Case Report

Synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy for pheochromocytomas in a patient with multiple endocrine neoplasia type 2a (MEN2A) syndrome: a case report

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Background: Pheochromocytoma is a rare neuroendocrine tumor, and bilateral pheochromocytomas is even less common. Due to the limited experience with such cases, this study aims to explore the optimal surgical strategy, assess the potential advantages of robotic surgery, and evaluate surgical outcomes for managing bilateral pheochromocytomas.

Case Description: This report presented a case of a 33-year-old woman with bilateral pheochromocytomas related to multiple endocrine neoplasia type 2a (MEN2A), who was successfully managed by synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy. This strategy reduced blood loss, improved cosmetic outcomes, preserved adrenal function, and gradually reduced the need for hormone replacement, ultimately leading to discontinuation of hydrocortisone therapy. The surgery was performed without significant complications. The patient recovered well and had normal blood pressure and hormone level at the 1-year postoperative follow-up.

Conclusions: Synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy is a safe, effective, and efficient approach for bilateral pheochromocytomas, and is favorable for rapid recovery and cosmetic demand. This treatment is more advantageous when dealing with multiple neuroendocrine tumors.

Keywords: Robotic-assisted minimally invasive surgery; bilateral pheochromocytoma; cortical-sparing adrenalectomy; multiple endocrine neoplasia type 2a (MEN2A); case report

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Introduction

Pheochromocytoma is a rare neuroendocrine tumor, often with malignant potential, for which surgical resection remains the primary treatment option. Pheochromocytomas are typically characterized by abundant vascular supply and proximity to major vessels and organs, necessitating meticulous surgical manipulation. Robotic-assisted surgery offers several advantages over traditional laparoscopic techniques, including enhanced three-dimensional visualization, increased precision due to wristed instruments

with seven degrees of freedom, stable imaging, higher magnification, and reduced surgeon fatigue. These advantages are particularly beneficial in complex cases such as pheochromocytoma, where precise and delicate tissue handling is critical to minimize complications (1-3).

Minimally invasive surgery, including both traditional laparoscopy and robotic-assisted techniques, is commonly employed for unilateral pheochromocytoma, regardless of whether transperitoneal or retroperitoneal approaches are used. These approaches are associated with benefits such as reduced blood loss, a low rate of conversion to open surgery, shorter hospital stays, and lower 90-day morbidity (4,5). However, simultaneous resection of bilateral pheochromocytomas is rare and presents unique challenges. Given the proximity of the tumors to surrounding organs, precise dissection is necessary to minimize intraoperative bleeding and preserve adrenal function. Furthermore, achieving effective cortical sparing while mitigating the risk of hemodynamic instability remains a significant surgical hurdle.

This case is notable due to the rare occurrence of bilateral pheochromocytomas in a patient with multiple endocrine neoplasia type 2A (MEN2A), a condition for which surgical experience and data on risks and outcomes are limited (6,7). The successful use of a robotic-assisted cortical-sparing approach in this instance provides valuable insights into optimizing surgical management for similar complex cases. We present this case in accordance with the CARE reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-24-371/rc).

Highlight box

Key findings

- This study demonstrates that synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy is a safe, effective, and efficient surgical approach for bilateral pheochromocytomas in patients with multiple endocrine neoplasia type 2a syndrome.
- The robotic technique allows precise dissection, reduced blood loss, adrenal function preservation, and improved cosmetic outcomes.

What is known and what is new?

- Bilateral pheochromocytomas are rare and challenging to manage, often requiring cortical-sparing surgery to preserve adrenal function. Robotic-assisted surgery offers advantages in precision and recovery.
- This report provides valuable insights into the successful application of a synchronous robotic-assisted bilateral approach, emphasizing its safety, time efficiency, and potential to reduce postoperative glucocorticoid dependency.

What is the implication, and what should change now?

