154 management included amiodarone for ventricular rate control, fluid
 155 resuscitation with 3,000 mL, and vasopressor support. Despite these
 156 interventions, the patient showed no clinical improvement. Consciousness
 157 deteriorated significantly, and peripheral oxygen saturation decreased to 88%.
 158 Urgent consultations with Endocrinology and the Intensive Care Unit (ICU)
 159 were requested, leading to a critical diagnosis of AC, supported by profoundly
 160 low serum cortisol ($3.803 \text{ nmol} \cdot L^{-1}$) and ACTH $<1 \text{ ng/L}$. With the consent of the
 161 family members, the patient was transferred to the ICU in the early morning of
 162 the third day after the operation. On admission, emergent interventions were
 163 initiated, including tracheal intubation, mechanical ventilation, sedation and

analgesia, norepinephrine infusion to stabilize blood pressure, intravenous hydrocortisone (300 mg/24 hours), piperacillin-tazobactam for infection control, strict glycemic management, and comprehensive organ function support. Following admission, the patient experienced three recurrent episodes of atrial fibrillation accompanied by hypotension. Sinus rhythm was restored promptly with electrical cardioversion, after which blood pressure stabilized (Figures 3c, d). Blood gas, electrolyte and lactate levels, rechecked during each episode, revealed no abnormalities. Intravenous hydrocortisone (300 mg/24 hours) was continued for 5 days, after which the dose was gradually tapered to 100 mg once daily, then 40 mg every 12 hours, and subsequently 30 mg every 12 hours via intravenous drip. Therapy was later transitioned to oral hydrocortisone, with standard replacement dosing of 20 mg, 10 mg, and 10 mg administered at breakfast, lunch, and dinner, respectively. The vital signs of the patient progressively stabilized. Comprehensive medical interventions were carried out to correct internal environmental disorders, strengthen anti-infection therapy, and support organ function alongside comprehensive nutritional care. Hydrocortisone dosing was gradually tapered, and vasoactive medications were carefully adjusted based on continuous blood pressure monitoring. Following a demanding 12-day ICU course characterized by steady clinical improvement, the patient was transferred to a general ward and eventually discharged.

3 Discussion and Conclusions

Clinical studies have identified more than 15 distinct tumor types of diverse origins associated with ectopic ACTH syndrome^[7]. Most of these tumors arise in

the lungs, pancreas, or thymus, most commonly as NETs [8, 9]. The typical manifestations include lung and thymic neuroendocrine, with occasional reports of multiple small pulmonary lesions [6]. NETs originate from neuroendocrine cells and may secrete hormones or bioactive substances such as ACTH, thereby inducing ectopic ACTH syndrome. Patients with this syndrome frequently present with clinical features such as central obesity, purple striae on the skin, hirsutism, refractory hypertension, hypokalemia with muscle weakness, hyperlipidemia, and diabetes^[10]. This patient presented the following characteristics: (i) middle-aged male, with a short disease course and acute onset; (ii) the typical clinical manifestations of Cushing's syndrome were relatively few, mainly presenting as hypokalemia and weakness in the lower extremities. (iii) markedly elevated cortisol levels with loss of circadian rhythm; failure of cortisol suppression with low-dose dexamethasone testing; persistently elevated ACTH levels without suppression after high-dose dexamethasone testing; (iv) enhanced CT scan demonstrating a well-defined thymic mass; and (v) pathological confirmation of a thymic NET. Collectively, these findings establish the diagnosis of a thymic NET associated with ectopic ACTH syndrome.

EAS represents a rare subtype of CS, yet recent years have witnessed a marked increase in reported cases. Global medical consensus now recognizes this condition ^[10]. Current expert recommendations emphasize that early detection and complete resection of the ectopic tumor remain the optimal therapeutic strategy ^[11, 12]. When the primary lesion is unresectable, treatment options include pharmacological intervention or surgical resection of the target glands,

212 followed by essential glucocorticoid replacement therapy^[11, 13]. However,
213 medical therapy is frequently limited by poor patient tolerance to adverse
214 effects, and in such cases, surgical excision of the affected glands has emerged
215 as a practical alternative^[13]. Currently, adrenal steroidogenesis inhibitors that
216 have been on the market for many years include ketoconazole, metyrapone,
217 mitotane, etomidate, and the recently approved osilodrostat. They reduce the
218 synthesis of glucocorticoids and the production and secretion of adrenal
219 androgens by inhibiting one or more adrenal enzymes^[14]. Although these drugs
220 can effectively control excessive cortisol, they have certain limitations: on the
221 one hand, they cannot restore the circadian rhythm of the hypothalamic-
222 pituitary-adrenal (HPA) axis, nor can they directly target tumors that secrete
223 ACTH^[15]. On the other hand, adrenal insufficiency is a common side effect of all
224 drugs used to treat EAS. For patients on the "block and replace" regimen (i.e.,
225 using high-dose adrenal steroidogenesis inhibitors to block endogenous cortisol
226 secretion while simultaneously receiving exogenous glucocorticoid replacement
227 therapy to prevent adrenal insufficiency), if the block is incomplete, there is
228 also a risk of excessive glucocorticoid replacement. In addition, the adverse
229 reactions of the drugs also limit their clinical application: for example,
230 ketoconazole has hepatotoxicity, metyrapone and osilodrostat may cause
231 accumulation of androgen and mineralocorticoid precursors (resulting in
232 hypokalemia), mitotane can cause cognitive function changes, and etomidate
233 may lead to severe dystonia^[16]. For patients with CS caused by ectopic ACTH
234 tumors who have long-term hypercortisolism, if the cortisol level exceeds the
235 normal upper limit by more than five times, severe complications, such as fatal

