

卵巢淋巴瘤和以淋巴结转移为主的 卵巢癌临床特征比较

高菲菲¹, 郭 垒², 薛 恺³, 盛伟琪⁴, 王 葳⁵, 李目杰⁶, 郑 重⁷, 李子庭⁷

1. 上海市第八人民医院妇产科, 上海 200235 ;
2. 濉溪县中医院妇产科, 安徽 淮北 235000 ;
3. 复旦大学附属肿瘤医院肿瘤内科, 复旦大学上海医学院肿瘤学系, 上海 200032 ;
4. 复旦大学附属肿瘤医院病理科, 复旦大学上海医学院肿瘤学系, 上海 200032 ;
5. 复旦大学附属肿瘤医院影像科, 复旦大学上海医学院肿瘤学系, 上海 200032 ;
6. 沈阳药科大学中药学院, 辽宁 沈阳 110016 ;
7. 复旦大学附属肿瘤医院妇瘤科, 复旦大学上海医学院肿瘤学系, 上海 200032

[摘要] 背景与目的: 卵巢淋巴瘤(ovarian lymphoma, OL)和以淋巴结转移为主的卵巢癌(ovarian cancer with bulk lymph node invasion, OC-BLN)常被相互误诊, 该研究通过比较两者间临床特点, 帮助鉴别。方法: 回顾2008年11月—2016年1月复旦大学附属肿瘤医院和上海市第八人民医院共14例OL和14例OC-BLN的临床特征、影像学资料及实验室检查数据进行对比分析。结果: 两组在年龄、症状、伴发腹水、发热、体重减轻和输尿管梗阻比率间差异无统计学意义, OL组卵巢肿块直径更大 [(13.04±5.94) cm vs (7.78±6.38) cm, $P=0.033$]、实性肿瘤比率更高(85.71% vs 28.57%, $P=0.006$)。卵巢淋巴瘤患者血清LDH/CA125比值为7.66±8.03, 高于卵巢癌组的0.31±0.27($P=0.009$)。以LDH/CA125值作为卵巢淋巴瘤诊断指标, 曲线下面积(area under the curve, AUC)可达0.952, 如选取1作为临界值, 灵敏度和特异度分别为91.7%和100%。结论: OL与OC-BLN存在的临床特征易混淆, 但通过卵巢肿瘤表现和血清LDH/CA125值的比较可帮助鉴别诊断, 从而更好地指导下一步的临床治疗。

[关键词] 卵巢淋巴瘤; 卵巢癌; 临床特征; CA125; 乳酸脱氢酶

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Comparison of the clinical characteristics of ovarian lymphoma and ovarian cancer with bulk lymph node involvement GAO Feifei¹, GUO Lei², XUE Kai³, SHENG Weiqi⁴, WANG Wei⁵, LI Mujie⁶, ZHENG Zhong⁷, LI Ziting⁷ (1. Department of Obstetrics and Gynaecology, Shanghai Eighth People's Hospital, Shanghai 200235, China; 2. Department of Obstetrics and Gynaecology, Suixi County Hospital of Traditional Chinese Medicine, Huaibei 235000, Anhui Province, China; 3. Department of Medical Oncology, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China; 4. Department of Pathology, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China; 5. Department of Diagnostic Radiology, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China; 6. School of Traditional Chinese Materia Medica, Shenyang Pharmaceutical University, Shenyang 110016, Liaoning Province, China; 7. Department of Gynecologic Oncology, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai 200032, China)

Correspondence to: ZHENG Zhong E-mail: alizheng@126.com

[Abstract] **Background and purpose:** Ovarian lymphoma (OL) is usually misdiagnosed as ovarian cancer with bulk lymph node invasion (OC-BLN), and vice versa. Therefore, to distinguish these two types of disease, we

compared their clinical characteristics in this study. **Methods:** This study retrospectively reviewed 14 OL and 14 OC-BLN patients from Fudan University Shanghai Cancer Center and Shanghai Eighth People's Hospital. The clinical characteristics, image and laboratory examination data were compared. **Results:** There was no significant difference in age, symptom, fever, weight loss and volume of ascitic fluid between the two groups. Comparing with OC-BLN, OL patients have larger tumor in ovaries [(13.04±5.94) cm vs (7.78±6.38) cm, $P=0.033$], and higher percentage of solid ovarian tumor (85.71% vs 28.5%, $P=0.006$). Lactate dehydrogenase(LDH)/CA125 was higher in OL (7.66±8.03) than OC-BLN (0.31±0.27, $P=0.009$). Using LDH/CA125 to diagnose OL, area under the curve (AUC) was 0.952. When the threshold value was set at 1, the sensitivity and specificity was 91.7% and 100%, respectively. **Conclusion:** OL and OC-BLN are easily to be misdiagnosed. OL has larger and more solid tumor than OC-BLN. LDH/CA125 can help to distinguish these two diseases and guide clinical decision making.