- This technique is particularly suitable for complex cases involving bilateral adrenal tumors or multiple neuroendocrine tumors.
- Increased adoption and expertise in robotic-assisted adrenal surgery may improve outcomes and expand its application in managing bilateral pheochromocytomas.

Case presentation

A 33-year-old woman was hospitalized due to bilateral adrenal tumors, elevated blood glucose and blood pressure for half a year.

Half a year ago, the patient's routine examination revealed an elevated blood pressure and blood glucose, with the maximum blood pressure reaching 210/150 mmHg and fasting blood glucose between 9 to 10 mmol/L. Contrasted computed tomography suggested multiple mixed-density tumors in both adrenal glands, with uneven enhancement; the largest tumor was as large as 4.3 cm × 3.8 cm × 4.0 cm (*Figure 1*). No obvious symptoms occurred during the course of disease.

The endocrinological tests were performed, which showed an elevated 24-hour urinary norepinephrine 185.6 μg (normal range: <76.9 μg), epinephrine 335.3 μg (normal range: <11 μg) and 3-methoxy-normetanephrine (3-NMN) 4.13 nmol/L (normal range: <0.9 nmol/L), and 3-methoxy-norepinephrine (3-MN) 11.18 nmol/L (normal range: <0.5 nmol/L). The serum normetanephrine, metanephrine, adrenocorticotropic hormone, plasma renin activity, and aldosterone were within normal ranges. Both somatostatin receptor imaging and ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) scintigraphy showed increased radioactive uptake in bilateral adrenal tumors, both imaging examinations suggested the diagnosis of bilateral pheochromocytoma (*Figure 2*). Thyroid ultrasound indicated multiple solid nodules. Serum calcitonin was 385 pg/mL (normal range: ≤6.4 pg/mL). Parathyroid hormone was 115 pg/mL (normal range: 15–65 pg/mL), serum calcium 2.45 mmol/L (normal range: 2.13–2.70 mmol/L); parathyroid ultrasound and parathyroid methoxyisobutylisonitrile (MIBI) imaging did not show significant abnormalities. The genetic test was performed and found the RET C.1900T>C mutation, the diagnosis of MEN2A was confirmed.

Considering the diagnosis of bilateral pheochromocytoma, the patient began phenoxybenzamine therapy 1 month prior to adrenal surgery. The past medical history and

