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Contents

Thrice Monthly Volume 10 Number 33 November 26, 2022

MINIREVIEWS

- 12066** Review of risk factors, clinical manifestations, rapid diagnosis, and emergency treatment of neonatal perioperative pneumothorax
Zhang X, Zhang N, Ren YY

ORIGINAL ARTICLE

Clinical and Translational Research

- 12077** Integrative analysis of platelet-related genes for the prognosis of esophageal cancer
Du QC, Wang XY, Hu CK, Zhou L, Fu Z, Liu S, Wang J, Ma YY, Liu MY, Yu H
- 12089** Comprehensive analysis of the relationship between cuproptosis-related genes and esophageal cancer prognosis
Xu H, Du QC, Wang XY, Zhou L, Wang J, Ma YY, Liu MY, Yu H
- 12104** Molecular mechanisms of Baihedihuang decoction as a treatment for breast cancer related anxiety: A network pharmacology and molecular docking study
Li ZH, Yang GH, Wang F
- 12116** Single-cell RNA-sequencing combined with bulk RNA-sequencing analysis of peripheral blood reveals the characteristics and key immune cell genes of ulcerative colitis
Dai YC, Qiao D, Fang CY, Chen QQ, Que RY, Xiao TG, Zheng L, Wang LJ, Zhang YL

Retrospective Study

- 12136** Diagnosis and treatment of tubal endometriosis in women undergoing laparoscopy: A case series from a single hospital
Jiao HN, Song W, Feng WW, Liu H
- 12146** Different positive end expiratory pressure and tidal volume controls on lung protection and inflammatory factors during surgical anesthesia
Wang Y, Yang Y, Wang DM, Li J, Bao QT, Wang BB, Zhu SJ, Zou L
- 12156** Transarterial chemoembolization combined with radiofrequency ablation in the treatment of large hepatocellular carcinoma with stage C
Sun SS, Li WD, Chen JL
- 12164** Coexistence of anaplastic lymphoma kinase rearrangement in lung adenocarcinoma harbouring epidermal growth factor receptor mutation: A single-center study
Zhong WX, Wei XF

Observational Study

- 12175** Prognostic values of optic nerve sheath diameter for comatose patients with acute stroke: An observational study

Zhu S, Cheng C, Wang LL, Zhao DJ, Zhao YL, Liu XZ

- 12184** Quality of care in patients with inflammatory bowel disease from a public health center in Brazil

Takamune DM, Cury GSA, Ferrás G, Herrerias GSP, Rivera A, Barros JR, Baima JP, Saad-Hossne R, Sasaki LY

- 12200** Comparison of the prevalence of sarcopenia in geriatric patients in Xining based on three different diagnostic criteria

Pan SQ, Li XF, Luo MQ, Li YM

Prospective Study

- 12208** Predictors of bowel damage in the long-term progression of Crohn's disease

Fernández-Clotet A, Panés J, Ricart E, Castro-Pocheiro J, Masamunt MC, Rodríguez S, Caballol B, Ordás I, Rimola J

Randomized Controlled Trial

- 12221** Protective effect of recombinant human brain natriuretic peptide against contrast-induced nephropathy in elderly acute myocardial infarction patients: A randomized controlled trial

Zhang YJ, Yin L, Li J

META-ANALYSIS

- 12230** Prognostic role of pretreatment serum ferritin concentration in lung cancer patients: A meta-analysis

Gao Y, Ge JT

CASE REPORT

- 12240** Non-surgical management of dens invaginatus type IIIB in maxillary lateral incisor with three root canals and 6-year follow-up: A case report and review of literature

Arora S, Gill GS, Saquib SA, Saluja P, Baba SM, Khateeb SU, Abdulla AM, Bavabeedu SS, Ali ABM, Elagib MFA

- 12247** Unusual presentation of Loeys-Dietz syndrome: A case report of clinical findings and treatment challenges

Azrad-Daniel S, Cupa-Galvan C, Farca-Soffer S, Perez-Zincer F, Lopez-Acosta ME

- 12257** Peroral endoscopic myotomy assisted with an elastic ring for achalasia with obvious submucosal fibrosis: A case report

Wang BH, Li RY

- 12261** Subclavian brachial plexus metastasis from breast cancer: A case report

Zeng Z, Lin N, Sun LT, Chen CX

- 12268** Case mistaken for leukemia after mRNA COVID-19 vaccine administration: A case report

Lee SB, Park CY, Park SG, Lee HJ

- 12278** Orthodontic-surgical treatment of an Angle Class II malocclusion patient with mandibular hypoplasia and missing maxillary first molars: A case report

