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3 例卵巢硬化性间质瘤的临床病理分析

黄佳佳¹, 郑洪¹, 谭娜¹, 黎成芳¹, 姚晋¹, 徐高强²

(遵义医科大学附属医院 1. 病理科; 2. 影像科, 贵州 遵义 563003)

[摘要] 收集了遵义医科大学附属医院3例卵巢硬化性间质瘤(sclerosing stromal tumor of ovary, SST)的临床及影像学资料, 采用光镜及免疫组织化学方法观察其病理特征并复习有关文献, 探讨SST的临床病理学特点、诊断、鉴别诊断及预后。3例SST患者平均年龄48.7岁, 主要临床表现为月经不调、绝经后阴道出血、盆腔包块等。肿瘤均为单侧发病, 表面光滑, 有完整包膜, 切面实性或囊实性, 灰黄灰白, 质韧。低倍镜下可见具有特点的假小叶形成。免疫表型示: 肿瘤细胞表达Vimentin, inhibin, TFE3及SMA。SST临床及影像学无明显特异性, 诊断主要靠常规病理学, 应注意与卵巢其他肿瘤鉴别。治疗推荐手术切除, 一般预后较好。

[关键词] 硬化性间质瘤; 卵巢; 临床病理特征

Clinicopathologic analysis of 3 cases of sclerosing stromal tumor in the ovarian

HUANG Jiajia¹, ZHENG Hong¹, TAN Na¹, LI Chengfang¹, YAO Jin¹, XU Gaoqiang²

(1. Department of Pathology; 2. Department of Imaging, Zunyi Medical University Hospital, Guizhou Zunyi 563003, China)

Abstract This paper collected the clinical and imaging data of 3 cases of sclerosing stromal tumor of ovary (SST) in our hospital, and observed the pathological features of the cases by means of microscopic and immunohistochemistry, with a review of literature. We investigated the clinicopathologic features, diagnosis, differential diagnosis and prognosis of SST. The average age of 3 patients was 48.7 years. The main clinical manifestations were irregular menstruation, postmenopausal vaginal bleeding, lower abdominal distention and pain. Tumors were unilateral, smooth surface, complete capsule, solid or cystic solid section, gray-yellow, gray-white, tough. At low magnification, characteristic pseudo lobules could be seen. Immunophenotype showed that tumor cells expressed Vimentin, inhibin, TFE3, and SMA. Ovarian sclerosing stromal tumors were rare and had no specific clinical and imaging features. The diagnosis mainly depends on routine pathology. We

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通信作者 (Corresponding author): 郑洪, Email: zhenghonghq@hotmail.com

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should pay attention to distinguishing them from other ovarian tumors. Surgical resection is recommended for treatment, and the prognosis is generally good.

Keywords sclerosing stromal tumors; ovarian; clinicopathological feature

卵巢硬化性间质瘤(sclerosing stromal tumor of ovary, SST)是一种起源于卵巢性索-间质的良性肿瘤,临床上较为罕见。患者通常无典型临床症状,影像学表现无明显特异性,在临床诊断中极易误诊,主要靠术后病理学检查。本文回顾性分析3例SST患者的影像学表现、临床病理特征及免疫组织化学染色结果,并复习文献,以提高对该病的认识。

1 临床资料

收集2010年1月至2018年10月遵义医科大学附属医院收治并明确诊断的3例SST患者的临床、影像及病理资料。

手术切除标本经4%中性甲醛缓冲液固定,常规脱水,石蜡包埋、切片,HE染色,免疫组织化学染色采用EnVision二步法,Vimentin, inhibin, Desmin, SMA, EMA, TFE-3, Ki-67蛋白定位于细胞质或细胞核,判断:无阳性染色、棕黄色、棕褐色依次计为阴性、弱阳性、强阳性。

3例患者年龄30~55(中位数37)岁。肿瘤均为单侧,其中右侧2例,左侧1例。临床主要表现为月经不调、下腹胀痛、尿频。B超盆腔实性肿物2例,囊实性肿物1例。合并子宫平滑肌瘤1例、子宫内膜增生症1例(表1)。