[**Key words**] Ovarian lymphoma; Ovarian cancer; Clinic characteristics; CA125; Lactate dehydrogenase

卵巢上皮性恶性肿瘤是女性常见的恶性肿瘤, 以腹膜播散转移为主要转移方式, 其次为淋巴结转移, 卵巢癌伴单独的淋巴结转移型约占10%^[1]。卵巢淋巴瘤(ovarian lymphoma, OL)包括原发性OL和继发性OL, 是一类少见疾病。OL以卵巢肿瘤为首发临床表现, 同时伴有腹膜后或全身淋巴结肿大, 常被误诊为卵巢癌, 行剖腹手术取得病理后方确诊^[2]。此外当卵巢癌表现为以淋巴结转移为主时仅仅通过影像学诊断亦会被误诊为OL。

OL以化疗联合靶向治疗为主。而以淋巴结转移为主的卵巢癌(ovarian cancer with bulk lymph node invasion, OC-BLN)以瘤体减灭手术为主结合化疗。如能在术前有效地鉴别两组疾病, 将有助于制定合理的治疗方案, 避免不必要的手术。因此, 本文将从临床表现、影像学表现和实验室检查等方面比较两组疾病的差异以寻找鉴别要点。

1 资料和方法

1.1 临床资料

收集2008年11月—2016年1月复旦大学附属肿瘤医院收治的以卵巢肿块为首发症状, 并经过病理证实的OL患者13例, 按相同标准收集上海市第八人民医院妇产科OL患者1例(经复旦大学附属肿瘤医院病理科会诊确认), 共14例OL患者(OL组)。同期复旦大学附属肿瘤医院收治的符合以下标准的OC-BLN患者(OC-BLN组): 病理证实上皮性卵巢癌, 且转移病灶主要为腹膜

后或全身淋巴结转移的ⅢA₁(ii)、ⅢA₂或Ⅳ期中淋巴结转移直径大于2 cm或伴有融合, 共14例患者。收集患者的临床特征并进行分析。

1.2 诊断

收集所有患者的影像学资料和病理学资料, 并对这些资料进行比较分析。同时, 检测患者的CA125和乳酸脱氢酶(lactate dehydrogenase, LDH), 并进行比较。

1.3 统计学处理

采用SPSS 20.0软件进行统计分析。计数资料以百分比(%)表示, 比较采用 χ^2 检验(Fisher-exact法); 计量资料以 $\bar{x}\pm s$ 表示, 连续正态分布数值的两组比较采用 t 检验。分类资料比较采用 χ^2 分析或精确概率法, 指标的诊断价值采用受试者工作特征(receiver operating characteristic, ROC)曲线, 计算曲线下面积(area under the curve, AUC)。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 临床特征比较

OL组中5例未行手术治疗, 通过体表淋巴结活检诊断, 9例行手术治疗, 在手术患者中有1例伴有腹膜浸润呈冰冻骨盆, 仅行肿块活检。OL患者病理均为B细胞淋巴瘤, 2例年轻患者均为Burkitt淋巴瘤, 大于20岁的OL中只1例(8.3%)为Burkitt淋巴瘤, 其余9例为弥漫大B细胞淋巴瘤, 2例因患者拒绝行活检, 无法具体分型。OC-BLN组中9例为高级别浆液性腺癌, 其余5例为低分化或未能分型腺癌。国际妇产科

联合会(International Federation of Gynecology and Obstetrics, FIGO)2013分期ⅢA₁(ii)期8例,ⅢA₂期2例,Ⅳ期4例。OL患者分期ⅡA期3例,ⅡB期1例,ⅢA期1例,ⅢB期1例,ⅣA期3例,ⅣB期5例,两组间临床特征比较见表1,两组间年龄分布虽然差异无统计学意义,但OC-BLN组中无小于40岁患者,而在OL中有2例小于20岁的患者(13岁和17岁)。两组就诊时首发症状、发热(体温38℃以上)、体重减轻(大于等于体重10%)、腹水量及肿瘤大小性质等比较见表1。