236 metabolic disorders (hypertension, hyperglycemia), mood swings and cognitive
237 impairments (such as depression), and infections or cardiovascular and
238 thromboembolic complications, often occur. Theoretically, the preoperative use
239 of drugs to reduce cortisol levels can help alleviate hypercortisolism-related
240 complications, improve postoperative recovery and wound healing, and reduce
241 the risk of infection. However, current data on perioperative or postoperative
242 outcomes are limited and heterogeneous; therefore, this treatment plan has not
243 been routinely adopted in most patients. The study conducted by Elena Valassi
244 et al^[17] based on ERCUSYN data shows that approximately one-fifth of patients
245 with CS received preoperative treatment mainly consisting of steroid synthesis
246 inhibitors; however, the incidence of postoperative complications did not
247 significantly decrease, and such treatment may interfere with the assessment
248 of early postoperative results. A retrospective multicenter study indicates that
249 using steroid production inhibitors for 4 months before surgery can normalize
250 cortisol levels in 50–72% of cases, but only approximately 33% of the cases
251 showed improvement in subjective symptoms^[18]. However, for patients with
252 severe life-threatening complications related to high cortisol levels, the rapid
253 normalization of cortisol levels is the most important objective. Before the
254 operation, the use of steroidogenesis inhibitors to benefit these patients is
255 necessary^[7, 19]. Excessive ACTH secretion in patients with EAS results in a
256 precipitous decline of both cortisol and ACTH levels following resection of the
257 ectopic tumor. At this point, owing to the insufficient supplementation of
258 exogenous hydrocortisone and the increased demand of the body caused by
259 surgical stress, the large amount of endogenous cortisol (stored in the

circulation) remaining in the body before the surgery can still meet the basic needs. However, within 12-66 hours after the surgery, the remaining cortisol is basically depleted, and the serum cortisol often drops below 20 µg/L. This stage is the peak period for adrenal crisis, and intensified glucocorticoid replacement therapy is required^[20]. This patient received hydrocortisone treatment after the removal of an ectopic ACTH tumor. During this period, the serum ACTH level was extremely low. This phenomenon is due to the fact that the overall HPA axis function has not yet recovered after the surgery, and exogenous glucocorticoids inhibit the HPA axis through a negative feedback mechanism^[21]. Therefore, the measured ACTH levels remained consistently at a low level. This low ACTH level does not indicate a failure of the treatment; instead, it suggests that the ectopic tumor has been successfully removed and that the body's HPA axis is currently in a state of reasonable inhibition by exogenous hormones. Within the first year after the surgery, the function of the HPA axis in most patients can gradually recover. To assess whether the ectopic ACTH has recurred, the serum ACTH level during the subsequent process of drug reduction requires close monitoring^[22]. Notably, after taking glucocorticoids, the blood drug concentration increases, and the measured total cortisol may be within the normal range or even higher. To assess the true function of the patient's adrenal glands, blood should be drawn before taking the first dose of the replacement hormone in the morning to determine "morning basal cortisol". At this time, the exogenous hormone has undergone metabolism overnight, the blood drug concentration is the lowest, and the measured value is closest to the level of endogenous secretion. However, in this

case, even with a daily hydrocortisone dose of 100 mg, the serum cortisol level in the morning was still below 5 µg/dL, suggesting that the patient's adrenal gland function had not yet recovered and there were clinical manifestations of AC. Notably, the goal of glucocorticoid treatment is not simply to "restore the cortisol levels to normal," but rather to "maintain stable vital signs of the patient and avoid the occurrence of AC."

