

女性生殖道同期发生的黏液性上皮化生和 肿瘤 14 例分析

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【摘要】 目的 探讨女性生殖道同期发生的黏液性上皮化生和肿瘤(synchronous mucinous metaplasia and neoplasia of the female genital tract, SMMN-FGT)的临床表现、病理特征、诊治方法及预后。**方法** 回顾性分析 2014 年 10 月至 2020 年 4 月复旦大学附属妇产科医院诊断的 14 例 SMMN-FGT 患者的临床资料和随访记录。**结果** 发病中位年龄为 46 岁(33~70 岁),初发症状主要为阴道排液(8/14)及卵巢囊肿(4/14)。所有行 HPV 检查的患者(13/14)结果均为阴性。所有患者均接受手术治疗,其中 7 例行全子宫+双附件切除术,4 例行广泛全子宫+双附件切除术+盆腔淋巴结清扫术,3 例行全子宫+双侧输卵管切除术,保留卵巢。术后病理提示 14 例病变累及子宫内膜,13 例累及宫颈,9 例累及输卵管,9 例累及卵巢,7 例同时累及宫颈、子宫内膜、输卵管及卵巢。8 例患者进展为恶性肿瘤,术后接受辅助治疗。随访 14~80 个月,1 例因复发死亡,13 例继续随访中。**结论** SMMN-FGT 是一组同时累及女性生殖道多个部位的黏液性病变,阴道排液多为其首发症状,其宫颈病变与 HPV 感染无关。治疗以手术为主,合并恶性病变患者须行辅助治疗,预后有待进一步随访。

【关键词】 女性生殖道; 胃型分化; 黏液细胞分化; 临床特征; 预后

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Clinical analysis of 14 cases of synchronous mucinous metaplasia and neoplasia of the female genital tract

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【Abstract】 Objective To investigate the clinical and pathological features, diagnosis, therapeutic and prognosis of synchronous mucinous metaplasia and neoplasia of the female genital tract (SMMN-FGT). **Methods** Clinical and follow-up data of 14 cases of SMMN-FGT diagnosed from Oct 2014 to Apr 2020 in the Obstetrics and Gynecology Hospital of Fudan University were retrospectively collected and analyzed. **Results** The patients were aged 33 to 70 years old (median 46 years old). The first symptoms were vaginal discharge (8/14) and ovarian cyst (4/14). HPV-negative results were found for all patients who underwent this test (13/14). All patients received surgical treatment, including total hysterectomy and bilateral adnexal resection in 7 cases; extensive total hysterectomy and bilateral adnexal resection and pelvic lymph node dissection in 4 cases; total hysterectomy and bilateral salpingectomy with ovarian preservation in 3 cases. The postoperative pathology showed involvement of the endometrium in 14 cases, of the cervix in 13 cases, of the fallopian tubes in 9 cases and of the ovaries in 9 cases. In 7 cases, lesions were seen in all

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organs of the female reproductive system (cervix, uterus, fallopian tubes and ovaries). Eight cases were diagnosed with malignant disease, and all of them received adjuvant therapy. All the patients were followed up for 14 to 80 months, and only 1 case was dead of recurrent disease. **Conclusion** SMMN-FGT is a series of mucinous lesions involving multiple areas of the female genital tract simultaneously. Abnormal vaginal discharge is the initial symptom. There was no association of cervical HPV-infection. Complete surgical resection remains the mainstay treatment. Patients who combined with malignant lesions require adjuvant therapy and continued follow-up is needed to evaluate long-term survival.

【Key words】 female genital tract; gastric adenomatous metaplasia; mucinous cell metaplasia; clinical characteristic; prognosis

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2009年Mikami等^[1]报道了一组病例,这些病例的特点为在女性生殖道(宫颈、子宫、输卵管、卵巢)多部位(2个及以上)同时出现胃型多灶性黏液性病变,并称之为女性生殖道同期发生的黏液性上皮化生和肿瘤(synchronous mucinous metaplasia and neoplasia of the female genital tract, SMMN-FGT)。目前全世界仅报道了34例^[1-18]。SMMN-FGT表现出一系列形态学改变,包含良性、恶性和非肿瘤性特征。由于该疾病十分罕见,容易漏诊误诊,无标准的治疗方案,预后也不明确,因此没有相关的临床指南。本文通过回顾性分析诊断的14例SMMN-FGT患者临床资料,探讨其临床特点、病理特征、诊治方法及预后情况,以期指导临床医师对该疾病的认识,并探索相应的诊疗措施。