1.1 影像学检查

3例患者行B超,结果示:附件区实性2例、囊

实性1例,边界清楚,肿瘤周边实性区可探及较丰富血流信号;3例行CT检查,平扫示:肿瘤边界较清楚、内部密度不均匀(图1A),占位肿块周边部及囊性区不增强,而部分中间实性区有早期增强(图1B)。影像学检查结果考虑有卵巢畸胎瘤、卵巢颗粒细胞瘤及卵巢囊腺瘤,B超及影像学检查均无硬化性间质瘤的诊断。

1.2 病理检查

肉眼观:肿瘤均为单侧发生,左侧1例,右侧2例,直径约4 cm,肿瘤圆形或类圆形,结节状,表面光滑。3例切面为实性,灰白质韧,其中1例为囊实性伴水肿,呈多囊状,囊腔大小不等,囊壁光滑,囊内含淡黄色液体。

镜下观:肿瘤呈不规则假小叶样结构(图2A),小叶间由胶原纤维区及水肿区相间隔(图2B);小叶内肿瘤细胞较丰富,瘤细胞以圆形、卵圆形、多边形的上皮样细胞为主,局部可见成纤维细胞,上皮样细胞胞质丰富透明,细胞核卵圆形,居中或偏位,似印戒样细胞,核染色质细,无病理性核分裂象(图2C)。间质内见薄壁小血管,扩张充血,并见分枝血管形成(图2D)。

1.3 免疫组织化学及特殊染色

3例患者肿瘤细胞中Vimentin, inhibin, TFE3均呈强阳性表达(图3A~3C),SMA阳性表达3例(图3D),Desmin阳性表达1例,EMA,CK均呈阴性表达,Ki-67指数<5%。PAS示印戒样细胞阴性。

表1 患者的临床资料

Table 1 Clinical data of patients

| 病例 | 年龄/岁 | 部位 | 临床症状 | 合并症 | 影像学 | 最大径/cm | 随访时间/月 |
|----|------|-----|---------|---------|-------|--------|--------|
| 1 | 55 | 左卵巢 | 绝经后流血 | 子宫内膜增生症 | 颗粒细胞瘤 | 5 | 36 |
| 2 | 30 | 右卵巢 | 月经不调,腹胀 | 无 | 畸胎瘤 | 4 | 26 |
| 3 | 37 | 右卵巢 | 尿频 | 子宫平滑肌瘤 | 囊腺瘤 | 5 | 10 |

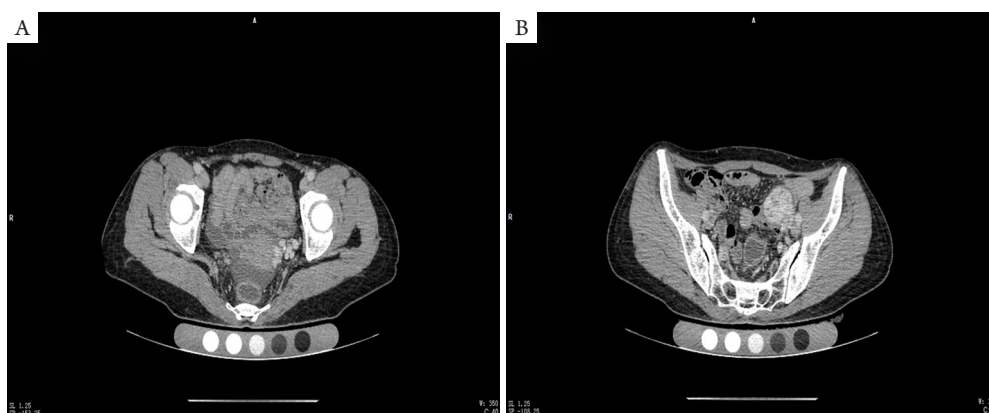


图1 患者CT图

Figure 1 CT images of patients

(A)CT增强扫描显示肿瘤边界较清楚、内部密度不均；(B)囊性区不增强，中间实性区有增强。

(A) Enhanced CT scan showed clear tumor boundaries and uneven internal density; (B) No enhancement in cystic areas and early enhancement in intermediate solid areas.

