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· 临床研究 ·

原发性乳腺淋巴瘤 8 例临床病理分析并文献复习

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摘要

目的: 探讨乳腺淋巴瘤的临床病理学特点及诊断要点。

方法: 收集 2009 年 1 月—2015 年 3 月确诊为乳腺淋巴瘤的病例资料, 进行临床资料、病理形态学及免疫组化分析, 并结合文献对该病的诊断及鉴别诊断进行讨论。

结果: 8 例均为女性, 发病年龄 35~82 岁, 6 例位于左乳, 1 例右侧, 1 例双侧。多数表现为无痛性肿块, 边界较清, 可活动。7 例为弥漫大 B 细胞淋巴瘤 (DLBCL), 1 例为黏膜相关淋巴组织淋巴瘤 (MALT), 免疫组化染色均表达 CD20、CD79a, 7 例 MUM1 阳性, 4 例 Bcl-2 阳性。治疗后 4 例患者获随访 3~25 个月, 均健在。

结论: 乳腺淋巴瘤少见, 常见类型为 DLBCL, 确诊依赖组织病理学和免疫组化染色。提高对乳腺淋巴瘤的认识, 对避免误诊是至关重要的。

关键词

乳腺肿瘤 / 诊断; 淋巴瘤; 诊断, 鉴别
中图分类号: R737.9

Primary breast lymphoma: a clinicopathologic analysis of 8 cases and literature review

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Abstract

Objective: To investigate the clinicopathologic characteristics and diagnostic criteria of primary breast lymphoma (PBL).

Methods: The cases diagnosed as PBL from January 2009 to March 2015 were collected, their clinical data, and pathological and immunohistochemical features were analyzed, and the diagnosis and differential diagnosis of this condition were discussed with a literature review.

Results: All the 8 cases were female, and age of onset ranged from 35 to 82 years. The tumor was located in left breast in 6 cases, in right breast in one case, and in both breasts in one case. The most common presentation was painless mobile mass with distinct borders. Seven cases were diagnosed as diffuse large B-cell lymphoma (DLBCL), and one was diagnosed as mucosa-associated lymphoid tissue lymphoma (MALT). Immunohistochemical staining showed that CD20 and CD79a positive expressions were found in all cases, 7 cases had mum-1 positive expression and 4 cases had Bcl-2 positive expression. After treatment, 4 patients were followed up for 3 to 25 months and all were alive.

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Conclusion: PBL is a rare condition, and DLBCL is the most common type. Its diagnosis depends on pathological and immunohistochemical examinations. Full awareness of this entity is important for avoiding misdiagnosis.

Key words Breast Neoplasm/diag; Lymphoma; Diagnosis, Differential

CLC number: R737.9

原发性乳腺淋巴瘤(primary breast lymphoma, PBL)临床少见,多为非霍奇金淋巴瘤,占有乳腺恶性肿瘤的0.04%~0.5%,占全身结外淋巴瘤的2.2%^[1]。本病进展快,预后较差,且术前诊断困难,为避免误诊,提高对该病的认识,笔者总结军事医学科学院附属医院病理科诊断为乳腺淋巴瘤的病例资料并复习国内外相关文献,探讨乳腺淋巴瘤的临床病理学及免疫组织化学特点、诊断与鉴别诊断要点及预后。

1 资料与方法

1.1 资料来源

收集军事医学科学院附属医院病理科2009年1月—2015年3月间病理诊断的乳腺淋巴瘤12例。按Wiseman等提出的诊断标准,8例为原发性乳腺淋巴瘤,4例为继发性。PBL中3例为手术标本,5例为穿刺标本。复习临床、影像学和病理资料,并进行随访。

1.2 病理检查方法

方法标本经4%中性甲醛液固定,常规脱水,石蜡包埋,切片厚4 μm,常规HE染色,光镜观察。免疫组化采用EnVision法。所用一抗CD3、CD20、CD79a、Bcl-2、Ki-67、MUM1、CK等及MaxVision试剂盒购自北京中杉金桥生物技术有限公司及福州迈新生物技术开发有限公司。操作步骤严格按试剂盒说明书进行。

2 结果

2.1 临床资料

8例原发性乳腺淋巴瘤均为女性,发病年龄跨度较大,35~82岁,平均发病年龄49岁,中位年龄45.5岁。发生于左乳6例,右乳1例,双乳1例。均以发现乳腺肿块就诊,均无乳头内陷、乳头溢