2.2 影像表现比较

5例OL患者和4例OC-BLN患者行盆腔

MRI,其表现见表2。对比行盆腔MRI的两组患者卵巢肿块具有共同之处,所有患者均表现为T1低或等信号,T2高信号,增强后强化。其中有1例OL和1例OC-BLN患者具有极为相似的影像学表现(图1)。通过细致对比研究发现,2例患者仍然有一定差异,OC-BLN患者肿块有一定的囊性成分,且肿块中强化更不均匀,存在中央“无强化坏死区”(图1)。结合其他患者CT表现,OL患者卵巢肿块表现为实性肿块占12/14(85.71%),明显高于OC-BLN,后者为4/14(28.57%), $P=0.006$ 。

表1 OL与OC-BLN临床特征比较

Tab. 1 Clinic characteristics of OL and OC-BLN

Characteristic	OL (n=14)	OC-BLN (n=14)	P value
Age/year median(range)	51.5(13-82)	45.5(33-69)	0.648
Initial symptoms			0.062
Abdominal distension/pain	11	5	
Bladder/rectum irritation	2	2	
Asymptom	1	4	
Others	0	3 ^a	
Ascites I/mL	600±937.26	267.86±545.47	0.262
Fever	4(28.6%)	0	0.098
Weight loss	6(42.9%)	3(21.4%)	0.420
Lymph nodes involved			0.420
Whole body	6	4	
Abdominal	8	10	
Hydronephrosis	5(35.1)	1(7.1)	0.165
Tumor size d/cm	13.04±5.94	7.78±6.38	0.033
Tumor type			
Solid	12(85.71)	4(36.36) ^b	0.006
Unilateral	8(57.10)	7(50.00)	1.000
LDH ρ_B /(U·L ⁻¹)	605.31±356.85	210.07±72.84	0.002
CA125 ρ_B /(U·mL ⁻¹)	270.24±514.83	1328.31±1306.66	0.029
LDH/CA125	7.66±8.03	0.31±0.27	0.009
CA19-9 ρ_B /(U·mL ⁻¹)	31.78±56.84	36.50±70.07	0.652

a: Each case of osphalgia, axillary mass and abnormal vaginal bleeding; b: Absence of imaging examination in one case

表 2 OL和OC-BLN患者盆腔MRI诊断结果比较

Tab. 2 MRI of OL and OC-BLN

Case	Tumor shape	Tumor size d/cm	Outline and invasion	Tumor component	T2	T1	Gd-DTPA enhanced T1
Case OL 1	Circular, lobulated	12.0×11.0×13.0	Clear boundary	Solid	Bright with dot more bright	Equal	Intense, inhomogeneous enhancement
Case OL 2	Irregular	5.2×3.4	Invasion to right pelvic wall and muscle	Cystic and solid, mainly solid	Bright	Uneven low	Intense enhancement
Case OL 3	Rough surface	8.2×5.5	Clear boundary	Solid, separation inside	Uneven bright	Dot bright within low signal	Inhomogeneous enhancement
Case OL 4	Irregular	9.1×8.6	Invasion to uterus and left pelvic wall	Solid	Bright	Low	Intense enhancement
Case OL 5	Irregular	11.0×7.7	Unclear boundary with uterus, right ureteral obstruction	Solid	Bright	Equal	Intense, inhomogeneous enhancement
Case OC-BLN 1	Irregular	2.7×3.5	Unclear boundary	Solid	Bright	Low	Intense, inhomogeneous enhancement
Case OC-BLN 2	Irregular	14.4×13.4×9.6	Clear boundary with compression of surrounding tissue	Cystic and solid with separation	Bright	Low	Inhomogeneous enhancement
Case OC-BLN 3	Circular	10.0×12.0×8.4	Clear boundary	Cystic and solid	Bright (solid)	Equal (solid)	Inhomogeneous enhancement (solid)
Case OC-BLN 4	Irregular	8.3×5.4	Unclear boundary	Solid	Mixed	Mixed	Inhomogeneous enhancement