Secondary adrenal insufficiency due to ACTH deficiency, though rare, affects approximately one in every ten thousand children and can arise from either congenital or acquired causes [23]. Rushworth et al. reported that the incidence of AC increases with advancing age, with annual hospitalization rates reaching 24.3 per 100,000 individuals aged 60–69 years[24]. Similarly, a prospective two-year German study involving 400 patients revealed an incidence of 8.3 AC events per 100 patient-years, with an associated mortality rate of 6.3%[25]. Early identification of AC is critical to improving patient outcomes. Allolio et al.[26] defined AC as the presence of two or more symptoms, such as nausea, vomiting, profound fatigue, fever, drowsiness, hyponatremia, hyperkalemia, or hypotension. However, manifestations, such as hypotension, fever, and shock, lack specificity and are frequently misdiagnosed as septic shock. In the present case, the patient's blood tests revealed only mild elevations in infection markers, including white blood cells and procalcitonin. These findings align with typical postoperative reactive changes and do not support the profile of severe infection-induced septic shock. Furthermore, patients with septic shock often develop oliguria due to impaired renal perfusion. In contrast, despite profound hypotension, this patient maintained a daily urine output of 2000–

5000 mL, which was inconsistent with septic shock. No unified diagnostic standard exists for AC. Its onset is abrupt, and its clinical manifestations are diverse and nonspecific [27]. To date, only one case of AC following surgery for a thymic NET tumor has been reported in the English-language literature [28]; that case manifested as acute respiratory failure and shock. What distinguishes the present report is the unusual recurrence of atrial tachycardia. Previous studies have shown that adrenal insufficiency can prolong the QT interval and trigger polymorphic ventricular tachycardia [29, 30]. However, the exact mechanism through which AC influences atrial electrophysiology and precipitates atrial tachycardia remains unclear [31]. Two potential pathways may have contributed to the clinical course in this case. First, preoperatively, the ectopic ACTH-secreting tumor induced hypercortisolism and hypokalemia, leading to myocardial injury and increased susceptibility to arrhythmias. Second, following tumor resection, ACTH levels dropped precipitously, and the long-suppressed HPA axis could not immediately compensate, resulting in adrenal atrophy and insufficient cortisol secretion. Cortisol plays a critical role in regulating intracellular calcium homeostasis. Rao et al.[32] demonstrated that adrenalectomized rats showed impaired sarcoplasmic reticulum calcium uptake, which was restored with exogenous cortisol supplementation. In the present patient, paroxysmal atrial tachycardia accompanied by profuse sweating occurred repeatedly during postoperative transfer to the ICU. Prompt treatment with high-dose glucocorticoids (with increased dosage and frequency), aggressive fluid resuscitation to correct dehydration, and electrical cardioversion rapidly normalized physiological parameters and terminated the

tachycardia. This response not only confirmed the diagnosis of AC but also demonstrated that AC can serve as a reversible cause of atrial tachycardia. Following resection of ectopic ACTH-secreting tumors, consensus supports the use of glucocorticoid supplementation to prevent AC. However, no unified standard currently exists for hormone replacement plans in the perioperative period ^[10]. Hydrocortisone remains the preferred drug because of its combined glucocorticoid and mineralocorticoid activity. Studies have shown that daily cortisol secretion in healthy individuals is approximately 15–30 mg, but secretion can rise to 100–300 mg under stress to meet metabolic demands. When adrenal function is impaired or the gland is surgically removed, the body cannot mount this compensatory increase, thereby predisposing patients to AC. In this patient, long-term hypercortisolemia caused severe disturbances in metabolism, immune function, and electrolyte balance. These pathological and physiological changes were not fully assessed and corrected before surgery. The tumor exhibited extensive adhesion to surrounding tissues, which made resection technically challenging, prolonged operative time, and increased intraoperative bleeding. However, the plasma half-life of hydrocortisone is only about 1.5 hours, yet supplementation during surgery was neither timely nor adequate. In addition, limited awareness among surgeons of the increased demand for glucocorticoids during surgical stress was also a contributing factor. The combined effect of these elements ultimately led to AC and recurrent atrial tachycardia. The combined effect of these elements ultimately led to AC and recurrent atrial tachycardia. Therefore, perioperative guidelines for glucocorticoid management in patients with adrenal cortical insufficiency

356 recommend that adults with any underlying cause of the condition receive a
357 100 mg intravenous hydrocortisone bolus at induction of anesthesia, followed
358 by a continuous infusion of 200 mg over 24 hours ^[23]. Mishra et al^[33] further
359 proposed administering hydrocortisone at 30 mg/h for the first 6 hours after
360 surgery, supplemented with 200 mg at 10 mg/h on the first postoperative day.
361 However, a recent systematic review of 71 studies demonstrated that cortisol
362 fluctuations during the perioperative period were highest in patients
363 undergoing open surgery or general anesthesia^[34]. Moreover, significant
364 interindividual variability in glucocorticoid responses means that some patients
365 remain undertreated and fail to achieve target cortisol concentrations ^[35].
366 Woodcock et al^[23] emphasized that, beyond continuous perioperative
367 treatment, a balanced and individualized supplementation strategy is essential,
368 requiring careful consideration of dosage, frequency, treatment duration, and
369 stress levels. Given the plasma half-life of hydrocortisone, continuous
370 intravenous administration during surgery is critical, followed by sequential
371 oral dosing with gradual postoperative tapering^[36]. In conclusion, for patients
372 with ectopic ACTH syndrome undergoing thymic tumor resection,
373 glucocorticoid supplementation must be meticulously individualized to prevent
374 an abrupt postoperative cortisol decline, which can precipitate relative cortisol
375 deficiency and AC. Regardless of the supplementation plan selected,
376 comprehensive perioperative monitoring of endocrine hormone levels is
377 mandatory. If relevant clinical symptoms emerge, AC due to insufficient
378 glucocorticoid supplementation should be a primary consideration, warranting
379 immediate adjustment of therapy. Finally, large-scale clinical studies to

establish the optimal glucocorticoid dosage and frequency in patients with ectopic ACTH syndrome after tumor resection remain limited. High-quality research is urgently needed to provide stronger evidence-based guidance.