Li GF, Zhang CX, Wen J, Huang ZW, Li H

- 12289** Multiple cranial nerve palsies with small angle exotropia following COVID-19 mRNA vaccination in an adolescent: A case report
Lee H, Byun JC, Kim WJ, Chang MC, Kim S
- 12295** Surgical and nutritional interventions for endometrial receptivity: A case report and review of literature
Hernández-Melchor D, Palafox-Gómez C, Madrazo I, Ortiz G, Padilla-Viveros A, López-Bayghen E
- 12305** Conversion therapy for advanced penile cancer with tislelizumab combined with chemotherapy: A case report and review of literature
Long XY, Zhang S, Tang LS, Li X, Liu JY
- 12313** Endoscopic magnetic compression stricturoplasty for congenital esophageal stenosis: A case report
Liu SQ, Lv Y, Luo RX
- 12319** Novel *hydroxymethylbilane synthase* gene mutation identified and confirmed in a woman with acute intermittent porphyria: A case report
Zhou YQ, Wang XQ, Jiang J, Huang SL, Dai ZJ, Kong QQ
- 12328** Modified fixation for periprosthetic supracondylar femur fractures: Two case reports and review of the literature
Li QW, Wu B, Chen B
- 12337** Erbium-doped yttrium aluminum garnet laser and advanced platelet-rich fibrin+ in periodontal diseases: Two case reports and review of the literature
Tan KS
- 12345** Segmental artery injury during transforaminal percutaneous endoscopic lumbar discectomy: Two case reports
Cho WJ, Kim KW, Park HY, Kim BH, Lee JS
- 12352** Pacemaker electrode rupture causes recurrent syncope: A case report
Zhu XY, Tang XH, Huang WY
- 12358** Hybrid intercalated duct lesion of the parotid: A case report
Stankevicius D, Petroska D, Zaleckas L, Kutanovaite O
- 12365** Clinical features and prognosis of multiple myeloma and orbital extramedullary disease: Seven cases report and review of literature
Hu WL, Song JY, Li X, Pei XJ, Zhang JJ, Shen M, Tang R, Pan ZY, Huang ZX
- 12375** Colon mucosal injury caused by water jet malfunction during a screening colonoscopy: A case report
Patel P, Chen CH
- 12380** Primary malignant pericardial mesothelioma with difficult antemortem diagnosis: A case report
Oka N, Orita Y, Oshita C, Nakayama H, Teragawa H
- 12388** Typical imaging manifestation of neuronal intranuclear inclusion disease in a man with unsteady gait: A case report
Gao X, Shao ZD, Zhu L

- 12395** Multimodality imaging and treatment of paranasal sinuses nuclear protein in testis carcinoma: A case report
Huang WP, Gao G, Qiu YK, Yang Q, Song LL, Chen Z, Gao JB, Kang L
- 12404** T1 rectal mucinous adenocarcinoma with bilateral enlarged lateral lymph nodes and unilateral metastasis: A case report
Liu XW, Zhou B, Wu XY, Yu WB, Zhu RF
- 12410** Influence of enhancing dynamic scapular recognition on shoulder disability, and pain in diabetics with frozen shoulder: A case report
Mohamed AA
- 12416** Acute myocardial necrosis caused by aconitine poisoning: A case report
Liao YP, Shen LH, Cai LH, Chen J, Shao HQ
- 12422** Danggui Sini decoction treatment of refractory allergic cutaneous vasculitis: A case report
Chen XY, Wu ZM, Wang R, Cao YH, Tao YL
- 12430** Phlegmonous gastritis after biloma drainage: A case report and review of the literature
Yang KC, Kuo HY, Kang JW
- 12440** Novel *TINF2* gene mutation in dyskeratosis congenita with extremely short telomeres: A case report
Picos-Cárdenas VJ, Beltrán-Ontiveros SA, Cruz-Ramos JA, Contreras-Gutiérrez JA, Arámbula-Meraz E, Angulo-Rojo C, Guadrón-Llanos AM, Leal-León EA, Cedano-Prieto DM, Meza-Espinoza JP
- 12447** Synchronous early gastric and intestinal mucosa-associated lymphoid tissue lymphoma in a *Helicobacter pylori*-negative patient: A case report
Lu SN, Huang C, Li LL, Di LJ, Yao J, Tuo BG, Xie R

LETTER TO THE EDITOR

- 12455** Diagnostic value of metagenomics next-generation sequencing technology in disseminated strongyloidiasis
Song P, Li X
- 12458** Diagnostic value of imaging examination in autoimmune pancreatitis
Wang F, Peng Y, Xiao B

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Retrospective Study

Diagnosis and treatment of tubal endometriosis in women undergoing laparoscopy: A case series from a single hospital

Hai-Ning Jiao, Wei Song, Wei-Wei Feng, Hua Liu

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Abstract

BACKGROUND

Tubal endometriosis (TEM) is a category of pelvic endometriosis (EM) that is characterized by ectopic endometrial glands and/or stroma within any part of the fallopian tube. The fallopian tubes may be a partial source of ovarian endometriosis (OEM). TEM is difficult to diagnose during surgery and is usually detected by pathology after surgery.