液等症状,其中1例自感疼痛,1例伴发热、乏力表现。肿块最大径1.5~6 cm,其中1例为双侧多发,最大灶直径为3.1 cm,位于右乳,累及右侧腋窝,余7例中5例局限于乳腺,累及同侧腋窝淋巴结1例,另1例累及其他结外器官(肝脾)及多处淋巴结。

肿物B超表现为不均质回声包块;钼靶X线示中等密度,无毛刺及钙化;CT示乳腺内软组织密度影,边缘光滑清晰。

2.2 病理检查结果

2.2.1 巨检 手术送检标本3例,2例为淡黄色结节,大小5 cm×4 cm×3.5 cm~1.5 cm×1 cm,质地均细腻,边界尚清。另例为肿物旋切术标本,肉眼观察为淡粉色条索样组织一堆,大小2.5 cm×1.8 cm×0.6 cm,质中。余为穿刺标本,大体观为灰白色或灰白灰黄色穿刺组织,长0.4~1.5 cm不等。

2.2.2 镜检 8例原发性乳腺淋巴瘤中,7例为弥漫大B细胞淋巴瘤(DLBCL),1例为黏膜相关淋巴组织淋巴瘤(MALT),无T细胞来源淋巴瘤和霍奇金淋巴瘤。

DLBCL瘤细胞弥漫浸润,乳腺正常结构消失,边缘可见残存乳腺导管及小叶结构,瘤细胞中等大小—大淋巴样细胞,异型性明显,染色质较粗,可见核仁,易见核分裂像(图1A-B)。MALT瘤细胞中等大小,核型略不规则,多数胞质丰富淡染,可侵及导管上皮,形成淋巴上皮病变(图1C)。

2.3 免疫组织化学

确诊依赖免疫组化标记结果(图2)。DLBCL:瘤细胞均不表达上皮来源标记CK,B细胞标记CD20、CD79a弥漫阳性,CD3、CD45R均不表达,Ki-67指数约50%~90%。MUM1阳性7例,CD10阳性2例,Bcl-2阳性4例。MALT:瘤细胞CD20、CD79a弥漫阳性,CD3、CD5、CD10、CD23、CyclinD1、TdT、CK不表达。

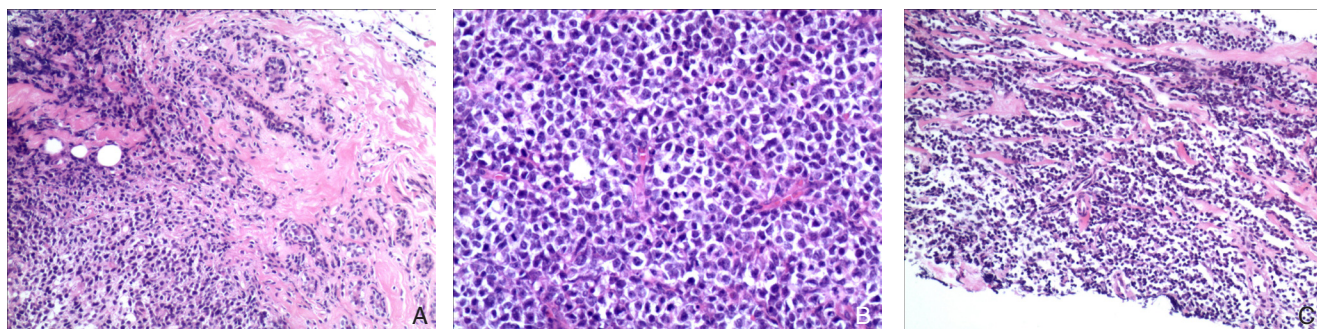


图 1 HE 染色 A: DLBCL, 瘤细胞浸润周围乳腺小叶间质 ($\times 100$); B: DLBCL, 可见核分裂像 ($\times 200$); C: MALT, 瘤细胞小到中等大小, 部分呈单核 B 细胞样 ($\times 100$)

Figure 1 HE staining A: DLBCL with intralobular interstitial tumor cell infiltration ($\times 100$); B: DLBCL presenting mitotic figure ($\times 200$); C: MALT with small- to medial-sized tumor cells and partial cells presenting a mononuclear b cell appearance ($\times 100$)