资 料 和 方 法

临床资料 收集2014年10月—2020年4月复旦大学附属妇产科医院诊治的14例SMMN-FGT患者临床资料,包括年龄、临床表现、诊治经过、术后病理及随访情况,并进行回顾性分析。临床资料均由医院电子病历资料库取得,所有患者均签署《关于收集及使用组织样本开展科学研究的知情同意书》。随访资料由门诊病历和电话随访获得。

标本处理 14例患者手术标本均以4%甲醛溶液固定,石蜡包埋,分别进行HE染色和免疫组织化学染色。免疫组织化学应用辣根过氧化物酶抗过氧化物酶复合物(PAP)法染色。检测指标包括:MUC6、P53、Ki-67、p16等,抗体均设立阴性和阳性对照。所有病理经我院病理科2名高年资医师读片

共同确认。

SMMN-FGT 诊疗标准^[1] SMMN-FGT需病理确诊,同时满足以下3个条件:1)同时发生;2)≥2个部位(宫颈、子宫内膜、肌层、输卵管、卵巢或腹膜等女性生殖器官);3)黏液性病变,具有胃型分化的特点。目前暂无排除标准。

结 果

临床资料 患者发病的中位年龄为46岁(33~70岁),均已生育,平均孕次3.0次(1~4次),平均产次1.4次(1~3次)。患者的首发症状为阴道排液8例,持续6~24个月不等,其中3例为诊断后追问病史发现。卵巢囊肿4例,阴道异常出血3例,妇科检查发现4例宫颈质硬,1例见黏液自宫颈管内溢出。2例患者有家族性黏膜皮肤黑色素斑胃肠道息肉综合征(Peutz-Jeghers syndrome, P-J综合征),4例患者曾因卵巢囊肿行手术治疗,术后病理均提示卵巢浆液性囊腺瘤。14例患者均常规行宫颈细胞学检查,其中3例结果异常。13例患者行HPV检查均阴性,另一例患者因拒绝行HPV检测结果未知。7例患者术前进行宫腔诊断性刮宫,3例患者进行宫颈活检,结果详见表1。12例患者术前行肿瘤指标检查,包含CA125、CA199、CEA、HE4、AFP、SCCA等,其中4例提示CA199升高,1例提示CA125升高。所有患者术前均行经阴道彩色多普勒超声检查评估(表1)。