AIM

To provide a clinical basis for the diagnosis and treatment of TEM.

METHODS

In this study, the data of 30 patients who underwent laparoscopic salpingectomy due to various gynecological diseases and had pathological confirmation of TEM at our hospital were retrospectively analyzed, and the clinical basis for the diagnosis and treatment of TEM was evaluated.

RESULTS

Among 1982 surgical patients, 30 met the study criteria. Among those, 6 patients had a history of infertility, 12 patients had a history of artificial abortion, 13 patients had a history of cesarean section, 1 patient had a history of tubal ligation, 4 patients had an intrauterine device, and 22 patients had hydrosalpinx. Sixteen patients (53.33%) conceived naturally and gave birth to healthy babies. Pathology showed that only 2 patients had TEM without any other gynecological diseases, while the others all had simultaneous diseases, including 26 patients with EM at other pelvic sites.

CONCLUSION

The final diagnosis of TEM depends on pathological examination since there are no specific clinical characteristics. The rate of TEM combined with EM (especially OEM) was higher than that of other gynecological diseases, which indicates that

TEM is related to OEM.

Key Words: Endometriosis; Fallopian tubes; Ovary; Laparoscopy; Infertility; Pathology

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Core Tip: Tubal endometriosis (TEM) is a category of pelvic endometriosis that is characterized by ectopic endometrial glands and/or stroma within any part of the fallopian tube. The fallopian tubes may be a partial source of ovarian endometriosis (OEM). In this study, 30 patients who underwent laparoscopic salpingectomy due to various gynecological diseases and were pathologically confirmed as having TEM at our hospital were retrospectively analyzed to provide a clinical basis for the diagnosis and treatment of TEM. The final diagnosis of TEM depends on pathological examination since there are no specific clinical characteristics. The rate of TEM combined with OEM was higher than that of other gynecological diseases, which indicates that TEM is related to OEM.

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INTRODUCTION

Endometriosis (EM) is a common, estrogen-driven chronic condition in which endometrium-like epithelial and stromal cells are implanted at ectopic sites beyond their native location, namely, the internal lining of the uterine cavity[1]. Tubal endometriosis (TEM) is a type of pelvic EM that is characterized by ectopic endometrial glands and/or stroma on any part of the fallopian tube. The causes of tubal dysfunction in EM may be hydrosalpinx, tubal blockage or adhesion formation. Up to 30% of women with EM have some form of tubal involvement[2]. Studies have suggested that the fallopian tubes may be a partial source of ovarian endometriosis (OEM)[3,4]. TEM is difficult to diagnose during surgery and is usually detected by pathology after surgery. In our study, the clinical and pathological characteristics of TEM were analyzed, and the correlation between TEM and OEM was analyzed to provide a clinical basis for the diagnosis and treatment of TEM.

MATERIALS AND METHODS

Patients

Among 1982 patients diagnosed with EM at Ruijin Hospital affiliated with Shanghai Jiao Tong University School of Medicine, 30 patients were diagnosed with pathologically confirmed TEM and underwent laparoscopy due to various gynecological diseases from January 2013 to December 2021. The clinical data and pathological features of the patients, including age, fertility and contraceptive status, clinical manifestations, concomitancy of other gynecological diseases, and surgical methods, were collected.

Diagnostic criteria of TEM

TEM was defined as the presence of ectopic endometrial glands and/or stroma in the fallopian tube, and 30 patients met this criterion.

In our study, we used immunohistochemistry to diagnose EM. Regarding the anatomical distribution of TEM, lesions of the proximal tube have been shown to mainly affect the mucosa, whilst lesions of the distal tube tend to affect the serosa/subserosa. Some authors have proposed that only lesions beyond the isthmus should be considered as TEM, whilst those proximal to the isthmus could be defined as endometrial colonisation. Thus, the limited evidence suggests lesions may be more prevalent beyond the isthmus and ampulla[1]. We will give consideration to potential lesions in the medial portion of the fallopian tube since TEM at this part could be confused with endometrial epithelization of the fallopian tube, and further research will be carried out in the future.

Statistical analysis

Normally distributed data are expressed as the means $\pm$ SD, while nonnormally distributed data are expressed as medians (ranges). Analysis of variance was used to compare the rates of TEM combined

with EM (especially OEM) and those of other gynecological diseases. $P < 0.05$ was considered to be statistically significant. All data were processed using SAS 9.0 statistical software (SAS Institute, Inc.).