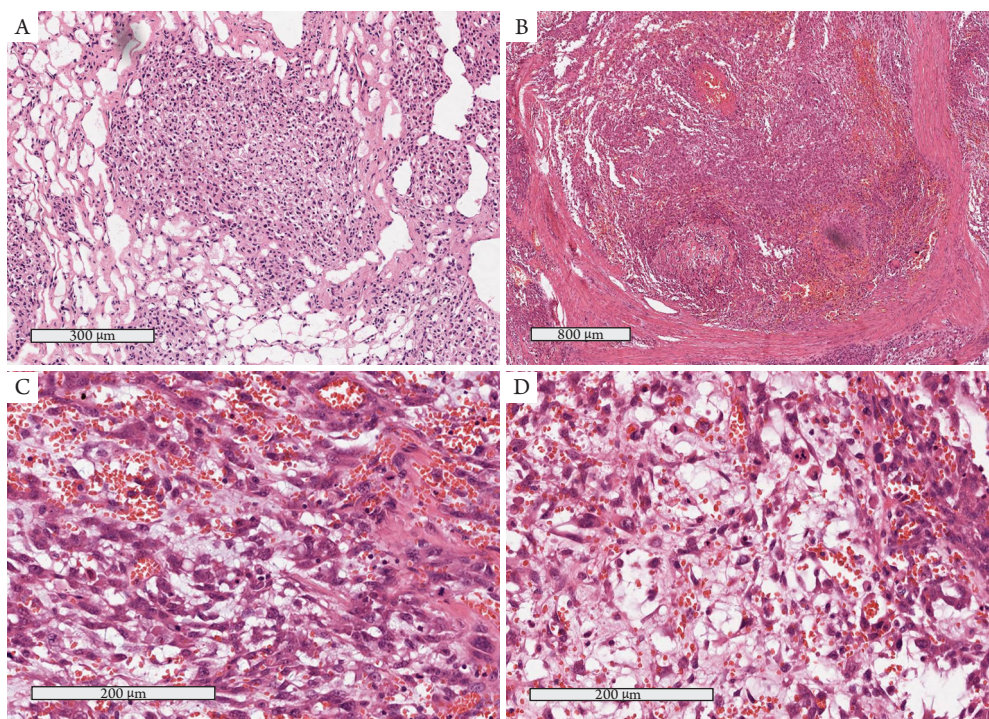


图2 肿瘤组织形态

Figure 2 Morphology of tumor tissue

(A)假小叶结构(HE, $\times 40$); (B)小叶内肿瘤细胞丰富, 周围胶原纤维围绕(HE, $\times 40$); (C)肿瘤细胞呈上皮样, 并见印戒样细胞(HE, $\times 200$); (D)间质扩张及分枝的薄壁血管充血(HE, $\times 200$)。

(A) Pseudolobular structure (HE, $\times 40$); (B) Pseudolobular is rich in cells and surrounded by fibrous tissue (HE, $\times 40$); (C) Tumor cells present epithelioid, and signet ring cells (HE, $\times 200$); (D) Interstitial dilatation and parenchyma hyperemia of branches (HE, $\times 200$).

