Paraganglioma of the Fallopian Tube Presenting as Isolated Fallopian Tube Torsion

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Abstract
A 32-year-old woman with no previous disease history was presented with worsening right-lower abdominal pain, which lasted for 4 days. On magnetic resonance imaging, a solid mass measuring 48 mm in longitudinal diameter connected with a tortuous structure that appeared to be a fallopian tube was identified in the right-lower abdomen. Because the right ovary was identified at a slightly distant location, isolated fallopian tube torsion with heterogeneous mass was suspected. The isolated fallopian tube torsion without ovarian involvement was laparoscopically confirmed. After detorsion, solid necrotized mass in the distal portion of the right fallopian tube near the fimbrial end became evident, followed by uneventful right salpingectomy with ovarian preservation. The pathological diagnosis was paraganglioma of the fallopian tube with positive cells for neural cell adhesion molecule, neuron-specific enolase, and S-100 protein in the viable peripheral foci of the massively necrotized hemorrhagic mass. Recurrence was not observed after 1.5 years.
Introduction

Pheochromocytoma and paraganglioma are related neuroendocrine tumors that exhibit similar histological features [1]. Pheochromocytoma arises in the adrenal gland, whereas paraganglioma can occur anywhere else from the extra-adrenal chromaffin cells in sympathetic and parasympathetic paraganglia [1].

Paraganglioma rarely occurs in the female genital organs [2] with reported sporadic cases in the uterus [3], ovaries [4–7], vagina [8], and vulva [9]; however, its occurrence in the fallopian tube has never been described. Isolated fallopian tube torsion (IFTT) without the involvement of the ipsilateral ovary is a relatively rare form of adnexal torsion [10]. IFTT may occur in association with intrinsic and extrinsic predisposing conditions [11]. We herein report a rare presentation of paraganglioma of the fallopian tube with IFTT treated with laparoscopic surgery after diagnosis by magnetic resonance imaging (MRI).

Case Report/Case Presentation

A 32-year-old, gravida three para two, woman experienced abdominal pain, which spontaneously subsided; however, 4 months later presented with worsening 4 days long right-lower abdominal pain. The patient was a smoker but did not report any preexisting medical conditions, including hypertension. At the initial examination, the patient was afebrile, and the vital signs were stable. Systolic and diastolic blood pressures were 134 and 73 mm Hg, respectively.

Blood examination showed normal values except for a slight elevation of C-reactive protein (0.18 mg/dL), white blood cell counts (9,100/L), and hemoglobin (15 g/dL). Serum tumor marker values, including carcinoembryonic antigen, CA125, CA19-9, alpha-fetoprotein, and squamous cell carcinoma antigen, were within the normal range.

Emergency computerized tomography (CT) without contrast enhancement and ultrasonography showed mass lesion in the right lower abdomen. MRI was requested to visualize the more precise structure of this mass, and dynamic CT was added to evaluate the blood supply to this tumor.

On MRI, a heterogeneous mass measuring 48 mm in longitudinal diameter (Fig. 1a, arrow) connected with a tortuous structure that appeared to be a fallopian tube (Fig. 1a, arrowhead) was identified in the right-lower abdomen. The right ovary (Fig. 1b, arrow), which appeared normal, was identified at a slightly distant location. Although solid abdominal mass, such as a gastrointestinal stromal tumor or malignant lymphoma, could not be completely ruled out, IFTT with heterogeneous mass was most suspected. On contrast-enhanced CT, loss of enhancement in this solid mass supported the diagnosis of IFTT with heterogeneous mass. Apparent abnormal lesions in other organs were not identified (data not shown).

Emergency surgical intervention was planned because of the worsening abdominal symptoms. The patient was counseled about the treatment options, and informed consent was obtained for laparoscopic surgery, which could be converted to laparotomy in case of failure.

