

A Patient with Paraganglioma Undergoing Laparoscopic Resection: A Case Report

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Abstract

Paraganglioma is a very rare extra adrenal nonepithelial tumor. The number of cases of laparoscopic surgery in Paraganglioma is small and controversial. This study encountered a case of successful transperitoneal laparoscopic surgery for a 56 mm paraganglioma in a 53-year-old female. Moreover, previous reports on laparoscopic surgery for paraganglioma are reviewed.

Keywords: Paraganglioma • Tumor

Introduction

Paraganglia are groups of neuroendocrine tissues of neural crest origin closely related to the autonomous nervous system. A tumor derived from the paraganglia is a Paraganglioma (PGL), which is an extra adrenal nonepithelial tumor [1]. The standard treatment is surgical treatment. Moreover, the safety of laparoscopic surgery has been reported in recent years.

Case Report

Patient: A 53-year-old female.

Chief complaints: Pointed out by medical checkup.

History of present illness: An abdominal mass was detected by ultrasound imaging during a medical checkup. The patient was then referred to the hospital for this study.

Past medical history: None.

Family history: None.

Blood test findings: Hemoglobin, 14.0 g/dL; Carcinoembryonic antigen, 3.0 ng/mL; Carbohydrate antigen 19-9, 6.7 U/mL; soluble interleukin-2 receptor, 205 U/mL.

Abdominal ultrasonography

A 56 × 43 mm hypoechoic tumor with a smooth margin, internal heterogeneity, and no blood flow signal was observed at the posterior wall of the gastric corpus and pancreas tail (Figure 1). Abdominal contrast-enhanced Computed Tomography (CT): A 56.7 × 37.9 × 54.7 mm low-grade tumor with poor contrast effect, smooth margin, and internal heterogeneity was observed between the posterior wall of the gastric corpus and the right margin of the abdominal aorta (Figure 2). Abdominal contrast-enhanced Magnetic Resonance Imaging (MRI): At the same site, T1-, T2-, and diffusion-weighted images showed low signal, faint and heterogeneous high signal, and faint high

signal, respectively. Fat component with capsule structure was not observed in fat-suppressed T2-weighted imaging. It could be continuous from the right margin of the aorta. However, the continuity with the gastrointestinal tract was not clear. Schwannoma and leiomyoma were considered as the diagnosis (Figure 3). Explanation of upper gastrointestinal endoscopy: No clear extrinsic compression was observed at the posterior wall of the gastric corpus.

Endoscopic ultrasound

A 47.3 × 31.3 mm hypoechoic tumor was observed at the posterior wall of the middle part of the gastric corpus suspected to be derived from the muscular

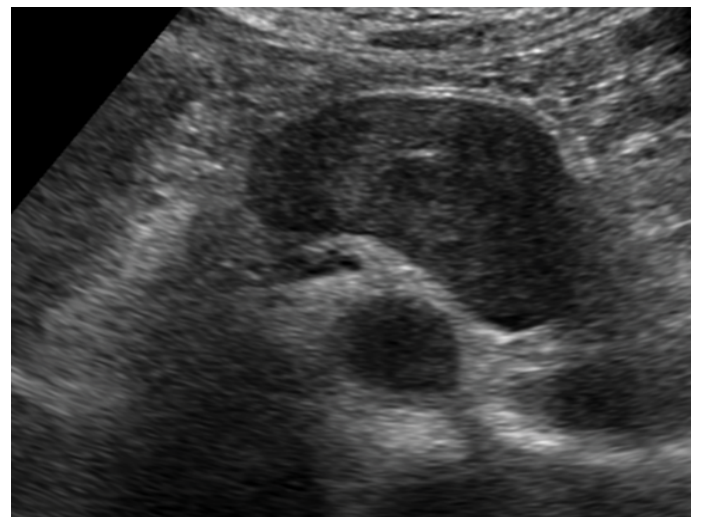


Figure 1. Abdominal ultrasonography image, A 56 × 43 mm hypoechoic tumor with a smooth margin, internal heterogeneity, and no blood flow signal at the posterior wall of the gastric corpus and tail of the pancreas.