诊治经过 患者均接受手术治疗,2例因术中提示侵犯宫颈可能行广泛全子宫+双附件切除术+盆腔淋巴结清扫术,其中病例7因术中冰冻提示内

表1 14例SMMN-FGT患者临床资料
Tab 1 Clinical characteristics of 14 patients with SMMN-FGT

Case No.	Age (y)	Primary symptom (s)	Time (mo)	TCT	HPV	Pre-operative biopsy	Preoperative pathology	History	Ultrasound	PE	Tumor biomarkers
1	56	AVD	8	NILM	(-)	D&C	Mullerian duct mixed tumor, adenocarcinoma to be excluded	(-)	(-)	(-)	CA199=94.64
2	37	AVD	24	NILM	(-)	Cervical Biopsy	Phyllodes hyperplasia	(-)	Cystic mass on the anterior cervix	Hard on Palpation	(-)
3	41	AVD/OC	12/2	NILM	(-)	/	/	(-)	BOC	Hard on Palpation	CA199=196.2
4	70	AVD	12	NILM	(-)	D&C	Mucinous cancer with inflammatory necrosis	Cesarean Section + Appendectomy	Uneven endometrium with hydrohystera	(-)	CA199=171.1
5	36	TCT(+)	0.33	AGC	(-)	Cervical Biopsy	Invasive adenocarcinoma on LEEP	Bilateral ovarian cystectomy (OMC)	Uneven density of cervix	Hard on Palpation	(-)
6	49	OC	2	NILM	(-)	/	/	Left ovarian cystectomy (OMC)+Right adnexal resection (OMC)	Uneven endometrium, multi-cystic mass anterior to the uterus	(-)	(-)
7	54	AVD	24	NILM	(-)	D&C	EEC	(-)	Cystic-solid mass in the cavity	(-)	CA199=121.47
8	33	AVB	2	NILM	(-)	D&C	GAS	P-J Syndrome + Cesarean Section + Intussusception release surgery	(-)	(-)	/
9	46	OC	2	NILM	(-)	/	/	Left adnexal resection (OMC)	ROC	(-)	(-)
10	46	AVD	24	AGC	(-)	D&C	Infiltrating dilatation of mucinous glands	Cholecystectomy + Cesarean Section	/	(-)	(-)
11	39	AVD	6	NILM	(-)	D&C	GAS	Removal of nasal polyps/Cesarean Section	Cystic-solid mass in the cavity near CS scar	Watery mucus spills out of the cervical canal	(-)
12	51	OC	2	NILM	/	/	/	Left adnexal resection (OMC)+Cholecystectomy	Multi-cystic at right ovary	(-)	(-)
13	37	AVB	3	NILM	(-)	D&C	GAS	Intestinal polyps + P-J Syndrome	(-)	(-)	/
14	52	AVD/AVB	12/1	AGC	(-)	Cervical Biopsy	Adenocarcinoma, origin uncertain	(-)	Cystic-solid mass on cervix	Hard on Palpation	CA125=154.20

TCT: Thinprep cytology test; PE: Physical examination; AVD: Abnormal vaginal drainage; NILM: Non-intrusive load monitoring; (-): Negative; D&C: Dilation and curettage; OC: Ovarian cyst; /: Untested; BOC: Bilateral ovarian cysts; AGC: Atypical glandular cell; LEEP: Loop electrosurgical excision procedure; OMC: Ovarian mucinous cystadenoma; EEC: Endometrioid endometrial carcinoma; AVB: Abnormal vaginal bleeding; GAS: Gastric-type mucinous carcinoma; P-J syndrome: Peutz-Jeghers syndrome; ROC: Right ovarian cyst; CS: Cesarean section.

膜癌侵犯宫颈行腹主动脉旁淋巴结清扫术;2例因术前提示宫颈腺癌,术中直接行广泛全子宫+双附件+盆腔淋巴结清扫术;3例因患者年轻未绝经,术中冰冻提示良性行全子宫+双侧输卵管切除术,保留双侧卵巢;1例患者术中冰冻提示转移性肿瘤可能,故单纯行全子宫+双附件切除术。12例为腹腔

镜手术,1例为经阴道手术,1例为开腹手术。术后均行病理学检查,明确诊断为SMMT-FGT,8例提示恶性病变,均接受紫杉醇+铂类(TP)方案化疗1~6个疗程不等,4例因宫颈恶性病变同时接受放疗(表2)。

表2 14例SMMN-FGT患者诊治经过及预后情况

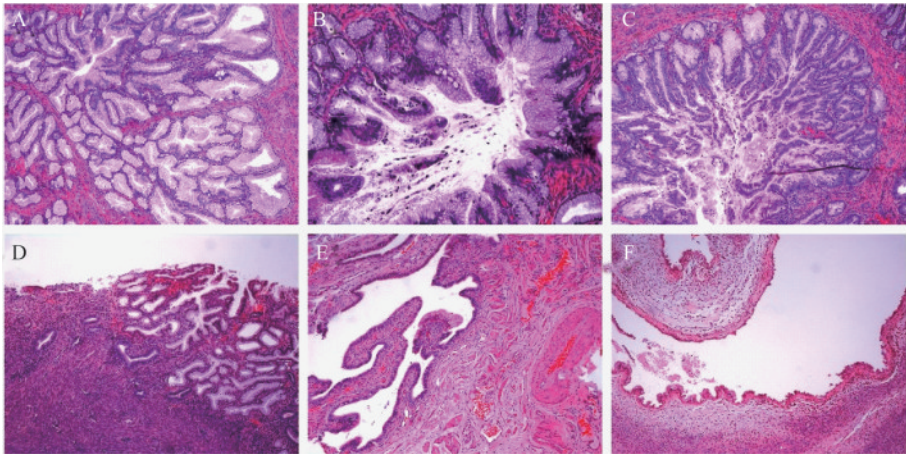
Tab 2 Diagnosis and prognosis of 14 patients with SMMN-FGT