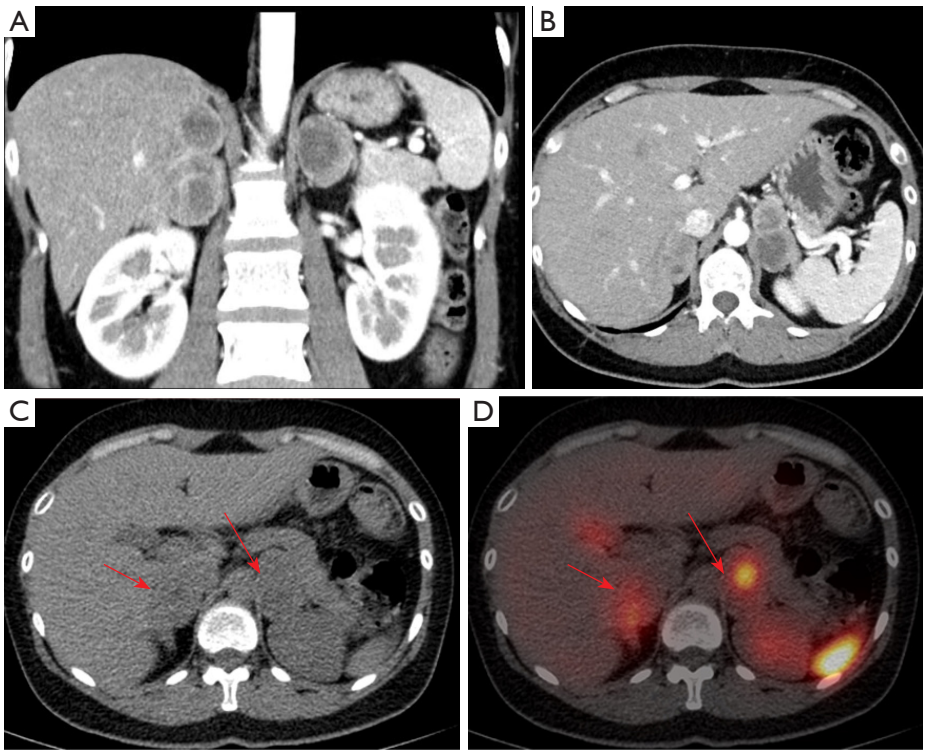

Figure 1 The imaging examination showed bilateral adrenal tumors. There were multiple tumors in left and right adrenals (A,B). ^{123}I-MIBG showed increased radioactive uptake in bilateral adrenal tumors (C,D). The arrows indicate bilateral adrenal tumors, demonstrating increased radioactive uptake in MIBG examination. MIBG, metaiodobenzylguanidine.

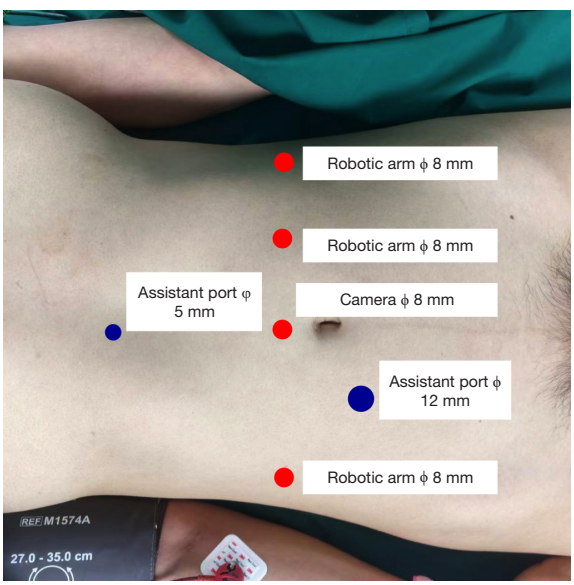

Figure 2 The positions of camera port, robotic arm ports, and assistant ports were annotated in the schematic diagram.

personal history were normal. Her mother and maternal grandmother died of a heart attack in their 30s, her maternal aunt died at 50 years old due to pheochromocytoma. Physical examination was normal.

The patient received synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy. The patient was placed in a supine position (*Figure 2*) and tilted the bed to the opposite of surgery side for about 30 degrees during the surgery. The camera port was placed on the upper edge of the umbilicus. After pneumoperitoneum was established, other 8-mm robotic ports were placed at the level of umbilicus on the left anterior axillary line, the edge of left rectus abdominis, and the right anterior axillary line, respectively. A 5-mm assistant port was placed immediately below the xiphoid process to elevate the liver and another 12-mm assistant port was placed at the level of umbilicus the edge of right rectus abdominis.

The patient experienced no significant intraoperative

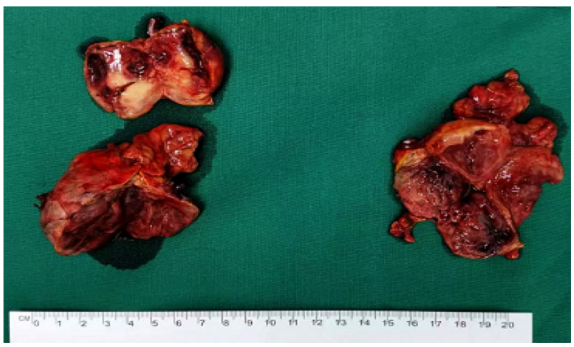

Figure 3 The specimens of bilateral pheochromocytomas. CT, computed tomography; MEN2A, multiple endocrine neoplasia type 2a.

or postoperative complications. The synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy was completed in 258 minutes, with an estimated blood loss of 150 mL. Multiple adrenal pheochromocytomas were resected, and part of adrenal glands were reserved (*Figure 3*). Hemodynamic parameters kept stable throughout the procedure. The patient recovered well postoperatively, with no significant bleeding, hypotension, or pancreatic-related complications observed. Bilateral drainages were extracted on the second- and third-postoperative day, respectively. The patient was discharged on the fourth-postoperative day. Pathologic result showed bilateral pheochromocytoma; immunohistochemistry results: AE1/AE3(–), chromogranin A (CgA)(+), Ki-67(index 3%), S-100 (supporting cells+), α-inhibin(–), synaptophysin (Syn)(+), SDHB(+), MGMT(–).