In conclusion, when ectopic ACTH syndrome is suspected, comprehensive endocrine hormone level assessments and targeted imaging are critical for accurate diagnosis and for establishing a solid foundation for preoperative planning. Surgical management of ectopic ACTH-secreting tumors requires multidisciplinary collaboration. During the perioperative period, glucocorticoid dosing must be administered precisely and adjusted according to the patient's clinical status. Clinicians should remain aware that the manifestations of AC are often subtle. In patients with EAS undergoing resection of ectopic ACTH tumors who develop sudden, life-threatening arrhythmias or shock, a high index of suspicion for AC is essential. Immediate initiation of glucocorticoid replacement therapy is critical to preserve life.

4 Abbreviations

AC: adrenal crisis; ACTH: adrenocorticotrophic hormone; CS: Cushing's syndrome; CT: computed tomography; EAS: ectopic adrenocorticotrophic hormone syndrome; ECG: electrocardiograph; FT3: free triiodothyronine; FT4: free thyroxine; HPA: hypothalamic-pituitary-adrenal; HB: hemoglobin; ICU: intensive care unit; NET: neuroendocrine tumor; TNET: thymic neuroendocrine tumors; TSH: thyroid-stimulating hormone;

Declarations

Ethics approval and consent to participate: Not applicable.

403 **Clinical trial number:** Not applicable.

404 **Consent for publication:** Written informed consent was obtained for the
405 publication of this case report and accompanying images.

406 **Availability of data and materials**

407 The datasets used and analyzed in this study are available from the
408 corresponding author upon reasonable request. The data and materials,
409 including all the clinical data of the patient, are included within the article.

410 **Conflict of Interest**

411 The authors declare that they have no competing interests.

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415 **Author Contributions**

416 F-XL: Conceptualization & study design, Writing—original draft.LB-M:
417 Corresponding author responsibilities, supervision, Writing—review & editing.
418 A-JJ: Corresponding author responsibilities, supervision, Writing—review &
419 editing. MW and GY: Data collection & curation. LK-H,W-J and RM-Z: Writing -
420 review & editing. All authors read and approved the final version of the
421 manuscript.

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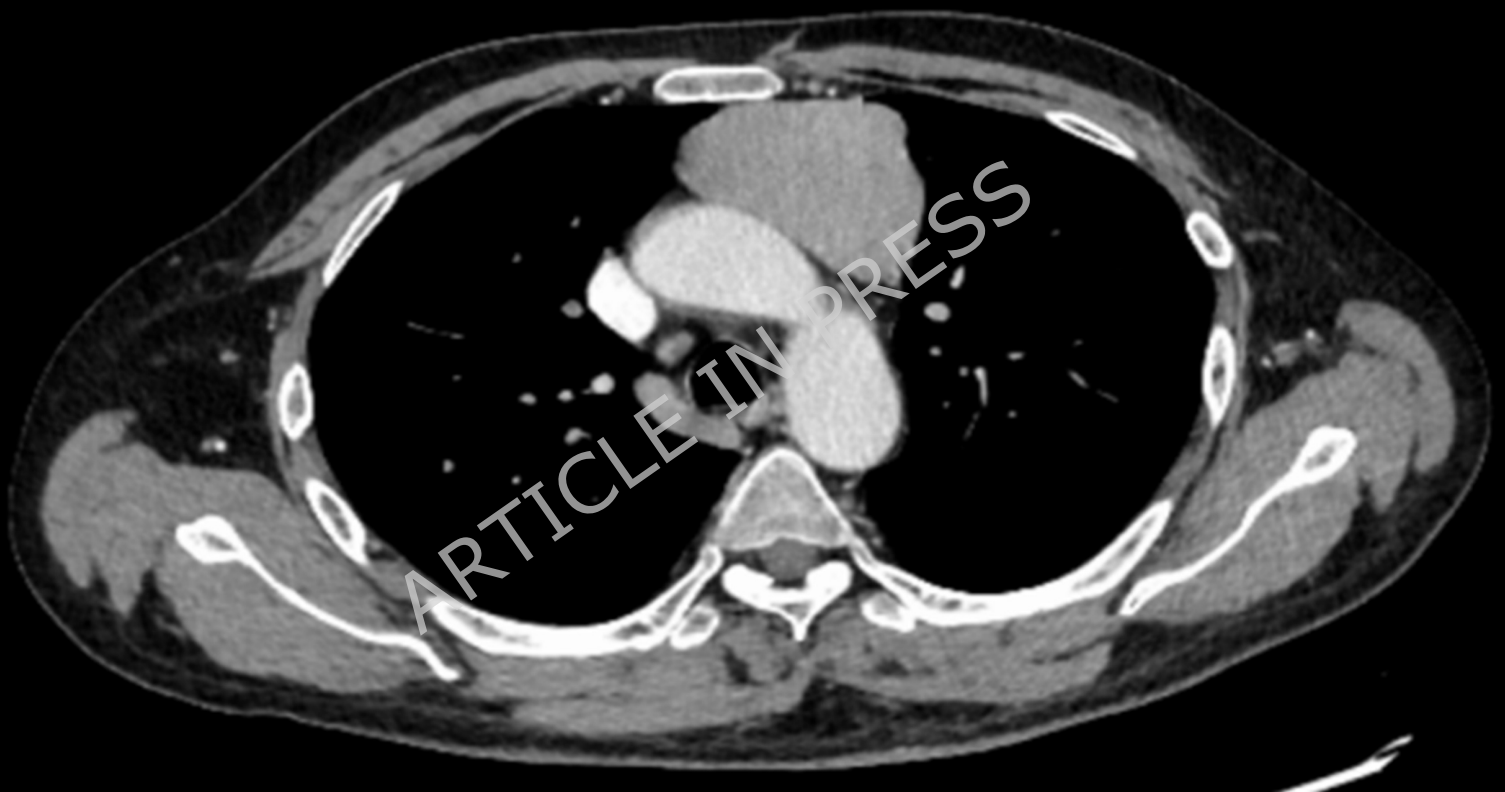
523 **Figure captions:**