RESULTS

Clinical manifestations

There were 1982 patients diagnosed with EM at our hospital who underwent laparoscopic surgery, including salpingectomy, cystectomy, and adenomyomectomy, and 30 of these patients were diagnosed with TEM, accounting for 1.51% of the patients (30/1982). Laparoscopic surgery was performed in all 30 TEM patients, including unilateral or bilateral salpingectomy in 27 and tubal cystectomy in 3. The mean age of the 30 TEM patients was 41.13 ± 10.33 years (14-74 years), and 1 of them was postmenopausal. There were 5 patients under 35 years old, 24 patients between 35 and 50 years old, and 1 patient over 50 years old. The mean number of pregnancies in the 30 patients was 1.23 ± 1.04 (0~4), including 0 pregnancies in 11 patients, 1 in 17 patients, and > 1 in 2 patients. The average number of births was 0.70 ± 0.60 (0-2), including 0 births in 11 patients, 1 birth in 17 patients, and > 1 births in 2 patients. 16 patients (53.33%) conceived naturally and gave birth to healthy babies.

Three patients had no sexual history, 6 patients had a history of infertility, 12 patients had a history of induced abortion, 13 patients had a history of cesarean section, 1 patient had a history of tubal sterilization, and 4 patients had contraceptive intrauterine devices (IUDs) (Table 1). A total of 20 patients had a history of intrauterine surgery (including induced abortion, cesarean section and IUD insertion). The incidence rate of TEM was higher in patients with an intrauterine operation history than in patients without an intrauterine operation history ($P < 0.05$). There were 6 patients with a history of a laparoscopic ovarian endometrial cystectomy and 1 patient with a history of a laparoscopic myomectomy.

Among the 30 patients, 9 patients had a chief complaint of progressive dysmenorrhea, 5 patients had chronic abdominal pain, 4 patients had menorrhagia, 6 patients had infertility, 3 patients had abnormal vaginal bleeding, and 15 patients were diagnosed with adnexal cysts by ultrasound. Of the 30 patients, 26 had dysmenorrhea. Preoperative ultrasound revealed that 9 patients had fallopian tube occupation, including 7 patients with suspected hydrosalpinx and 2 patients with undetermined fallopian tube occupation (suspected cancer). There were 19 patients (63.33%) who had a CA125 level over 35 U/mL, with an average level of 90.43 ± 98.95 U/mL.

Laparoscopic surgery

Laparoscopic surgery was performed in all 30 TEM patients, including unilateral or bilateral salpingectomy in 27 and tubal cystectomy in 3. There were fallopian tubal abnormalities in 26 patients, including hydrosalpinx in 22 patients, unilateral or bilateral fallopian tubal and ovarian adhesion and hydrosalpinx, tubal torsion and thickening of the fallopian tube in 10 patients, unilateral or bilateral distorted and enlarged fallopian tubes with violet lesions in 7 patients, unilateral or bilateral fallopian tube fimbria embedment in 5 patients, bilateral fallopian tube ampullary enlargement and stiffness with a history of bilateral tubal ligation in 1 patient, and unilateral or bilateral endometrial fallopian tubal cyst in 3 patients. There were 26 patients with EM in other parts of the pelvic cavity, 11 patients with uterine myoma, and 1 patient with uterine malformation (rudimentary uterus horn). The size and diameter of the lesions were noted to be 0.5-10 cm during intraoperative exploration. Clinical staging was performed for endometriotic lesions in other parts of the pelvic cavity. The RAF scores of the American Society for Reproductive Medicine (ASRM) staging ranged between 19 and 150 points, with an average score of 81.83 ± 35.14 points. There were 0 cases in stage I, 0 cases in stage II, 4 cases in stage III and 26 cases in stage IV (Figures 1 and 2).

Histopathological results

Postoperative pathology confirmed unilateral TEM in 26 cases and bilateral TEM in 4 cases. Endometrioid glands and/or epithelium were seen microscopically, surrounded by chronic hemorrhage, hemosiderin deposition, and/or irregular ectopic endometrial glands with endometrial stromal cells (Figure 3). TEM lesions were detected in the muscularis and mucosa of the fallopian tube in 4 patients (0.5-5 mm) and were found mainly in the serosa and the muscularis of the fallopian tube in 26 patients, with 6 of these patients having a history of infertility.

Only 2 patients had simple TEM, had no symptoms and were diagnosed with adnexal cysts by ultrasound. The remaining patients had one or more lesions, including other pelvic EM lesions in 26 patients (13 cases of OEM cysts and 13 cases of OEM accompanied by pelvic EM). The EM lesions that were in unilateral fallopian tubes and unilateral ovaries were all ipsilateral. There were 4 cases accompanied by adenomyosis, 5 cases with uterine myoma and 1 case with uterine sarcoma. A patient with left TEM combined with left rudimentary uterus horn and left OEM cyst underwent a laparoscopic left hysterectomy, a left salpingectomy and a left ovarian endometrial cystectomy (Table 1).