Two months after the surgery, the patient underwent bilateral thyroidectomy, lymphadenopathy lymph node dissection. Thyroid medullary carcinoma was diagnosed, and the lymph node metastasis happened in 2 of 27 lymph nodes.

The patient was followed up 1 year postoperatively, and no adverse events occurred. The patient had a blood pressure of 110–90/60–75 mmHg. Hydrocortisone therapy was gradually reduced and eventually discontinued. The 24-hour urinary norepinephrine and epinephrine, serum 3-MN and 3-NMN were within the normal range. After the thyroid surgery, the patient took levothyroxine replacement 150 μg daily, and maintained a normal thyroid function. The ultrasound showed no recurrence of thyroid carcinoma. Serum calcitonin, parathyroid hormone and serum calcium were normal.

We present a timeline of key events, from diagnosis through treatment to follow-up, providing a comprehensive overview of the patient's clinical course (*Figure 4*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Pheochromocytoma is a rare neuroendocrine tumor that typically presents as a solitary lesion. Approximately 8% of pheochromocytomas occur bilaterally, and this incidence increases to 37.5% in patients under the age of 18 years old (8). The incidence of pheochromocytoma with genetic abnormality is estimated to be 35–40%, with 25% of pheochromocytoma being attributed to genetic mutations (9,10). In patients with MEN2A, MEN2B, von Hippel-Lindau syndrome (VHL), and neurofibromatosis type 1 (NF-1), genetic anomalies are present in 42.6%, 19.1%, 9.6%, and 8.5% of cases, respectively, predisposing them to the development of bilateral pheochromocytomas (11). This patient, with a family history of pheochromocytoma, presented with bilateral adrenal tumors, thyroid medullary carcinoma, and a mutation in the *RET* proto-oncogene, leading to a diagnosis of MEN2A (12-14). This patient received synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy successfully, and provided valuable experience for similar surgeries.

The underlying causes for bilateral pheochromocytomas

The RET-related mechanism is associated with the activity of the Cluster 2 pathway. It further promotes tumorigenesis by regulating the mTOR signaling pathway. Additionally, the activation of kinase pathways facilitates the nuclear translocation of hypoxia-inducible factor 1-alpha, thereby influencing the expression of proteins related to tumor formation, ultimately leading to tumorigenesis (15,16). The genetic basis of pheochromocytoma, particularly involving immune-related pathways, has been increasingly recognized as a key factor in tumor pathogenesis. Wan *et al.* reported several immune-related biomarkers [such as fibroblast growth factor 2 (FGF2), FYN proto-oncogene (FYN), and vascular cell adhesion molecule 1 (VCAM1)] in