524 **Figure 1. (a, b)** An enhanced CT scan of the chest vividly revealed a thymic
525 mass extending into the anterior mediastinum and producing a pronounced
526 mass effect.

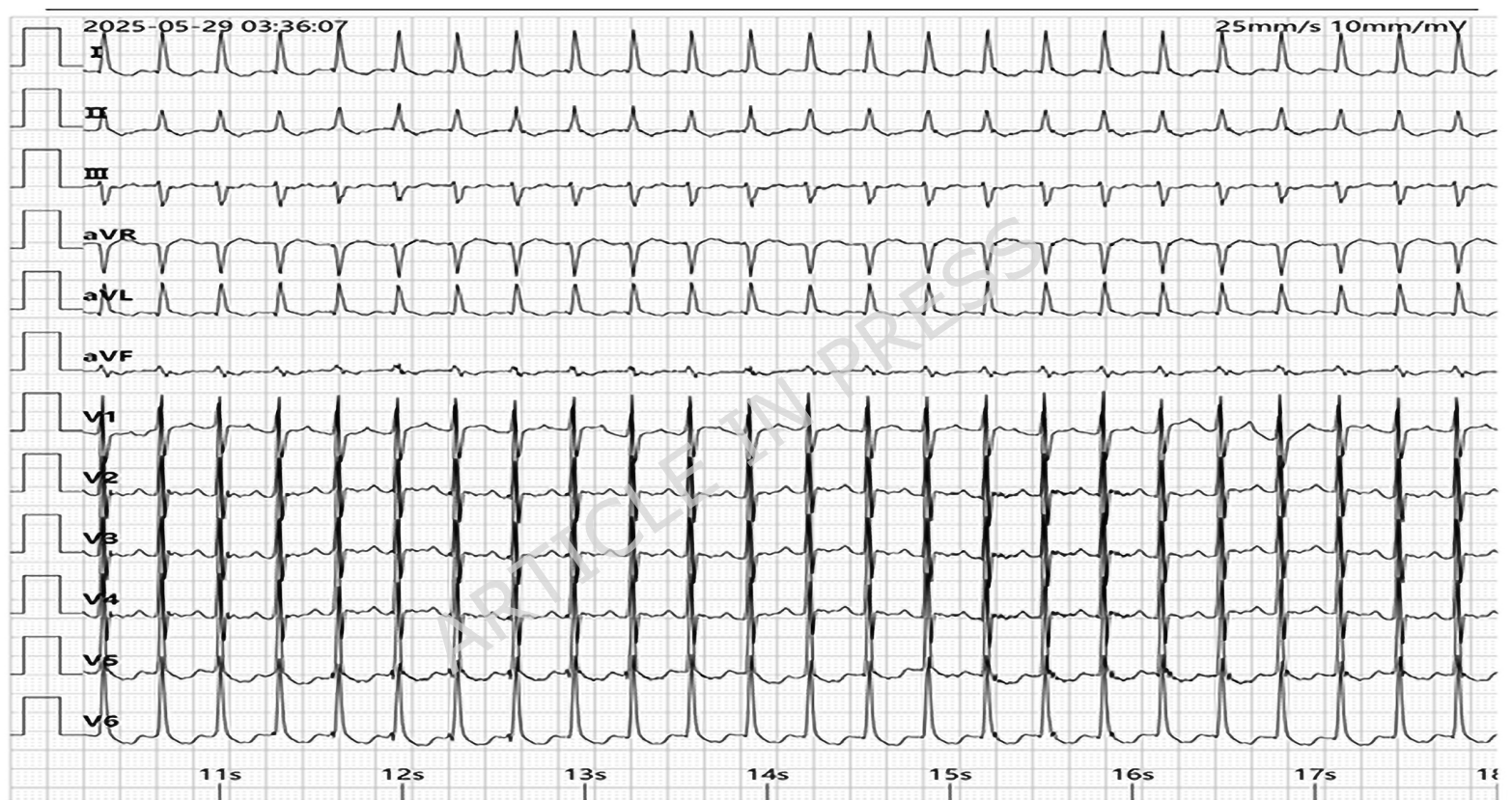
527 **Figure 2. (a, b)** Pathological findings of the mediastinal mass biopsy stained
528 with Hematoxylin and Eosin (100×). Immunohistochemistry showed the
529 following profile: CK(+); CgA(+); Syn(+); CD56(+); CD117(+/-); TTF-1(-); CD5(-
530); P63(-); Ki67(positive in 20% of tumor cells).