Gasless laparoscopic surgery was performed in a low Trendelenburg position under general anesthesia [12]. A 2.5-cm vertical umbilical incision was made to place the wound retractor (Alexis, small size; Applied Medical, Rancho Santa Margarita, CA, USA). To maintain the operative view, an intra-abdominal fan retractor system (Mizuho Co., Tokyo, Japan) was used for lifting the abdominal wall. An auxiliary 5-mm port (Kii advanced fixation sleeve; Applied Medical) was placed on the right lateral side of the abdomen to assist surgical manipulation.
A laparoscopic view through an ENDOEYE laparoscope (rigid 5-mm, 30 models; Olympus, Tokyo, Japan) identified isolated rotation of the right fallopian tube (Fig. 1c, arrow) without ovarian involvement (Fig. 1c, arrowhead). Careful detorsion revealed a detorted point of the right fallopian tube (Fig. 1d, arrow) and an uninvolved right ovary (Fig. 1d, arrowhead).

Further laparoscopic observation revealed a solid mass (Fig. 1e, arrow) attached to the distal portion of the right fallopian tube near the fimbrial end (Fig. 1e, arrowhead). Uneventful right salpingectomy was done by sealing and cut by the LigaSure Maryland jaw device (Medtronic, Tokyo, Japan). The duration of the surgery was 76 min, and estimated blood loss was 20 mL. The weight of the excised tissue was 54 g. The macroscopic appearance of the excised specimen showed a solid necrotized mass (arrow) arising from the right fallopian tube wall in the distal portion near the fimbrial end (arrowhead). The postoperative course was uneventful, and no recurrence was observed after 1.5 years.

Histological examination exhibited massive ischemic necrosis of excised tumor tissue and fallopian tube for the most part. In the viable peripheral tissue, closely packed nests, showing a “zellballen” appearance [4], were identified (Fig. 2a). Immunohistochemical staining was positive for neural cell adhesion molecule (CD56) (Fig. 2b), neuron-specific enolase (Fig. 2c), and S-100 protein (Fig. 2d) in viable tumor cells, while staining for the cytokeratin marker (AE1/AE3) and estrogen receptor (data not shown) was negative. The percentage of Ki-67 positive cells was <1% (data not shown). These histological characteristics confirmed the diagnosis of paraganglioma [2, 4] with potential low-grade malignancy.
Discussion/Conclusion

The dispersed neuroendocrine system throughout the body may give rise to neoplasms with neuronal and neuroendocrine features, such as paraganglioma [1, 2]. Half of paragangliomas arise from the organs of Zuckerkandl [2], which comprise a small mass of chromaffin cells derived from the neural crest along the aorta, while the histogenesis of a rare type of paragangliomas in the female genital organs remains controversial [3–9].

In paragangliomas of the ovary [4–7], which are most frequent in the female genital tract, potential developmental mechanisms include involvement of the ovary through the spread of paraganglioma from nearby extra-adrenal paraganglia or preexisting paraganglia within the ovarian parenchyma [5], although these hypothetical models have not yet been clarified. Alternatively, unidirectional differentiation to paraganglioma occurring within a tumor could be a rational explanation when paraganglioma of the ovary is associated with mature cystic teratoma [6].

The lack of clarity concerning the cellular origin appeared to be true for the paraganglioma of the fallopian tube described in the current report; i.e., paraganglioma of the fallopian tube can develop from extra-adrenal paraganglia that exist near the fallopian tube. Another possibility is that adrenomedullary cells in the adrenal rest of the fallopian tube [13], which have been rarely discovered and clarified without clinical significance, could be the origin.