Case No.	Preoperative diagnosis	Route	Surgery	FSP	Postoperative diagnosis	Postoperative management	Follow-up (mo)	Recurrence or progression	Prognosis
1	EC	PV	TAH+BSO	OMC	B	OB	80	N	AWOD
2	LEGH	LAP	TAH+BSO	(Cervix and endometrium) LEGH+OMC	M	TP*4	75	N	AWOD
3	OC	LAP	TAH+BSO	(Ovarian)MT	M	TP*3+RT	64	N	AWOD
4	EC	LAP	TAH+BSO+ EPH+BPLND	(Cervix; endometrium; myometrium) CA	M	TP*1+RT	63	N	AWOD
5	CA	LAP	RH+RSO+ BPLND+OMT+ AE	/	M	TP*6	60	N	AWOD
6	OC	LAP	TAH+LSO	SMMN-FGT	M	TP*3	52	N	AWOD
7	EC	LAP	TAH+BSO+ EPH+BPLND+ PALND	(Uterine; cervical canal)EC	M	TP*4+RT	36	Y	DOD
8	GEMA	OA	TAH+BS	(-)	B	OB	43	N (ovaries preserved with no sign of disease)	AWOD
9	OC	LAP	TAH+RSO	OMC	B	OB	42	N	AWOD
10	IEEG	LAP	TAH+BSO	(-)	M	OB	36	N	AWOD
11	GEMA	LAP	TAH+BS+BBO	(-)	B	OB	36	N (ovaries preserved with no sign of disease)	AWOD
12	OC	LAP	TAH+RSO	OMC	B	OB	33	N	AWOD
13	GEMA	LAP	TAH+BS	(Cervical canal ; endometrium) LEGH	B	OB	29	N (ovaries preserved with no sign of disease)	AWOD
14	CA	LAP	RH+BSO+ BPLND	Bilateral common iliac LN (-)	M	TP*4+RT	14	N	AWOD

FSP: Frozen section pathology; EC: Endometrial cancer; PV: Pre-vaginal surgery; TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo-oophorectomy; OMC: Ovarian mucinous cystadenoma; B: Benign diseases; OB: Observe; N: No; AWOD: Alive without disease; LEGH: Lobular endocervical glandular hyperplasia; LAP: Laparoscopy surgery; M: Malignant diseases; TP: Paclitaxel plus Cisplatin chemotherapy; OC: Ovarian cysts; MT: Metastatic tumors; RT: Radiotherapy; EPH: Extensive parametrial hysterectomy; BPLND: Bilateral pelvic lymph node dissection; CA: Cervical adenocarcinoma; /: Untested; RH: Radical hysterectomy; RSO: Right salpingo-oophorectomy; OMT: omentectomy; AE: Appendectomy; LSO: Left salpingo-oophorectomy; PALND: Para-aortic lymph node dissection; Y: Yes; DOD: Dead of disease; GEMA: Gastric-type endometrial mucinous adenocarcinoma; (-): Negative; OA: Open abdomen; BS: Bilateral salpingectomy; IEEG: Infiltrative expansion of endothelial glands; BBO: Biopsy of both ovaries; LN: Lymph nodes.

病理检查结果 所有患者均行术中快速冰冻病理检查,其中仅1例术中冰冻提示SMMN-FGT。大体观发现病灶切面可见多个大小不等的囊腔,内含黏液,部分呈蜂窝状结构,卵巢呈多房样改变。图1显示了病例2的宫颈、内膜、输卵管及卵巢的镜下表现。本组病例的病灶MUC6均呈弥漫着色或局灶状阳性;P53呈散在阳性或局灶阳性;P16染色9例为阴性,2例为部分或斑驳阳性,3例为阳性;Ki-67阳性指数依据不同的病理类型而不同。