531 **Figure 3. (a, b)** Recurrent ECG manifestations of atrial flutter were observed
532 on the patient's second postoperative day. **(c)** The ECG demonstrates the
533 reemergence of atrial fibrillation after transfer to the ICU. **(d)** The ECG
534 captured following electrical cardioversion successfully restored hemodynamic
535 stability after the patient's sixth episode of atrial fibrillation.

536

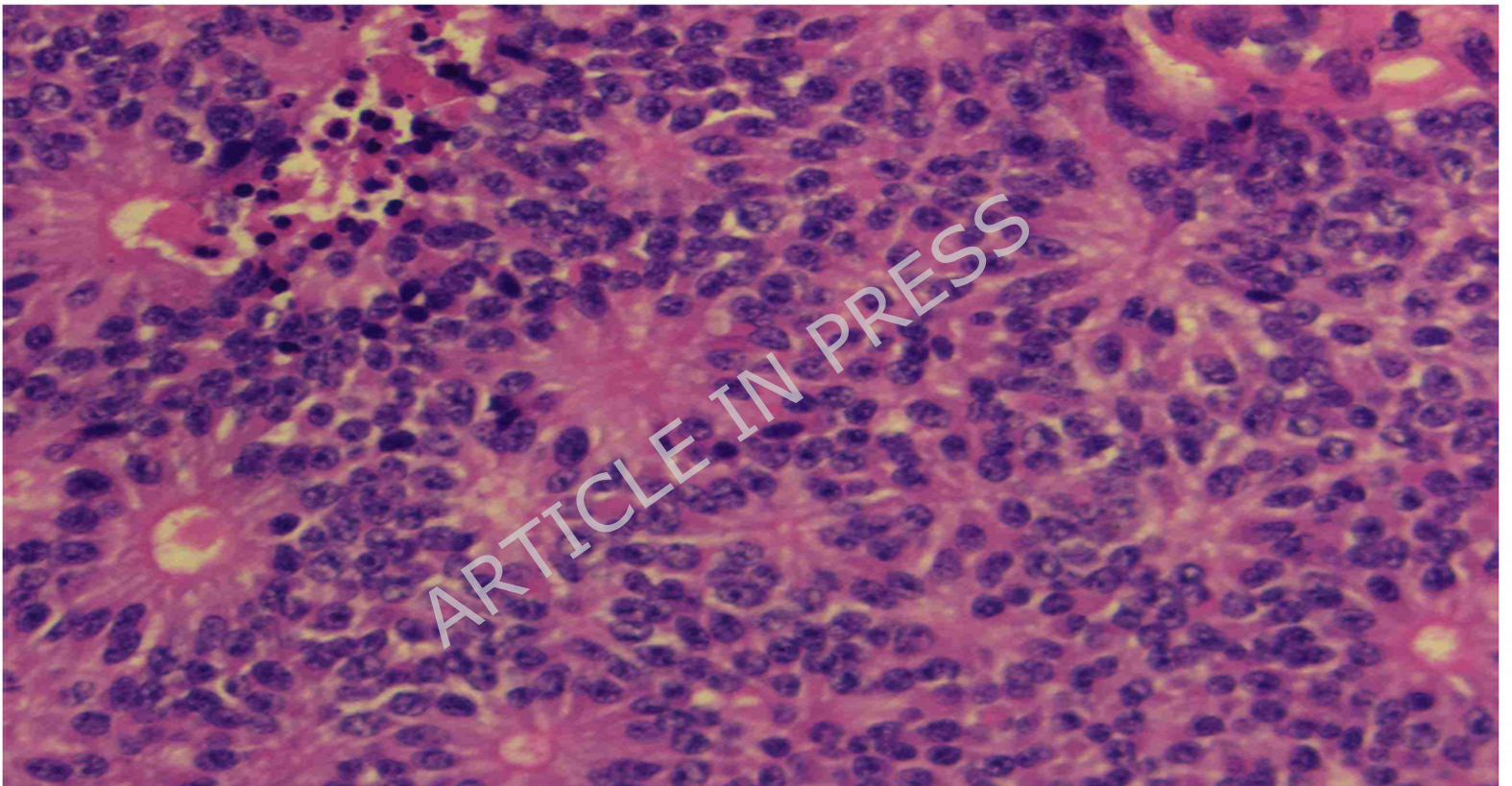


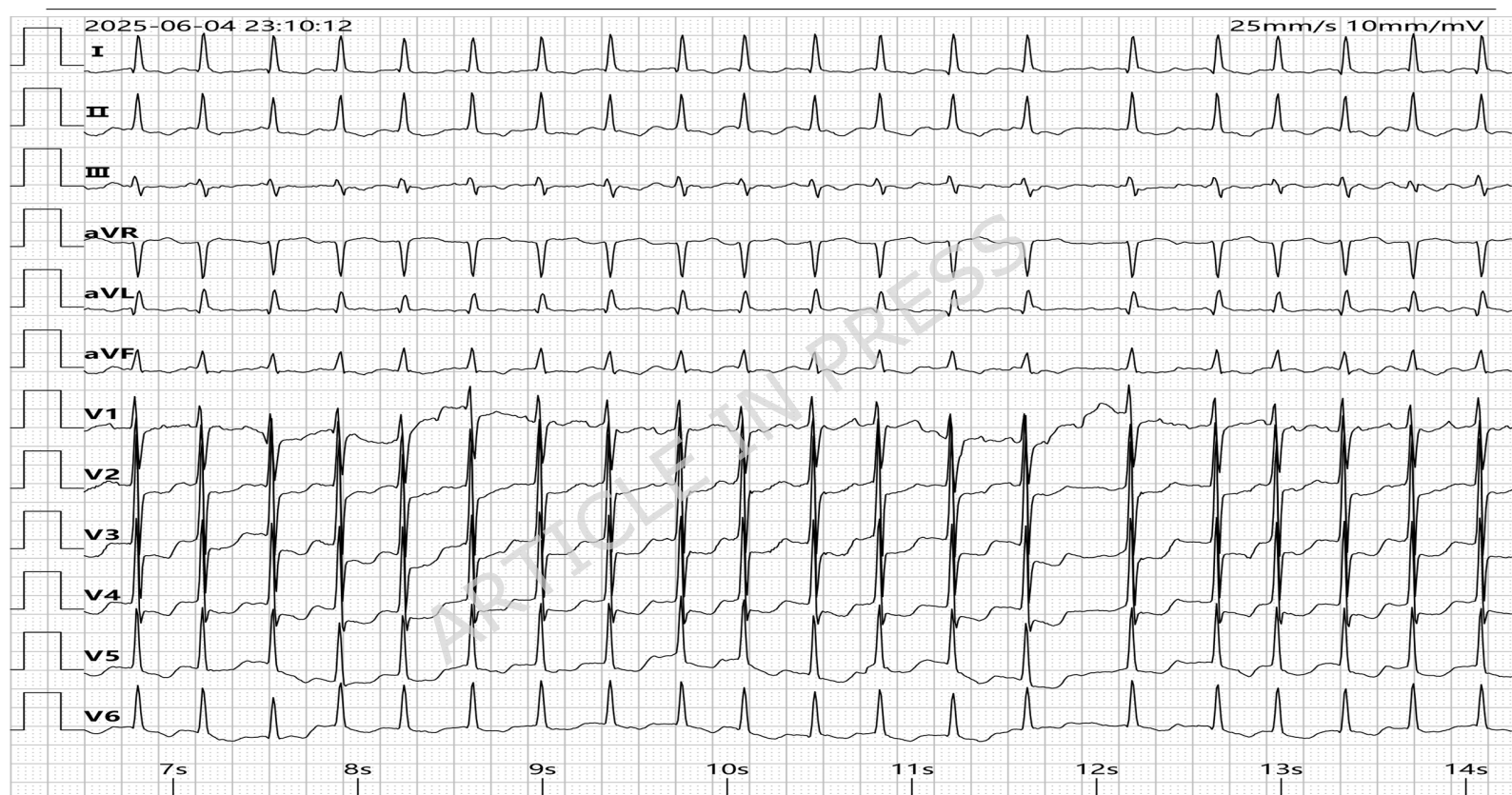






ARTICLE IN PRESS

A histological section of tissue, likely stained with hematoxylin and eosin (H&E), showing a dense population of cells with dark purple nuclei and pinkish cytoplasm/extracellular matrix. A diagonal watermark reading "ARTICLE IN PRESS" is overlaid across the center of the image.