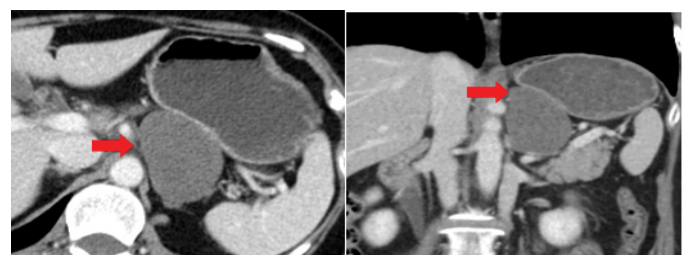


Figure 2. Abdominal contrast-enhanced computed tomography images, A 56.7 × 37.9 × 54.7 mm between the posterior wall of the gastric corpus and the right margin of the abdominal aorta (red arrows).

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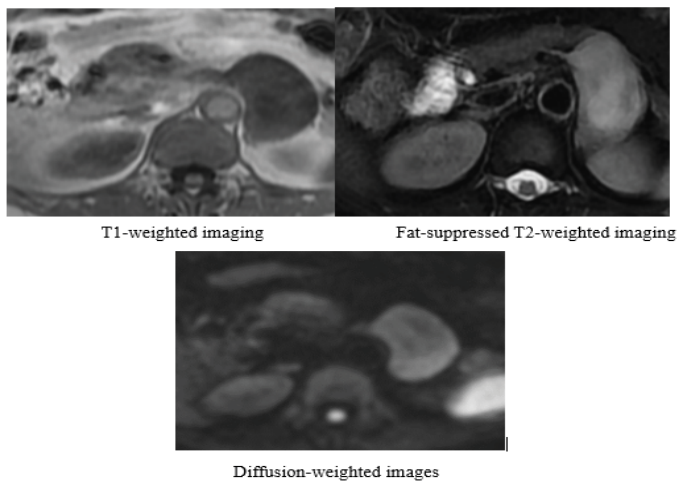


Figure 3. Abdominal contrast-enhanced magnetic resonance images, Low signal on T1-weighted imaging, faint and heterogenous high signal on T2-weighted imaging, and faint high signal on diffusion-weighted images. T1-weighted imaging; Fat-suppressed T2-weighted imaging; Diffusion-weighted images.

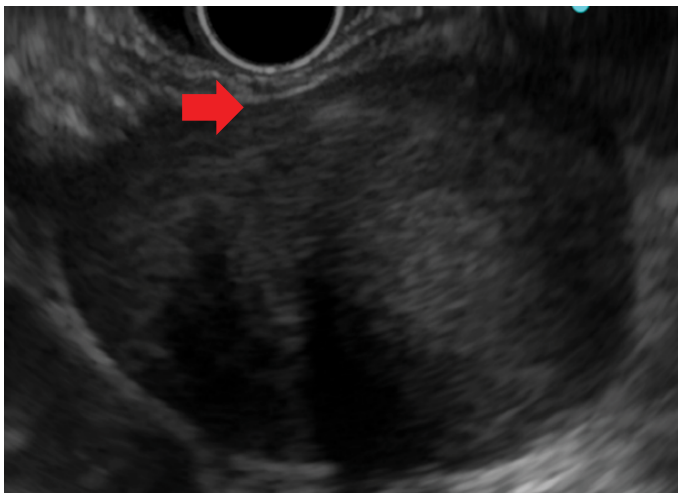


Figure 4. Endoscopic ultrasound image; A 47.3 × 31.3-mm hypoechoic tumor at the posterior wall of the middle part of the gastric corpus. It is suspected to be derived from the muscular layer of the fourth layer of the gastric wall (red arrow).

layer of the fourth layer of the gastric wall (Figure 4). Diagnosis with fine-needle aspiration was difficult due to insufficient amount of tissue.

Differential diagnoses

Based on the findings, Gastrointestinal Stromal Tumor (GIST) of the stomach, Schwannoma, and leiomyoma were listed as differential diagnoses. GIST of the stomach was most suspected, and the treatment modality was decided to be surgery.