本组病例中,13例有宫颈病变,其中微偏腺癌5例,胃型黏液腺癌4例,胃型浸润性低分化腺癌1例。微偏腺癌在2003版《WHO乳腺癌和女性生殖系统肿瘤病理学和遗传学分类标准》中是宫颈腺癌的1个亚型,而在2014版《WHO女性生殖器官肿瘤学分类》中属于胃型腺癌的一个高分化类型。本文涉及的胃型腺癌不包括微偏腺癌,两者单独列出^[14]。所有病例均有内膜病变,9例有输卵管病变,9例有卵巢病变。3例患者因年轻术中予保留卵巢(表3)。



A: Lobular endocervical glandular hyperplasia of cervix (5×); B: Gastric-type adenocarcinoma of cervix (10×); C: Atypical lobular endocervical glandular hyperplasia of cervix(5×); D: Lobar hyperplasia of the endometrium (5×); E: Glands metaplasia of the fallopian tube (5×); F: Mucinous cystadenoma of the ovary (5×).

图1 病例2的女性生殖道多部位黏液化生病灶HE染色

Fig 1 Hematoxylin and eosin (HE) staining of SMMN-FGT in case No. 2

表3 14例SMMN-FGT患者病理情况

Tab 3 Summary of histopathological findings of 14 patients with SMMN-FGT

Case No.	FSP	Postoperative pathology							Immunohistochemistry			
		Cervix	Uterus	Fallopian tube	Ovarian	Vaginal wall/ Parametrium	LVSI	LN	MUC6	P53	Ki-67	P16
1	OMC	Cervicitis	(Endometrium) ALEGH	(Right) MCM	(Left) MCM	/	/	/	(+)	(+)	5% (+)	(+)
2	(Cervix and endometrium) LEGH+OMC	ALEGH with GAS in situ	(Extensive superficial Endometrium) MCM	(Left) GAM	(Bilateral) OMC	/	(-)	/	/	(+)	10% (+)	(+)
3	(Ovarian)MT	(Whole cervical layer) GAS	(Deep Endometrium) GAS	(-)	(Bilateral) OMC	/	(-)	/	/	/	/	(-)
4	(Cervix; endometrium; myometrium) CA	(Whole cervical layer and nerves) GAS and MDA	(Deep Endometrium) GAS	(Right) Diffuse MCM	(-)	/	(-)	(-)	(+)	(+)	5% (+)	(-)

(续表3)

5	/	MDA	(lower uterine segment) MDA	(Right) Mucinous carcinoma	(Right) mucinous carcinoma	Vaginal wall (+); Parametrium (+)	(-)	(+)	(+)	(+)	2% (+)	(-)
6	SMMN-FGT	ALEGH, GAS	(Endometrium) GAS	(Left) GAS	(left) bord-line OMC	/	(-)	/	(+)	(+)	5% (+)	(-)
7	(Uterine; cervical canal) EC	(Whole cervical layer and nerves) GAS	(Deep Endometrium) GAS	(Right) Gastric-type MCM	(Right) Brenner tumor	(-)	(+)	Pelvic LN (+); para-aortic LN (-)	(+)	(+)	40% (+)	(-)
8	(-)	LEGH	(Endometrium) Multifocal gastric-type MCM	(Bilateral) Multifocal gastric-type MCM	Reserved, not checked	/	/	/	(+)	-	5% (+)	(+)
9	OMC	ALEGH	(Endometrium) ALEGH	(-)	(Right) OMC	/	/	/	(+)	(+)	10% (+)	(-)
10	(-)	MDA	(Endometrium; Myometrium) MDA	(-)	(Left) bord-line OMC	/	/	/	(+)	(+)	5% (+)	(-)
11	(-)	LEGH	(lower uterine segment) LEGH; (Endometrium) gastric-type MCM	(-)	Reserved, not checked	/	/	/	(+)	(+)	(+)	(+)
12	OMC	LEGH, ALEGH	(Endometrium) LEGH	(Right) LEGH	(Right) OMC	/	/	/	(+)	(+)	2% (+)	(-)
13	(Cervical canal; endometrium) LEGH	LEGH	(Endometrium) LEGH	(-)	Reserved, not checked	/	/	/	(+)	(+)	< 5% (+)	(-)
14	Bilateral common iliac LN (-)	(Whole cervical layer and nerves) GAS	(lower uterine segment) GAS; (endometrium) MCM	(Left) MCM	(-)	Vaginal wall (+); Parametrium (-)	(+)	(+)	(+)	(++)	40% (+)	(+)