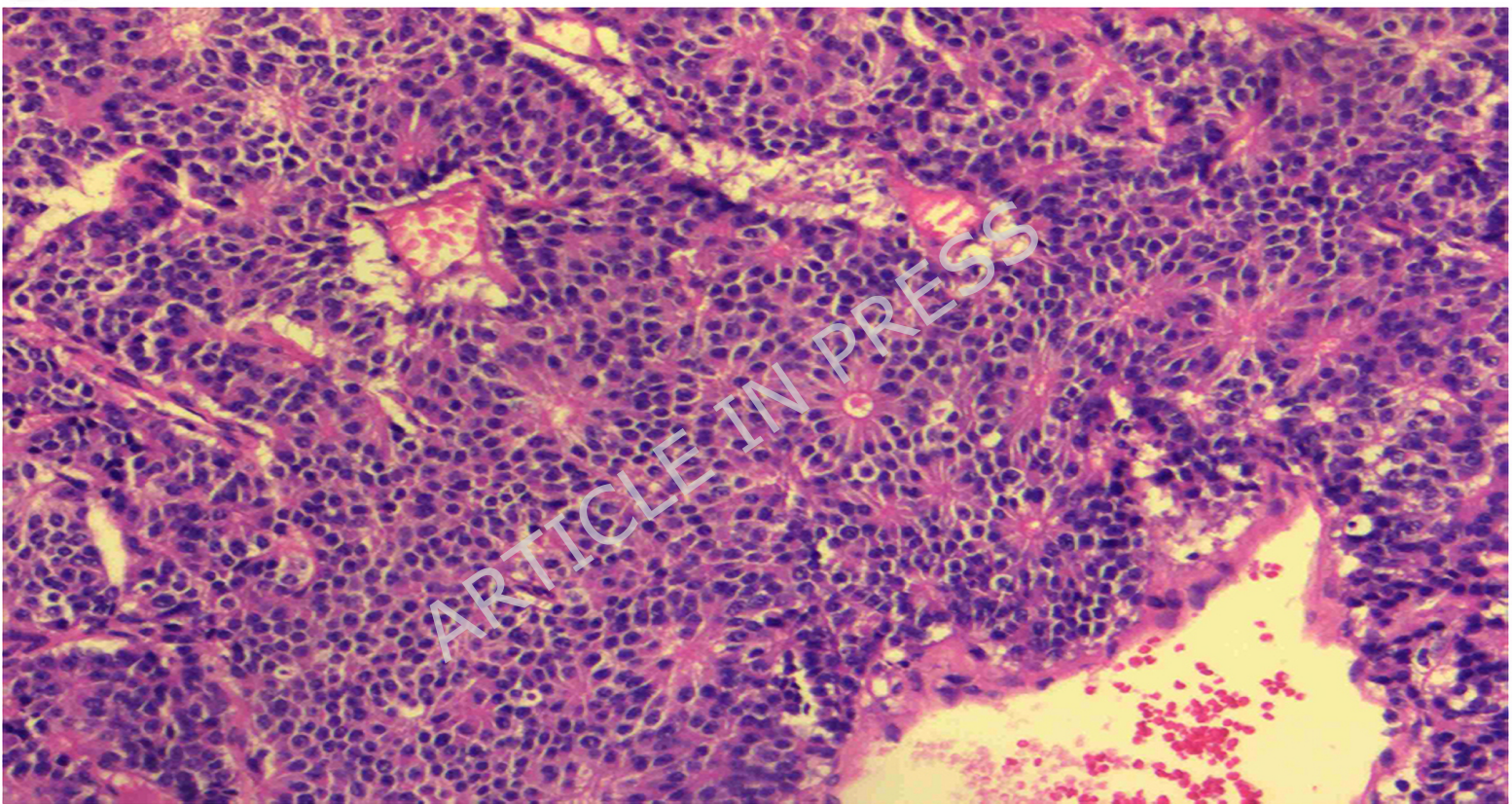


Table 1. Preoperative Endocrine Profile Evaluation in Patients

Parameter	8:00	16:00	23:59	Reference value
Baseline cortisol	41.385	34.936	29.757	AM:4.26-24.85;4PM:2.9-17.3; 12PM:0-6.72 (µg/dL)
Baseline ACTH	278.641	226.924	181.962	7.2-63.4 (pg/mL)
Baseline 24-hour urine cortisol	960			50-437 µg/24h
Low-dose dexamethasone suppression test				
cortisol	50.259			AM:4.26-24.85;4PM:2.9-17.3; 12PM:0-6.72 (µg/dL)
24-hour urine cortisol	1260.00			50-437 µg/24h
ACTH	195.017			7.2-63.4 (pg/mL)
High-dose dexamethasone suppression test				
cortisol	>60.000			AM:4.26-24.85; 4PM:2.9-17.3; 12PM:0-6.72 (µg/dL)
24-hour urine cortisol	1320.00			50-437 µg/24h
ACTH	249.933			7.2-63.4 (pg/mL)
Thyroid function				
FT3	4.34			3.1-6.8 (pmol/L)
FT4	20.6			12-22 (pmol/L)
TSH	0.164			0.27-4.2 (µIU/mL)

ACTH: adrenocorticotrophic hormone; FT3: free triiodothyronine; FT4:

free thyroxine; TSH: thyroid-stimulating hormone