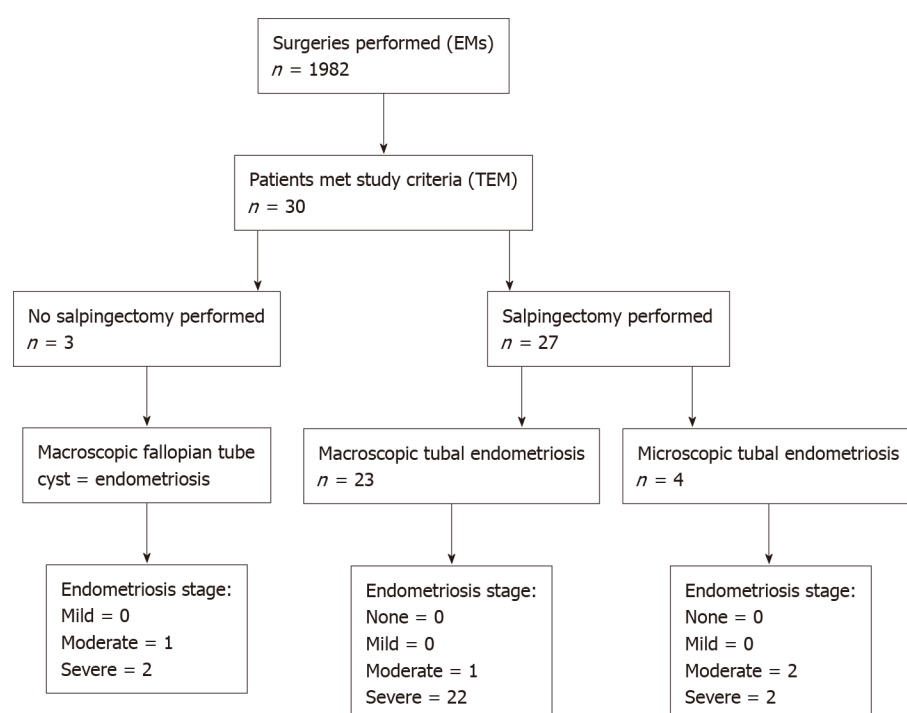
In our study, the rate of TEM combined with EM (especially OEM) was higher than the rates of other gynecological diseases ($P = 0.0001$). The TEM lesions of 4 patients who had no obvious abnormal appearance of their fallopian tubes were detected in the muscularis and mucosa of the fallopian tube

Table 1 Demographics and clinical pathological data for tubal endometriosis patients

Sample number	Age	G/P	Infertility	Intrauterine surgery	CA125 (U/mL)	Pathologic diagnosis			RAF scores of ASRM
						Fallopian tube and/or ovary	Uterine Anomaly	Deep infiltrating endometriosis	
1	45	1/1	No	Yes	53.2	Absence right fallopian tube and right ovary	Uterus normal	No	52
2	35	1/0	Yes	Yes	80.2	Absence left fallopian tube and left ovary	Uterus normal	Yes	82
3	46	2/1	No	Yes	10.2	Absence left fallopian tube	Uterine myoma	No	36
4	44	1/1	No	No	131.7	Absence left fallopian tube and left ovary	Uterus normal	No	82
5	27	0/0	No	No	52.1	Absence left fallopian tube and left ovary	Uterus normal	Yes	74
6	44	2/1	No	Yes	233.5	Absence left fallopian tube and left ovary	Uterine myoma	Yes	94
7	25	1/0	No	Yes	78.6	Absence left fallopian tube and left ovary	Uterus normal	No	92
8	48	1/1	No	Yes	49.9	Absence left fallopian tube and left ovary	Uterine myoma	No	92
9	40	3/2	No	Yes	49.3	Absence left fallopian tube and left ovary	Uterine sarcoma	Yes	48
10	47	1/1	No	No	21.3	Absence left fallopian tube and left ovary	Uterus normal	No	19
11	41	3/0	Yes	Yes	205.1	Absence bilateral fallopian tube and bilateral ovary	Uterus normal	Yes (rectal endometriosis)	150
12	28	0/0	No	No	102.6	Absence left fallopian tube and bilateral ovary	Uterus normal	Yes (ureteral endometriosis)	82
13	47	2/1	No	Yes	95.7	Absence bilateral fallopian tube and bilateral ovary	Uterine myoma	Yes	150
14	47	0/0	Yes	No	29.3	Absence left fallopian tube and left ovary	Uterine adenomyosis	No	92
15	28	0/0	No	No	168.5	Absence left fallopian tube and left ovary	Uterus normal	Yes (ureteral endometriosis)	144
16	74	2/2	No	Yes	10.1	Absence left fallopian tube and left ovary	Uterus normal	No	64
17	49	1/0	Yes	Yes	498.7	Absence bilateral fallopian tube and bilateral ovary	Uterine adenomyosis	Yes	144
18	49	3/1	No	Yes	45.2	Absence right fallopian tube and right ovary	Uterus normal	No	52
19	43	1/1	No	Yes	31.9	Absence right fallopian tube and right ovary	Uterine myoma	No	80
20	43	1/1	No	Yes	18.2	Absence left fallopian tube and left ovary	Uterine adenomyosis	No	116
21	40	1/1	No	Yes	28.8	Absence left fallopian tube and left ovary	Uterine myoma	Yes	92
22	42	1/1	No	No	105	Absence left fallopian tube and left ovary	Uterus normal	Yes	76
23	45	0/0	Yes	No	8.7	Absence right fallopian tube and left ovary	Uterus normal	Yes	76