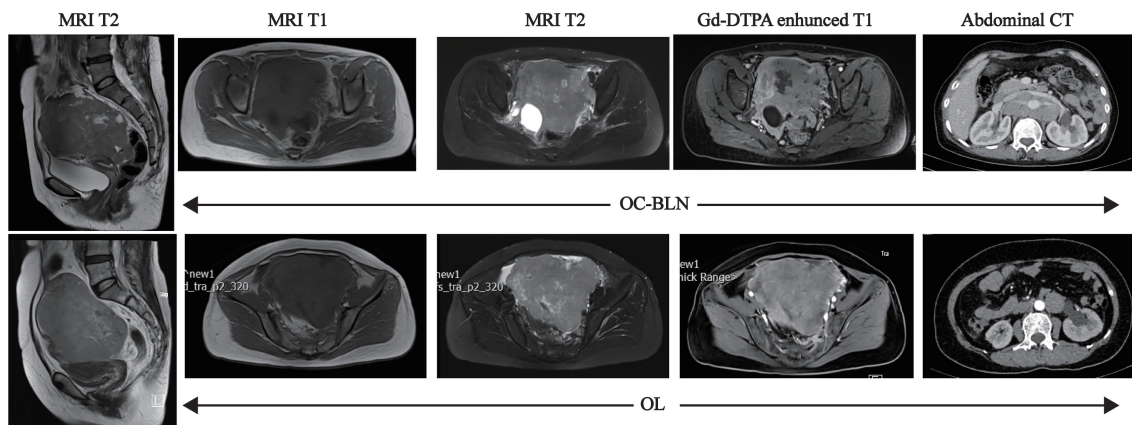


图 1 影像学相似的1例OC-BLN患者与OL患者盆腔MRI和腹部CT的比较

Fig. 1 A comparative MRI and abdominal CT in OC-BLN patients and OL patients

行PET/CT检测的OL患者1例, OC-BLN患者3例。OL患者卵巢肿块FDG代谢 SUV_{max} 为13.7, 腹膜 SUV_{max} 为3.5~21.7, 两侧肾上腺肿块 SUV_{max} 为9.6, 全身淋巴结 SUV_{max} 为1.8~9.0。而3例OC-BLN患者PET/CT表现附件肿块 SUV_{max} 为5.8~15.7, 全身淋巴结 SUV_{max} 为2.2~17.5。

3例OL行盆腔增强CT, 卵巢肿块表现为密

度均匀, 增强强化较均匀, 富血供肿块并伴有腹膜后淋巴结肿大。3例行盆腔增强CT的OC-BLN均表现盆腔囊实性肿块, 肿块边界均欠清, 并伴腹膜后多发肿大淋巴结。

2.3 实验室检查比较

OC-BLN组CA125的中位数是OL组的6.3倍, 相反LDH在OL组中的中位数是OC-BLN组

的3.06倍。两组间CA125和LDH的差异有统计学意义(表1), CA199在两组间差异无统计学意义(表1)。以CA125和LDH单独作为评价指标作ROC曲线(图2), AUC分别为0.899($P=0.01$)和0.866($P=0.003$)。但如果以LDH/CA125值作为诊断指标, AUC可达0.952, 如选取1作为临界值, 灵敏度和特异度分别为91.7%和100%。

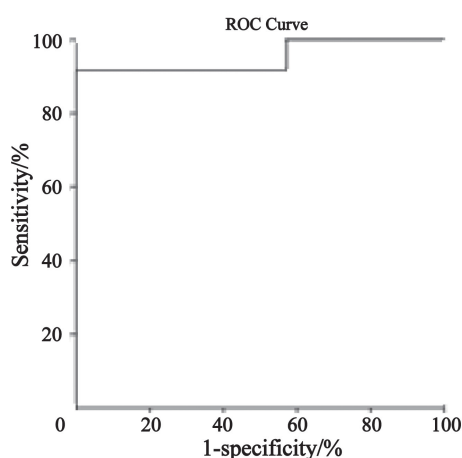


图2 LDH/CA125值诊断卵巢恶性淋巴瘤的ROC曲线

Fig. 2 LDH/CA125 value in the diagnosis of ovarian malignant lymphoma of the ROC curve