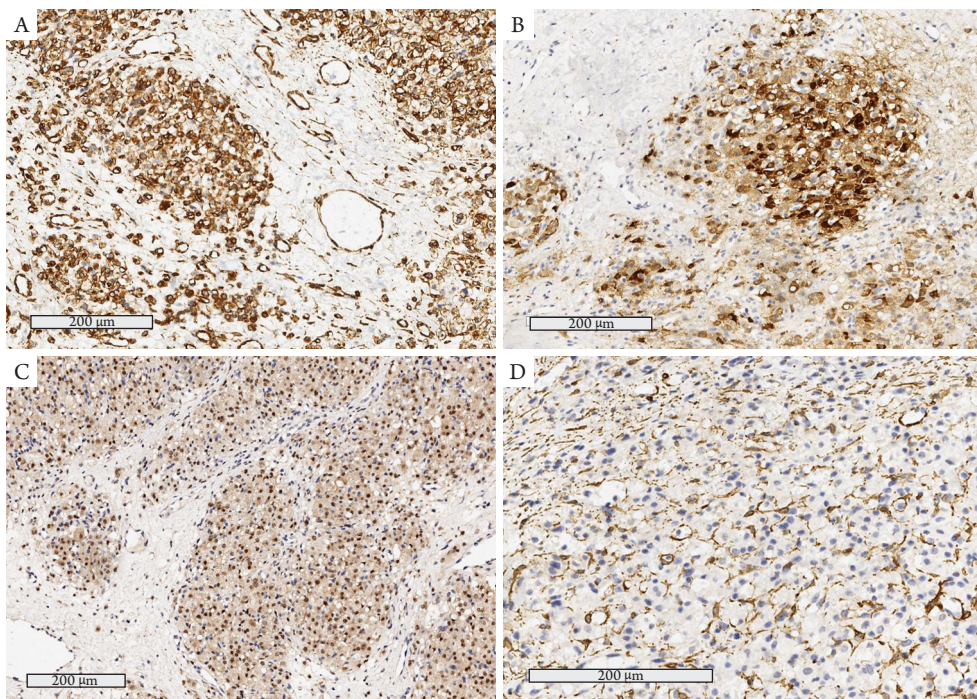


图3 肿瘤组织IHC染色(EnVision, × 200)

Figure 3 IHC of tumor tissues (Envision, × 200)

(A)肿瘤细胞Vimentin阳性; (B)肿瘤细胞inhibin阳性; (C)肿瘤细胞TFE-3阳性; (D)肿瘤细胞 SMA阳性。

(A) Vimentin is positive tumor cells; (B) Inhibin is positive in tumor cells; (C) TFE-3 is positive in tumor cells; (D) SMA is positive in tumor cells.

2 讨论

在卵巢性索-间质肿瘤分类中, SST是一种罕见的肿瘤, 起源于卵巢皮质中具有多向分化潜能的未分化间质细胞^[1], 可见于任何年龄段, 如年轻妇女、围绝经期女性, 婴幼儿也鲜有报道^[2]。卵巢性索间质肿瘤发生的分子机制尚不清楚, 因此针对这类肿瘤的分子遗传学研究很少。有报道^[3]显示: 97%(86/89)的成年型粒层细胞肿瘤出现FOXL2基因突变, 但在SST中未见报道。本组病例中2例较年轻, 1例为老年人, 临床表现为绝经后阴道流血, 近年亦有研究^[4]显示SST发生于绝经后老年患者, 因此, 若老年人群有卵巢肿瘤及绝经后流血, 在排除子宫内膜病变后, 应警惕此病。SST最常见的临床症状包括: 1)月经不调, 可表现为经量增多, 月经周期改变, 部分患者有性激素异常表现^[5]; 婴幼儿发生SST可继发性早熟^[6]。2)可触及盆腹部肿块, 可伴腹水, 需要与盆腔非卵巢来源的肿瘤鉴别。本组中1例影像学提示腹部肿块, 但未出现腹水。3)可合并其他症状如子宫平滑肌瘤、子宫内膜异位症等, 本组中1例患者合

并子宫平滑肌瘤。4)有研究^[7]指出实验室检查可有肿瘤标志物如CA125升高, 但本组病例中CA125正常。

SST在影像学上不具有特异性, 易误诊, 有学者^[8-9]总结了SST的CT及MRI影像特点, 主要包括以下几点: 1)早期周边显著强化, 后期向心性渐进; 2)早期明显均匀强化, 后期持续强化; 3)早期轻度强化, 后期持续强化, 但强化程度不如上述两种类型。本组病理中CT提示畸胎瘤、颗粒细胞瘤及卵巢囊腺瘤, 后经病理证实为硬化性间质瘤。