FSP: Frozen section pathology; LVSI: Lymph-vascular space invasion; LN: Lymph nodes; OMC: Ovarian mucinous cystadenoma; ALEGH: Atypical lobular endocervical glandular hyperplasia; MCM: Mucous cell metaplasia; (-): Negative; (+): Positive; LEGH: Lobular endocervical glandular hyperplasia; GAS: Gastric-type mucinous carcinoma; GAM: Gastric adenomatous metaplasia; MT: Metastatic tumors; MDA: Minimal deviation adenocarcinoma; /: Untested; EC: Endometrial cancer.

预后情况 生存时间自确诊之日算起,随访时间截止至2021年6月30日,随访时间为14~80个月。14例患者均完成随访,无失访。其中1例患者在术后36个月因复发死亡,保留卵巢的3例患者中1例术后29个月时体检发现卵巢囊肿暂未手术,余均未发现卵巢病变(表2)。

讨 论

SMMN-FGT十分罕见,目前国内外研究多为个案报道,其发病率、发病原因、组织发生、临床表现、病理特征、治疗手段及预后均无定论。既往报

道其发病年龄为33~71岁^[1,6,14]。本文报道的最小年龄33岁,与文献报道一致。本文回顾14例患者后发现,8例患者主诉阴道排液,其中排液过多者甚至让患者误认为是“漏尿”;3例恶性患者追问病史发现阴道排液症状已存在多时,因此对于阴道排液或有“漏尿”主诉的患者须警惕SMMN-FGT。卵巢囊肿及阴道异常出血也是SMMN-FGT的常见初始临床表现。

SMMN-FGT的术前诊断非常困难,文献报道其宫颈病变为非HPV相关,肿瘤标志物多为正常,当合并胃型腺癌时肿瘤标记物以CA199升高多见,CA125多正常或轻度升高,而CEA、AFP、HE4、

SCCA多正常。本文回顾的13例已行HPV检查的患者结果均为阴性,肿瘤指标仅5例异常,与文献报道一致,但本文的14例患者中10例进行了术前病理学检查,包括诊断性刮宫及宫颈活检,均提示有不同程度和类型的病变。因此,当患者出现大量阴道排液时,即使宫颈HPV及TCT检查、肿瘤标志物正常,也应该积极采用宫腔诊断性刮宫或宫颈活检等进一步诊断。当发现宫颈有胃型黏液分化的腺体时,建议进一步行子宫内膜、双侧输卵管卵巢的影像学评估,争取在术前明确诊断或为术中冰冻诊断提供更多的临床资料。Ikeda等^[17]在2015年报道了1例SMMN-FGT患者,病变除累及女性生殖道外,还累及尿道外口形成乳头状肿瘤,提示SMMN-FGT存在“超越”女性生殖道的可能性,对怀疑SMMN-FGT的患者应仔细评估,包括尿道外口。但在本组14例SMMN-FGT患者中均未发现病变累及尿道,这可能与妇产科手术的范围未包括泌尿道脏器有关。鉴于女性生殖道与泌尿道在组织胚胎分化时的同源性,建议密切关注确诊SMMN-FGT的患者泌尿道的病变可能。

SMMN-FGT的确诊有赖于病理检查,目前的诊断标准为:在组织学形态上发现2个及以上多器官(宫颈、子宫内膜、输卵管、卵巢)同时发生米勒管源性上皮向黏液上皮方向分化,包含简单型胃型黏液化生、叶状增生、不典型叶状增生、微偏腺癌、胃型腺癌、输卵管黏液上皮化生、卵巢黏液性囊腺瘤、卵巢交界性或黏液性癌等一系列表现^[1,14,18]。大体病灶切面可见多个大小不等的囊腔,内含黏液,部分呈蜂窝状结构。免疫组化提示MUC6高表达,Ki-67阳性指数与恶性程度有关^[14],本组14例病例大体标本及免疫组化均与文献报道一致。SMMN-FGT与胃型黏液分化密切相关,文献认为叶状增生、不典型叶状增生是胃型腺癌的癌前病变^[15]。本文报道的病例2和6其胃型黏液癌(gastric-type mucinous carcinoma, GAS)中合并叶状增生成分,并可见过渡形态。因此,我们推断SMMN-FGT是一组由良性病变随着时间推移逐渐向恶性发展的疾病,其早期诊断非常重要。