Surgical findings

Surgery was started in the lateral recumbent position with a transabdominal approach. Ports were inserted to form a reverse trapezoid with the umbilicus as the center. The tumor was separated from the gastric wall after the omental bursa was opened. The tumor was at a location surrounded by the left margin of the aorta, the upper margin of the renal artery, and the upper margin of the pancreas and the splenic hilum. The exfoliation of the retroperitoneum and the tumor was difficult. Thus, the pancreas was tunneled and lifted to achieve this (Figure 5). As feeding vessels were flowing from the left gastric artery toward the tumor, they were clipped, and the tumor was removed (Figure 6). The procedure was a laparoscopic tumorectomy. The surgical duration was 247 min, and the hemorrhage volume was 10 mL. There were no changes in the intraoperative vital signs.

Macroscopic findings

The macroscopic finding was a round tumor with a capsule with a clear boundary, and there was no necrosis on the cut surface. Moreover, yellow consolidation was observed (Figure 7).

Histopathological findings

Supporting tissues and capillaries were observed around the pleomorphic tumor cells and alveolar aggregates, exhibiting a Zellballen pattern were found. Further, many ganglion cells were observed (Figure 8).

Immunohistochemistry analysis

The following immunohistochemical findings were noted: S-100 (+) for

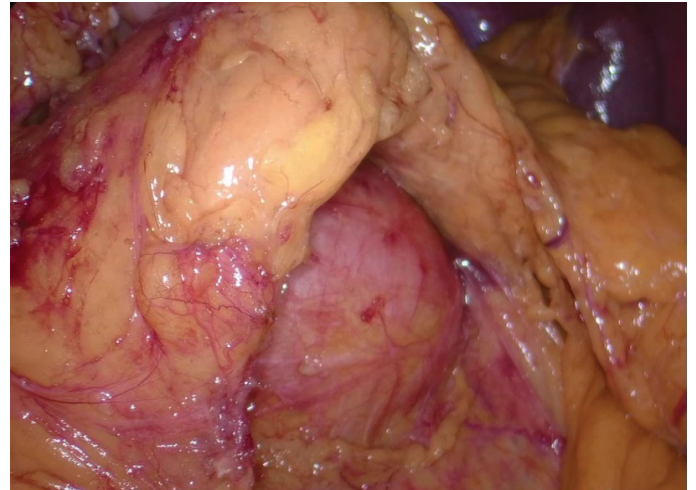


Figure 5. Surgical findings; The pancreas was tunneled and lifted; the tumor and the retroperitoneum were then exfoliated.

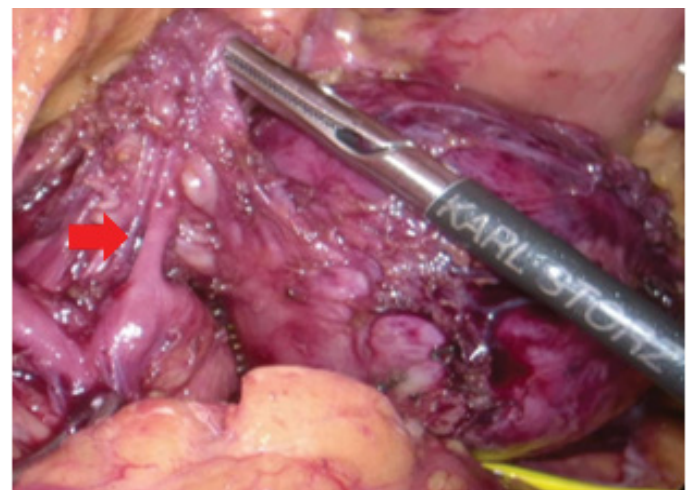


Figure 6. Surgical findings; Feeding vessels flow from the left gastric artery toward the tumor (red arrow).

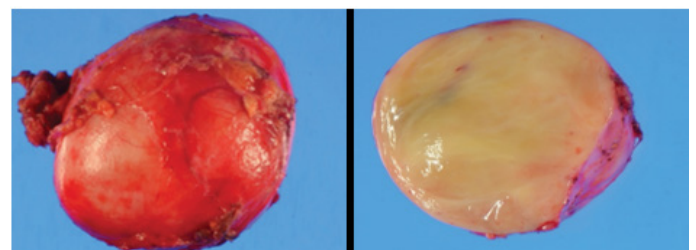


Figure 7. Macroscopic findings; A round tumor with capsule with a clear boundary was observed, and no necrosis existed on the cut surface. Moreover, yellow consolidation was observed.