在形态学上, SST典型形态表现为不规则假小叶样结构及印戒样细胞形成, 间质水肿伴胶原硬化; 小叶内瘤细胞以圆形、卵圆形或多边形的类上皮细胞为主, 夹杂数量不等的短梭形细胞, 上皮样细胞呈印戒样^[10]。本组3例均行术中冰冻检查, 但均未在术中确诊; 术中冰冻切片组织特点主要为肿瘤组织结节状排列, 结节内细胞杂乱无章分布, 肿瘤细胞呈梭形及圆形, 有部分病例可见印戒样细胞, 有的病例细胞形似黄素化卵泡膜细胞, 有的区域伴有黏液分泌。虽然形态多样,

但细胞总体较温和,冰冻切片上能正确做出良性肿瘤的诊断,术后石蜡标本组织尽管和纤维瘤、卵泡膜细胞瘤及硬化性间质瘤,类固醇肿瘤之间存在形态较差,但一般能做出正确判断。免疫组织化学检查示:Vimentin, inhibin, TFE-3及SMA均呈阳性表达,均不表达EMA,与Kaygusuz等^[11]的报道一致。转录因子结合IGHM增强子3(TFE3)是近期研究发现的可在SST中表达,且程度较强,这一发现有助于将SST与其他卵巢性索间质肿瘤区分开来。本组3例病例中,有2例TFE3呈强阳性表达,与Park等^[12]报道一致。

SST诊断上主要与以下几种卵巢病变相鉴别:

1)卵巢成人型粒层细胞瘤。成人型粒层细胞瘤多发生于围绝经期或绝经后女性,镜下组织形态多样化,常见核沟和Call-Exner小体;2)卵巢库肯勃格瘤。以卵巢转移性印戒细胞癌常见,肿瘤多源于胃,其次为结肠,常累及双侧卵巢,镜下无假小叶样结构,表现为卵巢间质中印戒状低黏附性含黏液癌细胞;而SST中空泡状或印戒样瘤细胞质内不含黏液而含脂质,可询问病史并用特殊染色加以鉴别;3)卵泡膜细胞瘤及纤维瘤。发病年龄较SST晚,表现为较一致的梭形细胞,血管不多,免疫组织化学检查TFE3, SMA呈阴性表达。

SST在生物学行为上属于良性肿瘤,临床治疗主要以手术切除为主,切除肿瘤后疗效较好,复习文献尚未有复发及恶变报道^[13-16]。本组随访12~46个月无复发。SST主要依靠常规病理学诊断,临床表现与影像学检查无明显特异性;术中冰冻未见典型结构的诊断困难,甚至可误诊为恶性卵巢肿瘤^[17]。日常工作中病理医生需对这种罕见肿瘤加以认识,特别是术中冰冻切片,掌握其组织学要点,结合临床表现、影像学表现综合诊断,如术中未确诊,应选取合适的标本取材,或选取多块标本,提高诊断准确率,避免临床过度治疗。