由于SMMN-FGT的临床表现和病理表现复杂多变,需要与其他有类似临床及病理表现的疾病相鉴别,包括:(1)普通型宫颈腺癌累及生殖道^[19];(2)单纯性胃型腺癌和或微偏腺癌^[20];(3)转移性腺

瘤:消化道高分化黏液腺癌转移到卵巢和宫颈时^[21];(4)女性生殖系统多部位原发恶性肿瘤(multiple primary malignant carcinomas, MPMC):是指同一女性生殖系统器官中,同时或先后原发于同一器官不同部位,或2个甚至更多器官的恶性肿瘤^[22]。MPMC与SMMN-FGT的区别在于,SMMN-FGT的病变同时发生,且均为黏液性病变并具有胃分化特性,而MPMC可先后发生病变,两种肿瘤病理类型可相同或不同。

SMMN-FGT是一组同时发生于女性生殖道多部位的病变,其组织发生起源仍然未知^[23]。Mikami等^[1]报道的6例SMMN-FGT患者中,6例病变累及内膜,5例累及宫颈,5例累及输卵管,2例累及卵巢。本文报道的14例SMMN-FGT患者中,14例子宫内膜发生病变,13例累及宫颈,9例输卵管发生病变,9例累及卵巢,提示SMMN-FGT最常累及内膜,其次为宫颈。因此,我们推测SMMN-FGT可能起源于子宫内膜或者优先在内膜发生病变,这一推断还需更多的大样本临床研究或动物模型的基础研究加以证实。

本文报道的14例SMMN-FGT患者中有2例P-J综合征,其中1例已证实存在*STK11/LKB1*基因突变。众所周知,P-J综合征可表现为多种女性生殖道肿瘤,包括宫颈胃型腺癌、黏液性肿瘤、卵巢环状小管性索肿瘤^[24]。因此,当患者确诊SMMN-FGT后,应建议患者进行肿瘤遗传学评估,进行*STK11*基因检测,及时发现P-J综合征。

SMMN-FGT的发病率极低,因此治疗方面尚无相关指南或专家共识,目前报道的所有病例初始治疗均为手术。本文中3例术中病理提示为良性的患者,因为年轻,保留了卵巢。术后随访29~43个月,未见复发,提示诊断为SMMN-FGT良性病变的患者,存在保留卵巢的可能,但这一结论需大样本长期随访进一步确认。本文报道的恶性病例中,微型腺癌和/或胃型腺癌患者术后随访均超过36个月。病例3因术中冰冻病理提示转移性癌,仅行全子宫+双附件切除术,术后病理提示宫颈微偏腺癌浸润宫颈全层,向上累及子宫内膜及宫体肌层,双卵巢黏液性癌,但患者并未补充手术,术后接受含铂类化疗后放疗,现随访64个月,存活且无复发。Mikami报道的6例SMMN-FGT患者随访13~102个月,仅1例术后62个月死亡^[1]。单纯宫颈胃型腺

癌及微偏腺癌在预后方面没有差异,5年生存率仅25%^[25]。说明SMMN-FGT中微偏腺癌要比单纯性微偏腺癌预后好,提示对于晚期SMMN-FGT患者仅行单纯性全子宫+双附件切除术后,辅助治疗仍然可获益。然而,最终结论还需要更长时间的随访和更多的临床研究来进一步论证。

综上所述,SMMN-FGT的常见初始症状为阴道排液,所有病例均有内膜病变累及,因此对于有阴道排液的患者,无论是否有HPV感染,均建议行宫腔及宫颈组织活检。SMMN-FGT是一组由良性向恶性逐渐发展的病变,因此早期诊断非常重要。即使出现了恶性病变,如宫颈微偏腺癌或胃型腺癌,手术加辅助治疗仍然使患者受益,其预后较单纯宫颈微偏腺癌或胃型腺癌更好。这是一种罕见病,因此有待更多的临床研究和机制探索。

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利益冲突声明 所有作者均声明不存在利益冲突。

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(上接第389页)

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