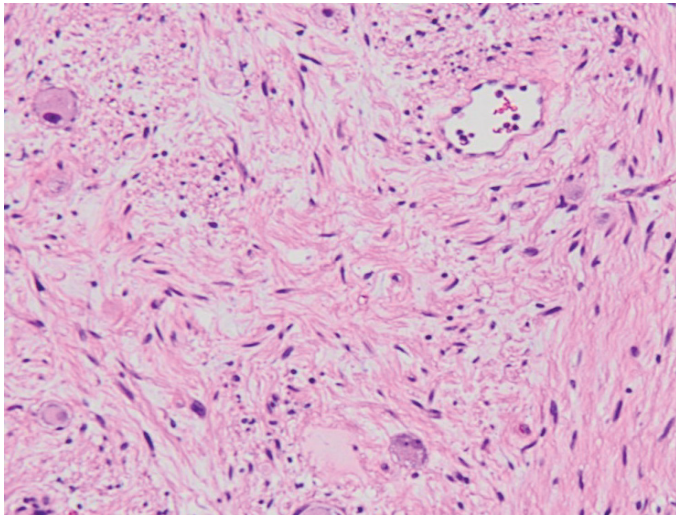


Figure 8. Histopathological findings; Supporting tissues and capillaries were observed around the pleomorphic tumor cells and alveolar aggregates, exhibiting a Zellballen pattern.

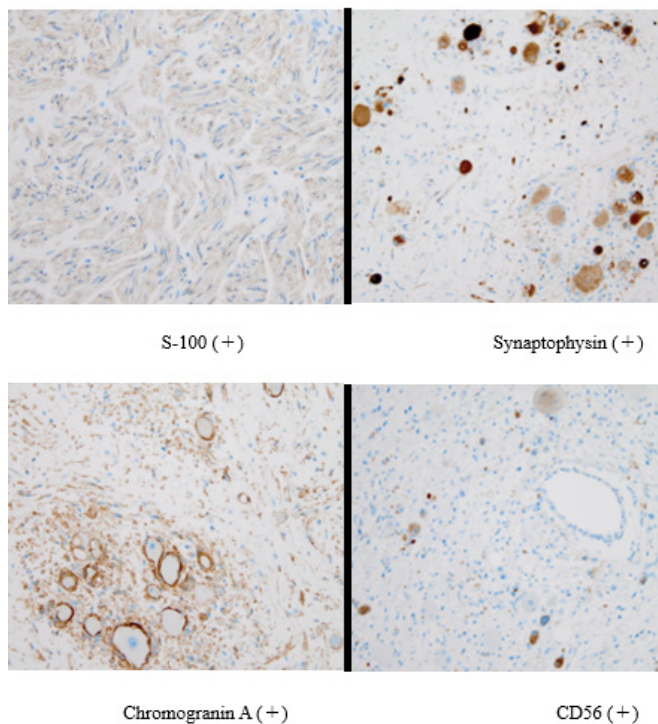


Figure 9. Immunohistochemistry staining; S-100 (+); Synaptophysin (+); Chromogranin A (+); CD56 (+).

supporting cells, synaptophysin (Syn) (+) and CD56 (+) for ganglion cells and chromogranin A (CgA) (+) for ganglions. Ki67 index was below 1% (Figure 9).

Final diagnosis: PGL

Post-operative progress: Pancreatitis was noted on postoperative day 3. The patient was discharged based on independent gait on postoperative day 12.

Discussion

PGLs are currently clinically and biologically divided into two groups, based on the parasympathetic and the sympathetic nervous system involvement, according to the World Health Organization classification. PGLs arising from the parasympathetic ganglia mainly affect the head and neck. Thus, PGLs are described as two subgroups based on location, namely head and neck PGL