3 讨 论

OL与OC-BLN的治疗策略不同。满意的细胞减灭术、有选择的人群中系统淋巴结清扫能提高卵巢癌生存^[3]。OL治疗原则以化疗为主^[4-5], 无需行彻底的“肿瘤细胞减灭术”。国外文献报道, OL化疗完全缓解率为64%^[4], 对于年轻患者, 全身化疗还可以保留生育功能^[6]。我国文献中多数OL患者首次治疗都采用了手术治疗, 甚至采用了类似OC-BLN的瘤体减灭术^[5,7-9], 这主要有两个原因, 一是由于诊断困难, 二是妇产科医师受到OC-BLN治疗原则影响, 甚至认为OL的治疗原则也应该行瘤体减灭术, 甚至系统的腹盆腔淋巴结清扫^[7,10]。然而, 目前国内外文献并无证据显示对OL行彻底的瘤体减灭术能获益。相反全面的瘤体减灭术创伤大, 手术风险大, 并发症多, 反而可能使患者恢复慢, 影响后续化疗。我们的病例中有1例术后出现嗜血细胞综合征。手术是否为嗜血

细胞综合征的诱因尚未见相关报道。因此对OL的准确诊断, 可以避免不必要的手术治疗, 制定合理的处理方案。

通过OL和OC-BLN的临床资料对比发现, 在发病年龄、症状及影像学表现上两者都较为相似, 也提示两者间鉴别诊断较为困难。但进一步分析发现, 两者在卵巢肿块大小和性质、实验室检查等指标上存在差异。

与文献报道相似, OL最常见的病例类型是弥漫性大B细胞淋巴瘤。其次为Burkitt淋巴瘤, 在小于20岁的年轻患者中Burkitt淋巴瘤比例高, 国外有6岁^[11]、10岁^[6]、24岁^[12]及30岁^[13]患卵巢Burkitt淋巴瘤的报道。对OL和OC-BLN的临床特征进行比较发现, OL以腹痛、腹胀诊断最为多见, 卵巢肿瘤体积较大、卵巢肿瘤表现以实性为主。B症状是OL患者常见症状, 而在卵巢癌中较少见, 以发热为例, OL中有4例发热, 而OC-BLN无发热, 虽然差异无统计学意义但仍有一定临床提示价值。

国内外的病例报道OL的MRI表现与我们的结论相似。结合许玲辉等^[14]、Ferrozzi等^[15]和刘东等^[16]的报道, OL的MRI表现为实性T1等或低信号、T2中高信号、中和轻度不均匀强化, 可伴中央不强化区, DWI呈明显高亮信号, 平均卵巢肿瘤大小为7.9 cm。OC-BLN同样表现为盆腔巨大肿块, 伴有腹膜后淋巴结肿大, 但MRI表现为肿块更加不均匀和更多的囊性成分。胡喜斌等^[17]报道和比较了1例OL与5例其他类型卵巢肿瘤的MRI表现, 结果显示, OL T1WI等信号、T2WI稍高信号软组织肿块影, 信号均匀, 而无性细胞瘤中心可见少量囊变坏死。PET/CT在淋巴瘤的诊断和分期中起重要作用, 有文献报道, OL患者SUV_{max}通常超过15, 而OC-BLN患者则很少超过15^[18]。本研究结果也显示, OL患者SUV_{max}最大达21, 而OC-BLN患者有1例附件SUV_{max}达15.7, 淋巴结达17.5。是否可通过设定合适的SUV_{max}值加以鉴别还有待更多病例研究。增强CT在鉴别两组疾病上较困难, 需要指出OL也可表现为腹膜增厚转移。

LDH是OL活动期的标志物,并非OL特有,本研究也显示,LDH在部分OC-BLN患者中亦有升高,但总体上OL患者LDH水平高于OC-BLN。相反CA125也在OL患者中升高但升高程度亦低于OC-BLN患者。如结合两项指标,我们采用LDH/CA125作为指标鉴别两组疾病,AUC可达0.952,高于LDH和CA125单独使用。

总之,以卵巢肿块为表现的OL的鉴别诊断要点如下:①年龄小于20岁需警惕卵巢Burkitt淋巴瘤;②卵巢肿块影像学表现为实性肿块,密度较均匀,MRI表现T1低或等信号,T2高信号,增强后强化,肿块直径可以较大;③可伴或不伴腹水,B症状,注意浅表淋巴结的活检具有重要的诊断价值;④LDH/CA125帮助鉴别。

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