24	47	1/1	No	Yes	60.3	Absence left fallopian tube and left ovary	Uterus normal	No	56
25	39	1/1	No	Yes	8.6	Absence bilateral fallopian tube and bilateral ovary	Uterus normal	No	114
26	42	4/1	No	Yes	175.8	Absence left fallopian tube and left ovary	Septate Uterus	No	92
27	42	1/1	No	Yes	64.6	Absence right fallopian tube and right ovary	Uterus normal	No	36
28	37	0/0	Yes	No	159.7	Absence right fallopian tube	Uterus normal	No	24
29	14	0/0	No	No	118.5	Absence left fallopian tube and left ovary	Left uterus unicornis and right rudimentary uterus horn	Yes	82
30	36	2/1	No	Yes	17.5	Absence right fallopian tube and right ovary	Uterine adenomyosis	No	62

ASRM: American Society for Reproductive Medicine.



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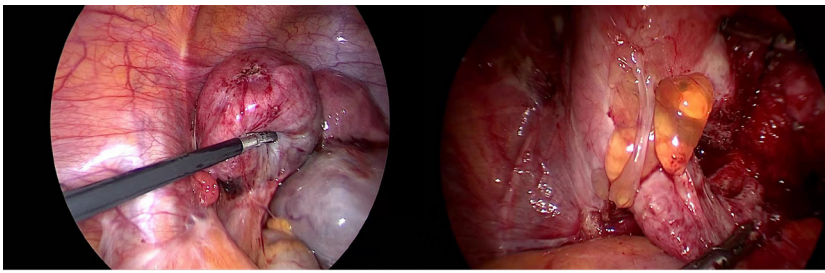
Figure 1 Study participant with tubal endometriosis at Ruijin Hospital. EMs: Endometriosis; TEM: Tubal endometriosis.

(0.5-5 mm). The TEM lesions of 26 patients who had abnormal appearances of their fallopian tubes were mainly found in the serosa and the muscularis of the fallopian tubes.

DISCUSSION

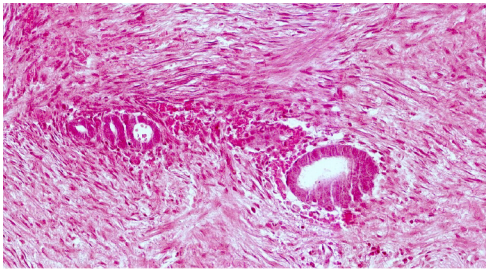
Incidence rate of TEM

In our study, 1982 patients, including 30 patients [1.51% (30/1982)] with TEM, were diagnosed with EM by surgery at our hospital during the same period. In a review of 2063 EM cases published in 1945 by Clement *et al*[5], EM lesions were located in the fallopian tube in 6 cases, accounting for 0.29% of the patients. There are few reports on TEM, and the incidence rate of TEM has varied greatly. This may be related to the fact that the clinical characteristics of TEM are not obvious and that the diagnosis of TEM



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Figure 2 Laparoscopic surgery was performed in tubal endometriosis patients.



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Figure 3 Histopathological results of the tubal endometriosis patient after laparoscopic surgery (histopathological sections were stained with hematoxylin and eosin, and cell morphology was observed at 200 × microscope).

requires surgical and pathological diagnostic verification. In recent years, with the promotion of the concept of preventive salpingectomy during hysterectomy, TEM was found in the postoperative pathological examinations of fallopian tubes without any obvious abnormalities. Therefore, more large-sample data and epidemiological investigations are needed to determine the exact incidence rate of TEM.