参考文献

- Gulati A, Kaushik R, Sharma J. Sclerosing stromal tumor of the ovary associated with benign endometrioid peritoneal implants[J]. *Indian J Pathol Microbiol*, 2009, 52(4): 594-595.
- 周景, 刘光, 丁华野, 等. 幼儿卵巢硬化性间质瘤1例及文献复习[J]. *诊断病理学杂志*, 1997, 4(4): 217-218.
ZHOU Jing, LIU Guang, DING Huaye, et al. A case report and literature review of ovarian sclerosis mesenchymal tumor in children[J]. *Journal of Diagnostic Pathology*, 1997, 4(4): 217-218.
- Shah SP, Köbel M, Senz J, et al. Mutation of FOXL2 in granulosa-cell tumors of the ovary[J]. *N Engl J Med*, 2009, 360(26): 2719-2729.
- Lee CM, Lim S, Cho HY, et al. Sclerosing stromal tumor of the ovary in postmenopausal women: a report of two cases[J]. *J Menopausal Med*, 2015, 21(2): 115-159.
- Chaurasia JK, Afroz N, Maheshwari V, et al. Sclerosing stromal tumour of the ovary presenting as precocious puberty: a rare neoplasm[J]. *BMJ Case Rep*, 2014, 2014: pii: bcr2013201124.
- Squillaro AI, Zhou S, Thomas SM, et al. A 10-month-old infant presenting with signs of precocious puberty secondary to a sclerosing stromal tumor of the ovary in the absence of hormonal elevation[J]. *Pediatr Dev Pathol*, 2019, 22(4): 375-379.
- 王园园, 潘庆, 韩小于, 等. 核分裂象易见的卵巢硬化性间质瘤合并Meigs征及CA125升高一例[J]. *中华病理学杂志*, 2018, 47(12): 967-969.
WANG Yuanyuan, PAN Qing, HAN Xiaoyu, et al. A case of the easily visible sclerotic ovarian mesenchymal tumor combined with Meigs and elevated CA125[J]. *Chinese Journal of Pathology*, 2018, 47(12): 967-969.
- 王志涛, 邹煜, 李奎. 卵巢硬化性间质瘤的CT、MR表现及其病理基础[J]. *浙江医学*, 2016, 38(14): 1170-1173.
WANG Zhitao, ZOU Yu, LI Kui. CT, MR and pathological basis of ovarian sclerosing stromal tumor[J]. *Zhejiang Medical Journal*, 2016, 38(14): 1170-1173.
- 武新英, 王丽萍, 杨小兵, 等. 卵巢硬化性间质瘤CT表现与临床病理探究[J]. *中国CT和MRI杂志*, 2014, 12(6): 43-47.
WU Xinying, WANG Liping, YANG Xiaobing, et al. CT and clinicopathological study of ovarian sclerosing stromal tumor[J]. *Chinese Journal of CT and MRI*, 2014, 12(6): 43-47.
- 冯敏, 廖欣, 刘娟, 等. 卵巢硬化性间质瘤13例临床病理分析[J]. *四川大学学报(医学版)*, 2015, 46(1): 155-158.
FENG Min, LIAO Xin, LIU Juan, et al. Clinical and pathological analysis of 13 cases of ovarian sclerosing stromal tumor[J]. *Journal of Sichuan University. Medical Science Edition*, 2015, 46(1): 155-158.
- Kaygusuz EI, Cesur S, Cetiner H, et al. Sclerosing stromal tumour in young women: clinicopathologic and immunohistochemical spectrum[J]. *J Clin Diagn Res*, 2013, 7(9): 1932-1935.
- Park CK, Kim HS. Clinicopathological characteristics of ovarian sclerosing stromal tumor with an emphasis on TFE3 overexpression[J]. *Anticancer Res*, 2017, 37(10): 5441-5447.
- 冯盼盼. 卵巢硬化性间质瘤临床病理特征及鉴别诊断分析[J]. *中国卫生标准管理*, 2016, 7(7): 178-179.
FENG Panpan. Clinical and pathological features and differential diagnosis of ovarian sclerosing stromal tumor[J]. *China Health Standards Management*, 2016, 7(7): 178-179.

14. Bennett JA, Oliva E, Young RH. Sclerosing stromal tumors with prominent luteinization during pregnancy: a report of 8 cases emphasizing diagnostic problems[J]. *Int J Gynecol Pathol*, 2015, 34(4): 357-362.
15. Pai RR, Shaktawat SS, Khadilkar UN, et al. Sclerosing stromal tumour of the ovary a clinicopathologic spectrum[J]. *Indian J Pathol Microbiol*, 2005, 48(3): 370-372.
16. 李海梅, 余金霞, 杨海军. 卵巢硬化性间质瘤 10 例临床病理分析[J]. *中国癌症防治杂志*, 2018, 10(2): 132-136.
- LI Haimei, YU Jinxia, YANG Haijun. Clinical and pathological analysis of 10 cases of ovarian sclerosing stromal tumor[J]. *Chinese Journal of Oncology Prevention and Treatment*, 2018, 10(2): 132-136.
17. 彭丽秀, 谭琛, 陈晓琼, 等. 卵巢硬化性间质瘤 1 例报告并文献复习[J]. *中国实用妇科与产科杂志*, 2012, 28(9): 716-717.
- PENG Lixiu, TAN Chen, CHEN Xiaoqiong, et al. A case report and literature review of ovarian sclerosing stromal tumor[J]. *Chinese Journal of Practical Gynecology and Obstetrics*, 2012, 28(9): 716-717.

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