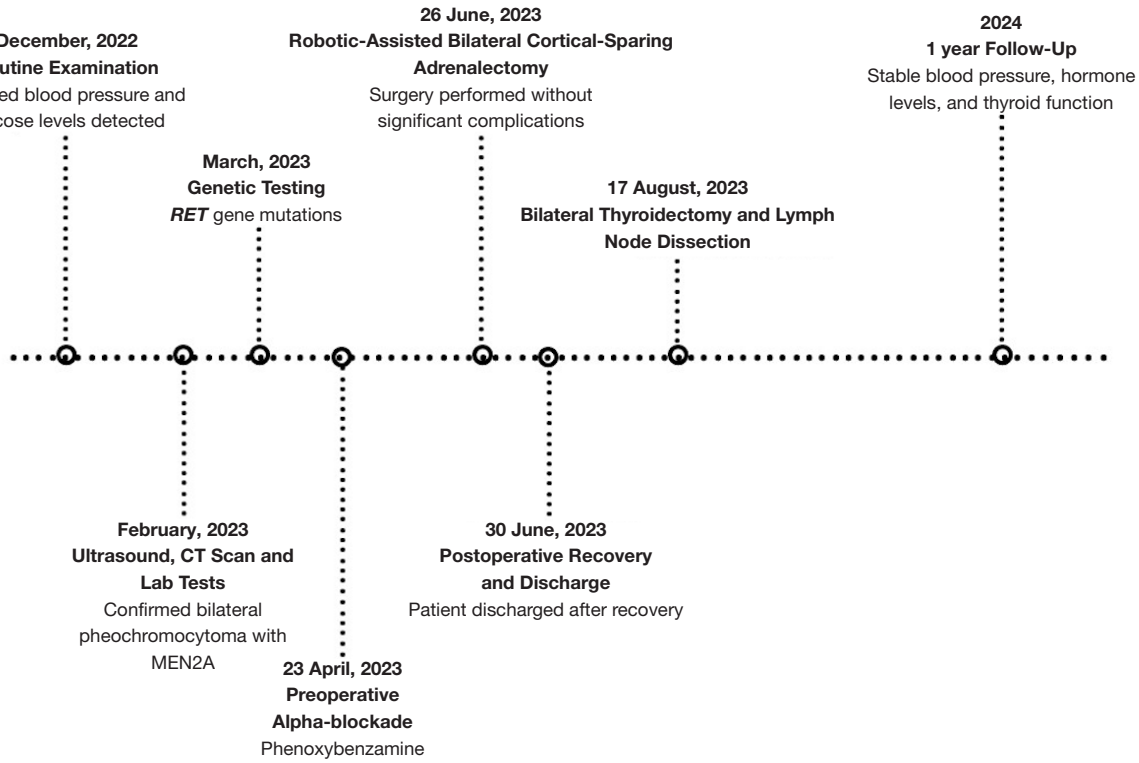

Figure 4 Timeline of key events in the diagnosis, treatment, and follow-up of this patient. CT, computed tomography.

pheochromocytoma and paraganglioma (17). These genetic alterations increase the risk of bilateral adrenal tumors development, highlighting the critical role of genetic counseling and early detection.

Comparison of retroperitoneal and transperitoneal approach in robotic-assisted adrenalectomy

Pheochromocytomas are always large, the bleeding, adhesion or complications are more likely to happen during the surgeries. The retroperitoneal approach has the advantages of little impact on intestinal functions and reaching the adrenal tumors more directly. Gokceimam *et al.* showed that the thickness of perinephretic fat being independently associated with operative time in retroperitoneal laparoscopic adrenalectomy, which indicated that enough operating space is critical for a successful retroperitoneal surgery (18). The transperitoneal approach provides obvious anatomic landmarks and has enough space to deploy the fourth robotic arm and multiple assistant ports, both are quite important in complex pheochromocytomas surgeries. Although the bowel function may be affected, it is always acceptable.

Advantages of synchronous transperitoneal bilateral robotic-assisted surgery

In this case, synchronous transperitoneal bilateral pheochromocytoma resection was successfully performed. During the transperitoneal surgery, the patient's position was adjusted simply by tilting the surgical bed and re-targeting the robot, which was much more time-efficient compared to two separate unilateral retroperitoneal surgeries that require reposition, disinfection, docking, and re-targeting. Nomine-Criqui *et al.* reported the operative time of unilateral adrenalectomy between 120 to 231 minutes (19). Pokharkar *et al.* showed the operative time of transperitoneal bilateral robotic pheochromocytoma surgery as 235 min, far less than operative time of two unilateral surgeries (7).