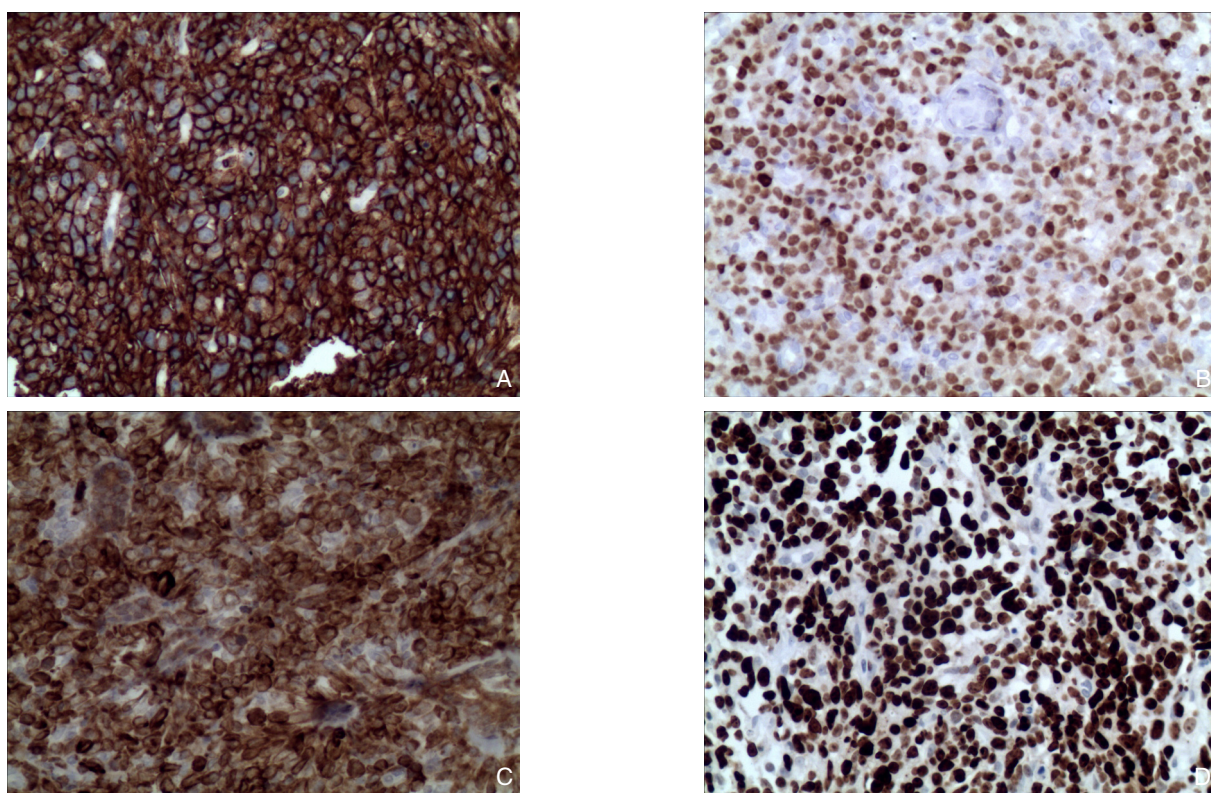


图 2 免疫组化染色 ($\times 200$) A: 瘤细胞弥漫表达 CD20; B: MUM1 阳性; C: Bcl-2 阳性; D: Ki-67 高表达

Figure 2 Immunohistochemical staining ($\times 200$) A: Tumor cells with diffuse CD20 expression; B: MUM1 positive expression; C: Bcl-2 positive expression; D: High Ki-67 expression

2.4 治疗及随访

7例DLBCL患者进行治疗: 4例乳腺切除(其中1例腋窝清扫), 1例肿物旋切术, 2例未手术直接化疗。7例均行化疗(R-CHOP或CHOP方案)。1例联合放疗。4例得到随访资料: 随访时间3~25个月, 均健在, 其中1例在获得CR后于确诊后第12个月发现宫颈复发转移, 中枢神经系统受侵, 23个月对侧乳腺复发。1例MALT确诊后患者回当地。

3 讨论

3.1 概述和流行病学特点

原发性乳腺淋巴瘤罕见, 占非霍奇金淋巴瘤的0.38%~0.70%, 结外淋巴瘤的2.2%, 占乳腺恶性肿瘤的0.04%~0.5%^[1]。Wiseman等^[2]提出了诊断标准: 乳腺肿块经病理学(细胞学)证实为淋巴瘤; 以往无其他部位淋巴瘤史; 乳腺是首发部位, 同时或随后可以有同侧腋窝淋巴结累及,