Clinical manifestation of paragangliomas is variable because they can be either functional or nonfunctional [1–10]. When paragangliomas occur from extra-adrenal chromaffin cells in

Fig. 2. Histopathological examination showing paraganglioma of the fallopian tube. a Hematoxylin and eosin staining showed closely packed foci of viable cells showing a “zellballen” appearance. Scale bar, 50 μm. b Positive immunohistochemical staining for neural cell adhesion molecule (CD56). Scale bar, 50 μm. c Positive immunohistochemical staining for NSE. Scale bar, 50 μm. d Positive immunohistochemical staining for S-100 protein. Scale bar, 50 μm. NSE, neuron-specific enolase.
parasympathetic paraganglia, they are usually nonfunctional; however, paragangliomas arising from sympathetic paraganglia could possess the ability to secrete catecholamine, which produces symptoms due to catecholamine excesses, such as the classic triad of headaches, palpitations, and profuse sweating [1].

However, because sympathetic paragangliomas could exhibit either secretory or nonsecretory ability, the production of catecholamines by paraganglioma may not correlate with specific symptoms [1, 2]. In the current case of paraganglioma without exhibiting the classic triad of headaches, palpitations, and profuse sweating, significant elevation of blood pressure was not observed at triage. Therefore, paraganglioma of the current case appeared either nonfunctional or nonsecretory, although the levels of catecholamines were not unfortunately measured.

Preoperative diagnosis of nonfunctional paraganglioma is challenging due to the lack of characteristic symptoms associated with catecholamine excess [1, 2]. As a result, a definitive diagnosis could only be made based on histological findings of the surgically excised specimen when a typical “zellballen” appearance [4] with positive immunohistochemical staining for neuronal markers [2–4], such as CD56, neuron-specific enolase, and S-100 protein, is identified.

In the current case without signs of hypertension at triage, there were significant difficulties in diagnosing paraganglioma because most part of the tumor was severely damaged due to prolonged ischemia caused by IFTT. However, as shown in Figure 2, conventional histological staining showed “zellballen” appearance in the barely survived peripheral tissue, suggesting that the current tumor is a paraganglioma of the fallopian tube. This diagnosis was confirmed further by showing positive immunohistochemical staining of neuronal markers.

Although widely recognized [5], the malignant potential of paraganglioma is a significant concern from oncological aspects. Paraganglioma is a slowly growing tumor with a tendency to show benign disease course or low latent malignancy [8]. A combination of extensive necrosis, identifiable mitotic figures, or vascular invasion in the histological specimen, which could be suggestive of a more aggressive nature in general, remains controversial to determine metastatic potential and likelihood of recurrence of paragangliomas [1, 7].

Consequently, clinical diagnosis of malignant potential of paraganglioma is determined by the presence or future development of metastases [5]. However, the time between initial therapy of paraganglioma and identification of subsequent advanced disease conditions, such as metastases, is highly variable [1, 2].

As primary treatment, surgical debulking of paraganglioma with involved tissue is needed because these tumors are resistant to chemotherapy and radiotherapy [1, 2]. In the current case, unilateral salpingectomy was performed for surgical excision in an emergency setting. Additional surgical staging and adjuvant therapy were not given as the low-malignant potential of the current tumor was assumed based on the results of Ki-67 immunohistochemistry showing a low index <1%, and the patient chose regular follow-up by CT. After the treatment for paraganglioma, further long-term follow-up is needed to detect recurrence, the additional appearance of primary tumors, or metastatic disease [4].

In conclusion, paraganglioma of the fallopian tube is an extremely rare entity, the cancerous potential of which remains unknown. Further accumulation of cases would be needed to reveal its histogenesis, clinical characteristics, and malignant potential.

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Statement of Ethics

The authors state that they have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, written informed consent was obtained from the patient for publication of this case report and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors report no conflicts of interest. The authors have no relationships with the companies that may have a financial interest in the information contained in the manuscript.

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Author Contributions

Akihiro Takeda, Kazuko Watanabe, Wataru Koike, and Shiori Tsuge reviewed the relevant scientific literature and wrote the original manuscript. Kazuko Watanabe interpreted the pathology. Wataru Koike interpreted the imaging. All the authors were involved in reviewing and editing the manuscript and figures. All the authors approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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