and sympathetic PGL [1]. Sympathetic PGLs, originating from the chest and abdominal sympathetic nerves, account for 80% of all PGLs [2]. Moreover, 85% of sympathetic PGLs occur beneath the diaphragm and are particularly observed in the retroperitoneum around the adrenal and renal areas around the organ of Zuckerkandl and the bladder [3,4]. In addition, they are observed in the chest and heart [5,6]. PGL is usually characterized by catecholamine-related symptoms, such as persistent/paroxysmal hypertension, diaphoresis, palpitation, headache, and anxiety neurosis [7]. The sudden release of catecholamine makes it severe, with symptoms such as pulmonary edema, cerebral hemorrhage, hypertensive crisis, and cardiovascular disorders [8-10]. However, about 10% of asymptomatic PGLs may be discovered with the advancements in imaging [11]. Biochemical tests confirm the excessive secretion of catecholamine or metanephrine [10]. Free metanephrine in the blood and urine is a specific marker for chromaffin tumors and is superior to catecholamine [12]. In addition, blood metanephrine evaluation is superior to 24-h urinary metanephrine evaluation in sensitivity and specificity [13]. Furthermore, the test for the detection of urinary vanillylmandelic acid has the lowest sensitivity. PGL can be diagnosed with almost 100% certainty when metanephrine in the blood and urine is more than four times the normal upper limit. As this case was initially suspected as GIST of the stomach, blood and urine tests could not be performed before surgery. In the imaging studies performed in the current case, contrast-enhanced CT revealed consolidation with a contrast effect. Moreover, in MRI tests, T1- and T2-weighted images showed low and high signals, respectively. ¹²³I-meta-iodobenzylguanidine is a high-sensitivity test and it is useful for adrenal tumors or metastases [14].

Further, patients with PGL are also recommended to undergo genetic screening to detect genetic mutations that cause the disease. As many as 20 susceptibility genes have been currently discovered for PGL and pheochromocytoma. Germline mutations such as those in RET, VHL, SDHA, SDHB, SDHC, SDHD, SDHAF2, and MAX are related to PGL [15,16]. Patients with family history and below the age of 50 years are recommended to undergo genetic screening [17]. Proper preoperative management becomes necessary if excessive secretion of catecholamine is confirmed before surgery. Preoperative preparation by administering α -adrenergic blockers, β -adrenergic blockers, or calcium channel blockers and communication between the anesthesiologist–surgeon team during surgery are important. The standard treatment for PGL is surgical resection. A PubMed search for reports on laparoscopic surgery for abdominal PGL with paraganglioma/laparoscopic revealed 12 case reports, including this case, in a 10-year period from 2010 to 2020 (Table 1) [18-28]. The average age was 44.9 years [22-28], and the male: female ratio was 5:7. Laparoscopic approaches consisted of the transperitoneal approach in 11 cases and trans thoracoabdominal approach in 1 case. Peritoneal approach was performed in the supine and lateral recumbent positions in six and five cases, respectively. No cases were found with the retroperitoneal approach of surgery. Tumor location was with a ratio of right:left=7:4 at the aortic bifurcation in 1 case, above the renal artery in 6 cases, and under the renal artery in 6 cases. The average maximum tumor diameter was 52.5 mm (28-82 mm), the average surgical duration was 177 min (100-325 min), the average hemorrhage volume was 77.6 mL (little-340 mL), and the average duration of hospitalization was 5.2 days (2-12 days). Only pancreatitis, in terms of complications, was noted in the present case. In addition, tumor location was compared above and below the renal artery, and the average surgical duration for cases with the tumor above the renal artery and below the renal artery were 208.8 and 130.6 min, respectively. The respective average hemorrhage volumes were 114.3 and 16.6 mL. The surgical duration was longer and the hemorrhage volume larger for tumors above the renal artery.

Pancreatitis was confirmed in the present case, and this is a point for reflection. Pancreatitis occurred because the pancreas had been tunneled for the dorsal tumor treatment. The retroperitoneal approach in the lateral recumbent position instead of the supine position was considered the best method. Ensuring accurate preoperative diagnosis, tumor location, and size and performing the surgery in the best position is necessary. The safety and effectiveness of laparoscopic surgery for pheochromocytoma have been extensively reported. However, laparoscopic surgery for PGL is controversial. The comparison between laparoscopic surgery and laparotomy for PGL has been reported in a small-scale experiment, and a decrease in hemorrhage volume and duration of hospitalization has been reported in this study [29].

Table 1. Cases of laparoscopic surgery for abdominal paraganglioma performed during 2010–2020 by PubMed search.