Bilateral pheochromocytomas are sometimes part of syndromes, and may coexist with pancreatic neuroendocrine tumors, paragangliomas and other intra-abdominal neuroendocrine tumors (8,20,21). For such patients, transperitoneal surgery can not only remove bilateral pheochromocytomas but also treat coexisted abdominal or retroperitoneal tumors at the same time. Lang *et al.*

reported a simultaneous surgery of pelvic paraganglioma and pheochromocytoma with dual docking, which improved the efficiency significantly (22).

The synchronous transperitoneal surgery has a better cosmetic effect. In this case, we placed only six ports, including four robotic ports and two assistant ports. These are less than those used in two separate unilateral retroperitoneal surgery, which requires at least eight ports; and are less than those used in previous reported bilateral transperitoneal surgery as well (7). Furthermore, we took out the multiple tumors from only one incision, while two separate unilateral retroperitoneal surgery requires two incisions to take out bilateral tumors. Bilateral pheochromocytoma is more common in young patients, and this approach reduces the total length of incisions and improves the cosmetic effects significantly.

Although our patient showed an uneventful postoperative recovery, previous studies have reported unusual postoperative manifestations such as skin hyperpigmentation, diagnosed adrenal insufficiency (23,24). This highlights the variability in postoperative outcomes even among successful adrenalectomy cases. Therefore, we utilized robotic surgery to precisely resect bilateral pheochromocytomas while preserving as much of the normal adrenal tissue as possible, aiming to reduce the risk of postoperative glucocorticoid deficiency.

In more critical cases of pheochromocytoma crisis, veno-arterial extracorporeal membrane oxygenation (ECMO) combined with urgent adrenalectomy may be employed, as described by Lichter *et al.* (25). Compared to these severe situations, our case represents a relatively straightforward clinical course, further supporting the efficacy of robotic-assisted adrenalectomy in suitable candidates.

Compared to traditional laparoscopic surgery, robotic system has a better ergonomic design, and provides a three-dimensional visualization, high magnification, and dexterous robotic arms, and therefore ensured the precise and complete tumor resection, maximized the preservation of normal adrenal tissue, and reduced the risk of bleeding, tissue injuries, conversion to open surgery and tumor recurrence (26-29).

Anesthesia risks of synchronous bilateral robotic-assisted pheochromocytoma resection

Anesthesia risk is an important concern in this surgery. In this case, the patient had taken α-receptor blocker (phenoxybenzamine) for 2 months preoperatively, and the hemodynamic parameters were stable during the surgery. Many studies have shown that the bilateral laparoscopic pheochromocytoma resection is safe in well-prepared patients (7,30,31). Robotic and laparoscopic surgeries have similar anesthesia risk and bilateral robotic surgery will not increase the anesthesia risk. In the case reported by Pokharkar *et al.*, the blood pressure and heart rate were stable during the bilateral robotic-assisted pheochromocytoma surgery as well, which confirmed that bilateral robotic surgery may not increase the risk of anesthesia (7).

Drawbacks of robotic surgery

Robotic surgery has the disadvantages as well. Firstly, the absence of tactile feedback may result in the inappropriate compression or traction of tumor. This may lead to excessive releasing of catecholamine and even tumor rupture or vessel breakage, increasing the risk of bleeding, hemodynamic instability and tumor relapse (32). Secondly, a smooth robotic surgery relies heavily on the good cooperation of the assistant, the absence of tacit cooperation in emergency situation like bleeding episode will cause serious consequences. Thirdly, the robotic surgery is much more expensive than traditional laparoscopic surgery and cannot be covered by insurance in China (33).

Conclusions

Synchronous transperitoneal robotic-assisted bilateral cortical-sparing adrenalectomy is a safe, effective, and efficient approach for managing bilateral pheochromocytoma, offering superior cosmetic outcomes. This approach may be particularly beneficial for patients with neuroendocrine tumors involving multiple intra- or retro-peritoneal sites. Accumulating more experience with robotic-assisted surgery and addressing its limitations are essential.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-24-371/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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