Etiology and pathogenesis

TEM lesions can be divided into three types: serosal (subserosal) TEM, intraluminal TEM and post-tubal ligation TEM. The most common type of TEM is serosal (subserosal) TEM, which is frequently accompanied by EM in other parts of the pelvis. Intrauterine surgery increases the incidence of EM, which may increase the incidence rate of TEM[6]. Most of the patients had a history of intrauterine surgery and tubal ligation, indicating that tubal ligation and intrauterine surgery may increase the incidence rate of TEM. In 1981, Rock *et al*[7] reported that the incidence of TEM could be as high as 63% after laparoscopic tubal electrocoagulation sterilization. The mechanism of the induction of TEM after tubal ligation may be related to the following three factors[8]: (1) Fistulas formed by tubal ligation may induce endometrial implantation directly; (2) the position of the tubal ligation is located between the isthmus and ampulla. Ligation stimulates the activation of the tubal intima, incurs tubal submucosa, muscularity and serosa to convert into or tends to transform into endometrial tissue, and finally forms lesions; and (3) factors related to infection may cause EM lesions to directly invade the fallopian tube, leading to TEM and changes in the fallopian tube structure, or TEM may be indirectly caused by the inflammatory response. In addition, the pathogenic factors of EM, such as menstrual reflux and genetic factors, may also be applicable to TEM[9] However, further study is needed to confirm this.

Clinical manifestations and diagnosis of TEM

TEM lacks specific clinical manifestations. Routine examinations (*e.g.*, ultrasound studies and serum tumor marker measurements) cannot be used to obtain a definite diagnosis[10]. None of the cases reported in China or in our study were diagnosed before surgery. McGuinness *et al*[11] found that TEM was more common than we expected. In patients with pelvic pain, adnexal cysts or infertility, 12% of the patients had visible tubal lesions through laparoscopic surgery, and 42.5% had only microscopic lesions confirmed by postoperative pathology. There are no separate clinical staging criteria for TEM. The modified revised American Fertility Society staging criteria of the ASRM can be used for reference. The EM was scored according to the lesion location, size, scope and adhesion of EM lesions to evaluate the severity of the disease and to select treatment plans.

Different parts of the fallopian tube may cause different clinical manifestations[12]: (1) If the lesion involves the isthmus or interstitium of the fallopian tube, the lesion can cause infertility by proximal

fallopian tube obstruction; (2) lesions involving the middle fallopian tube are rare and are more common in patients with severe EM; and (3) if the lesion involves the ampulla of the fallopian tube, it will lead to obstruction and cause hydrops and blood accumulation and will also cause local diverticulum formation or thickening and distortion of the fallopian tube, which can eventually lead to infertility or dysmenorrhea.

Prospective studies have shown that EM is associated with an increased risk of subsequent infertility [13]. However, among patients with histologically confirmed EM, those patients who were confirmed to have OEM did not have a higher risk of infertility [4]. These results suggest that TEM and other types of EM may be more correlated with infertility [14].

Among the 30 included patients, 26 had dysmenorrhea, 5 had chronic abdominal pain, and 6 had infertility. Preoperative gynecological ultrasound examinations revealed 9 cases of fallopian tube occupation, including 7 cases of suspected hydrosalpinx and 2 cases of undetermined fallopian tube occupation (suspected cancer). If a patient has the clinical symptoms of dysmenorrhea or infertility, salpingography and laparoscopic exploration should be recommended, even if the ultrasound examination only suggests the existence of OEM, to determine whether there are fallopian tube structure abnormalities and to detect and manage the possible coexisting TEM [10].

EM is closely associated with the occurrence of EM-associated ovarian cancer, especially endometrioid ovarian cancer and ovarian clear cell cancer [15], and the pathogenic mechanisms include gene mutation, apoptosis, inflammatory/immune conditions, and oxidative stress [16,17]. EM can also transition into extraovarian tumors, such as tumors of the fallopian tube, bladder and peritoneum, accounting for approximately 21% of the cases of EM complicated by malignant tumors [18]. The malignancy of TEM, as one category of EM, remains to be further studied. No cases of ovarian fallopian tube cancer were found in our study, but there was 1 case of primary uterine sarcoma.

TEM treatment

As one category of EM, TEM is treated following the general principles for the treatment of EM, including reducing and removing lesions, relieving and controlling pain, treating and promoting fertility, and preventing and reducing recurrence [19].

TEM is often detected during laparoscopic exploration of OEM or other pelvic lesions. Surgery, drugs and combination therapy can be used simultaneously. If the patient desires fertility preservation, conservative surgery, such as salpingography and laparoscopic salpingoplasty, can be used according to the lesion site. During the operation, attention should be given to the prevention of adhesions, such as the use of anti-adhesion agents or anti-adhesion membranes (Interceed®). No bleeding should be found on the wound surface; otherwise, the adhesions will be more serious [12,20], and postoperative GnRH-a therapy may be needed. The fallopian tube on the lesion side should be removed if the patient has no desire for fertility preservation or if the patient should need to undergo a hysterectomy because of other gynecological diseases. According to the guidelines for the treatment of EM, combined drug therapy is recommended after surgery to reduce EM recurrence.