No	Author	Age	Sex	Approach Method	Tumor Location	Maximum Diameter of Tumor (Mm)	Surgical Duration	Hemorrhage Volume (ML)	Complication	Duration of Hospitalization
1	The current case 2020	53	Female	Transperitoneal	Above the left renal artery	56	247	10	pancreatic fistula	12
2	Ahmed 2020 ¹⁸	23	Male	Transperitoneal Lateral recumbent position	Aortic bifurcation	50	NA	NA	None	NA
3	Xiang 2020 ¹⁹	45	Male	Transperitoneal Lateral recumbent position	Under the right renal artery	72	120	50	None	5
4	Pietro 2020 ²⁰	26	Male	Transperitoneal	Under the left renal vein	35	130	少量	None	3
5	Antonios 2019 ²¹	69	Female	Transperitoneal	Under the right renal artery	45	142	少量	None	3
6	Tomoaki 2019 ²²	72	Male	Transperitoneal Lateral recumbent position	Above the right renal artery	70	231	200	None	NA
7	Hisataka 2018 ²³	51	Female	Transperitoneal	Above the right renal artery	26	325	340	None	7
8	Mohammad 2018 ²⁴	24	Female	Transperitoneal Lateral recumbent position	Under the left renal artery	35	NA	NA	None	5
9	Zar 2017 ²⁵	26	Female	Transperitoneal	Above the right renal artery	82	120	40	None	5
10	Hrishikesh 2016 ²⁶	22	Female	Transperitoneal Lateral recumbent position	Under the left renal artery	80	125	40	None	4
11	Yutaka 2015 ²⁷	64	Male	Transperitoneal	Above the right renal artery	28	230	36	None	6
12	Altug 2010 ²⁸	64	Female	Transthoroabdominal Lateral recumbent position	Above the right renal artery	48	100	60	None	2

In addition, the comparative study between patients with pheochromocytoma and PGL undergoing laparoscopic surgery reported that laparoscopic PGL had a longer surgical duration. However, no significant difference existed in hemorrhage volume and duration of hospitalization [30]. The selection of the laparoscopic approach is determined by the surgeon's preferences and skills, and the patient's physique, body mass index, tumor size, and location [31]. Some reports have indicated that the retroperitoneal approach shortens the surgical duration [32,33]. In addition, reports also exist on the single-site and robotic surgeries [34,35]. In terms of histological features, sympathetic PGLs and pheochromocytomas consisting of polygonal cells, called chromaffin cells, exhibit amphophilic to basophilic cytoplasm. Tumor cells are separated by the capillary plexus and arranged in an alveolar pattern (Zellballen architecture). Cytological characteristics include granular cytoplasm, prominent nucleoli, vesicular nuclei, pseudo-inclusions inside nuclei, and so on. There may be secondary changes like hemorrhage, hemosiderin deposition, sclerosis, and pigmentation of the lipofuscin or melani [2,36].

Immunohistochemistry could confirm the pathological diagnosis and assist in making a differential diagnosis with other microscopically similar tumors. CgA is the most specific feature and helps distinguish PGLs from other neuroendocrine tumors. PGLs are usually positive for Syn, which is less specific than CgA because diffused positive Syn staining is also observed in adrenal cortical carcinomas [37-39]. CD56 is also an important neuroendocrine marker [40,41]. PGLs are usually negative for keratins. A Ki-67 proliferation index >3% significantly predict the malignant potential and prognosis of PGLs. In addition, Pheochromocytoma of the Adrenal Gland Scaled Score (PASS), proposed by Thompson et al. in 2002, is an index showing the malignancy potential of malignant pheochromocytomas [42]. Malignant PGLs show a PASS score of ≥ 4 . Of the 12 parameters of PASS, necrosis, capsular invasion, vascular invasion, cellular monotony, high mitosis, atypical mitotic figures, and nuclear hyperchromasia were significant predictors of malignancy [43]. The tumor in this case had a Statistical Package for the Social Sciences score of 1 and was highly likely to be benign. However, malignant PGL has been reported to be 10%-20% of the reported cases, [44] and the malignancy risk

is reported to be high despite young age and tumor size. Thus, strict follow-up is important [42,45].

Conclusion

In conclusion, a laparoscopic tumorectomy by the transperitoneal approach was performed for a case of PGL. Laparoscopic surgery for PGL is generally not recommended. However, in the present case, it was completely safely resected after examining previous studies and reported cases. Fully understanding the preoperative diagnosis, tumor size, and location and performing the surgery with the best approach method and surgical position is important.

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