但当累及的淋巴结大而乳腺肿块小或肿块位于腋尾,则考虑淋巴结起源的恶性淋巴瘤;无同时存在的广泛播散的淋巴组织增生性疾病;骨髓穿刺结果正常。

3.2 临床表现

PML发病年龄跨度大,据文献^[3]报道发病年龄17~95岁,平均年龄54岁。也有文献^[4]报道平均发病60岁。绝大多数为女性,男性少见^[5-6]。临床表现常为无痛性肿块,生长较快,边界清楚,很少见乳头凹陷及橘皮样变。有文献^[3]报道以右侧多见。可伴腋窝淋巴结肿大。影像学检查与早期乳腺癌区分困难,确诊需依靠病理形态和免疫组化染色。

本研究中8例淋巴瘤,均为女性,发病年龄35~82岁,平均发病年龄49岁,比文献报道相对年轻。发生部位以左乳多见,与国外文献^[7]报道不符,但与国内报道^[8]一致。

3.3 病理组织学特点、免疫组化特点

原发乳腺淋巴瘤多为NHL, B细胞来源肿瘤多见。类型包括DLBCL、MALT及滤泡性淋巴瘤(FL)、伯基特淋巴瘤、套细胞淋巴瘤、T细胞淋巴瘤、霍奇金淋巴瘤等^[9-11]。以DLBCL最为多见,占46%~71%^[12], MALT约占8.5%~35%^[13], FL占2%~44%^[14-15]。T细胞淋巴瘤和HL罕见。

本组DLBCL7例, MALT1例。各组形态与淋巴结内相同肿瘤形态一致。其诊断需要结合免疫组化染色结果。

DLBCL瘤细胞弥漫表达CD20、CD79a, 部分表达MUM1、Bcl-2、Ki-67; MALT淋巴瘤常弥漫表达CD20、CD79a, EMA染色示淋巴上皮病变, FL除弥漫表达CD20、CD79a等B细胞标记, 还表达Bcl-2。T细胞淋巴瘤则表达CD2、CD3、CD5等T细胞标记。

3.4 鉴别诊断

乳腺淋巴瘤在活检或穿刺标本中, 结合形态和免疫组化染色结果, 可以诊断。但在冷冻切片中, 由于冷冻对细胞形态的影响且没有免疫组化染色的帮助, 极易误诊。

浸润性小叶癌: 经典型浸润性小叶癌肿瘤细胞常呈单个或单行排列浸润于间质中, 细胞较小, 常向心性包绕导管呈“列兵”样结构。有时乳腺淋巴瘤细胞也可围绕导管或小叶, 甚至呈

“列兵”样排列, 与浸润性小叶癌鉴别困难。此时需要仔细观察, DLBCL瘤细胞较大, 核分裂较多, 有坏死, 无导管或小叶原位癌改变。免疫组化染色, 小叶癌表达细胞角蛋白, 淋巴瘤表达相应淋巴细胞标记。髓样癌: 瘤细胞呈片状、合体状排列, 异型明显, 有丰富的淋巴细胞和浆细胞浸润, 无腺管状结构, 有时容易与淋巴瘤混淆, 免疫组化染色表达CK, EMA等, 不表达CD20等淋巴细胞标记。淋巴细胞性乳腺炎: 有时易与小淋巴细胞淋巴瘤混淆。淋巴细胞乳腺炎细胞通常可见淋巴细胞、浆细胞、组织细胞等, 而小淋巴细胞淋巴瘤形态相对一致, 成片浸润, 有细胞异型。

3.5 治疗及预后

目前对于PBL的治疗方案尚无公认的统一标准。关于PBL治疗效果的文献通常例数较少, 时间跨度较大, 难以得到有力的数据。有学者^[16-17]认为应对I、II期的患者采取手术、化疗加放疗的方案, 而对III期患者则以化疗为主, 辅以放疗和姑息手术。关于手术在PBL中的作用, 目前存在很大争议。早期认为根治术加放疗有效; 现在有学者^[18-19]总结前期文献认为乳腺根治术没有必要, 肿物局部切除加放疗即可获得满意结果。但也有学者^[20]认为乳腺根治术可以降低肿瘤负荷, 有其重要作用。

有文献^[21]报道, Ann Arbor分期可能是影响预后的重要因素。而且对于分期较晚, 增殖活性高的PBL容易发生中枢神经系统转移复发。需定期检测颅脑CT或MR检查。

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