In addition, assisted reproductive technology, especially gamete intrafallopian transfer, can significantly increase the rate of intrauterine pregnancy [21].

Correlation between TEM and OEM

In our study, 2 patients had simple TEM; the rest had one or more lesions, including 26 patients with pelvic EM in other areas (13 with OEM cysts and 13 with OEM and pelvic EM). The EM lesions of the unilateral fallopian tube and unilateral ovary were ipsilateral. There were 4 cases of adenomyosis, 5 cases of uterine myoma and 1 case of uterine sarcoma. One patient had left TEM combined with a left rudimentary uterine horn and a left OEM cyst. The rate of TEM combined with EM (especially OEM) was higher than that of other gynecological diseases ($P = 0.0001$), which indicates that TEM is related to OEM.

Zheng *et al* [22] reported the oviduct source of OEM. Their team validated FM03 and DMBT1 as specific markers for tubal mucosal epithelium and endometrium, respectively, in 32 cases of OEM. The results showed that FM03 expression was high and DMBT1 expression was low in 18 patients (56%). Fourteen patients (44%) had low FM03 expression and high DMBT1 expression. The results showed that approximately 60% of the cells in EM were derived from the fallopian tubes, and 40% were derived from the uterus. The histological origin of OEM may be the tubal epithelium [23]. The results of this study also indicate that TEM and OEM may have a certain correlation. The etiology of TEM has not been determined thus far, but it may be associated with OEM. This is an original perspective to some extent, but a large number of clinical studies are needed to verify it.

Xue *et al* [24] found that there were 168 cases (55.08%) of left TEM, 93 cases (30.49%) of right TEM, and 44 cases (14.43%) of bilateral TEM among 305 TEM patients. They believed that TEM is an asymmetrical disease and that the left side is more susceptible. However, in our study, a left-sided susceptibility to TEM was not found due to the limited sample size. These perspectives are new. A large number of scientific studies and clinical studies are still needed for verification.

Limitations

This study is limited by several factors. First, the sample size, constituting 1982 patients with EM and 30 with identifiable TEM, was small. Second, owing to the study's retrospective nature, it was difficult to assess the significance of salpingectomy in postoperative pain relief in patients with tubal disease, especially because all patients had EM on other pelvic organs as well.

CONCLUSION

The fields of infertility and EM management would benefit from further studies that evaluate the role of fallopian tubes and the anatomical location of EM lesions in patients with infertility and pelvic pain.

The pathogenesis and mechanism of TEM have not been determined, but the correlation between TEM and OEM remains to be studied. The treatment of EM may help to increase the natural pregnancy rates, but further studies are needed for confirmation. The study of TEM will provide new ideas for the treatment of female infertility and other diseases and thus has very important clinical significance.

ARTICLE HIGHLIGHTS

Research background

Tubal endometriosis (TEM) is characterized by ectopic endometrial glands and/or stroma within any part of the fallopian tube. TEM is difficult to diagnose during surgery and is usually detected by pathology after surgery.

Research motivation

The fields of infertility and EM management would benefit from further studies that evaluate the role of fallopian tubes and the anatomical location of endometriosis (EM) lesions in patients with infertility and pelvic pain.

Research objectives

To provide a clinical basis for the diagnosis and treatment of TEM.

Research methods

In this study, the data of 30 patients who underwent laparoscopic salpingectomy due to various gynecological diseases and had pathological confirmation of TEM at our hospital were retrospectively analyzed, and the clinical basis for the diagnosis and treatment of TEM was evaluated.

Research results

Pathology showed that only 2 patients had TEM without any other gynecological diseases, the rest had one or more lesions. The EM lesions of the unilateral fallopian tube and unilateral ovary were ipsilateral. One patient had left TEM combined with a left rudimentary uterine horn and a left ovarian endometriosis (OEM) cyst. The rate of TEM combined with EM (especially OEM) was higher than that of other gynecological diseases ($P = 0.0001$), which indicates that TEM is related to OEM.

Research conclusions

The final diagnosis of TEM depends on pathological examination since there are no specific clinical characteristics. The pathogenesis and mechanism of TEM have not been determined, but the correlation between TEM and OEM remains to be studied. The treatment of EM may help to increase the natural pregnancy rates, but further studies are needed for confirmation.

Research perspectives

The study of TEM will provide new ideas for the treatment of female infertility and other diseases and thus has very important clinical significance.

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FOOTNOTES

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