

原发性乳腺鳞状细胞癌1例并文献回顾

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摘 要

目的: 探讨乳腺化生性鳞状细胞癌的临床特征、诊断和治疗。方法: 通过分享1例乳腺化生性鳞状细胞癌的临床、病理资料及诊治过程, 查阅和回顾相关文献, 讨论乳腺化生性癌的诊治方法和思路。结果: 患者术后病理: (右侧)根治切除乳腺标本外上象限见化生性癌-鳞状细胞癌(组织学II级, 镜下浸润范围 3.1×1.4 cm), 见导管原位癌(中级别, 筛孔型, 约占70%), 区域淋巴结: 右侧腋窝淋巴结内见癌转移(1/14)。病理学分期: ypT2N1aMx。免疫组化结果: ER(-), PR(-), HER2(2+), Ki-67(+, 约30%), CK5/6(+), CK14(-), P53(弱+), E-Cadherin(+), P120Catenin(膜+), EGFR(+), D2-40示脉管癌栓(+)。结论: 病理检查及免疫组化分析对于明确乳腺化生性鳞状细胞癌的诊断至关重要, 以根治性手术为主结合化疗的综合治疗是目前最合理治疗方法。

关键词

乳腺鳞状细胞癌, 乳腺化生性癌, 免疫组化, 手术

Primary Squamous Cell Carcinoma of the Breast: A Case Report and Literature Review

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Abstract

Objective: To investigate the clinical features, diagnosis and treatment of mammary hyperplastic squamous cell carcinoma. **Methods:** By sharing the clinical and pathological data and the diagnosis and treatment process of a case of mammary hyperplastic squamous cell carcinoma, the relevant literature was reviewed to discuss the diagnosis and treatment methods and ideas of mammary

hyperplastic carcinoma. Results: The postoperative pathology of the patient was as follows: (right) radical resection of the breast specimen showed chemoplastic carcinoma-squamous cell carcinoma (histological grade II, scope of infiltration 3.1×1.4 cm) in the upper outer quadrant, ductal carcinoma *in situ* (medium grade, ethmoid type, accounting for about 70%), regional lymph nodes: cancer metastasis was found in the right axillary lymph node (1/14). Pathological stage: ypT2N1aMx. Immunohistochemical results: ER(-), PR(-), HER2(2+), Ki-67(+, about 30%), CK5/6(+), CK14(-), P53(weak +), E-Cadherin(+), P120Catenin(membrane +), EGFR(+), D2-40 indicating vascular cancer thrombolus(+). Conclusion: Pathological examination and immunohistochemical analysis are very important for the diagnosis of mammary hyperplastic squamous cell carcinoma. Radical surgery combined with chemotherapy is the most reasonable treatment at present.

Keywords

Squamous Cell Carcinoma of the Breast (SCC), Metaplastic Carcinoma of the Breast, Immunohistochemistry, Surgery

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1. 引言

乳腺化生性癌是一种侵袭性肿瘤, 占所有乳腺恶性肿瘤的比例不到 1% [1]。当 90% 以上的恶性细胞为鳞状细胞时, 诊断为乳腺鳞状细胞癌(squamous cell carcinoma of the breast, SCC), 占所有乳腺癌的不到 0.1% [2], 因其罕见性, 对于化生性乳腺癌的诊断及后续治疗存在一定的困难和争议, 目前化生性乳腺鳞癌主要以病理诊断为主[3] [4], 影像诊断为辅, 而对乳腺鳞癌的治疗依旧参考常规乳腺癌的治疗指南。本文通过分享 1 例由青岛大学附属医院乳腺病诊疗中心收治的原发性乳腺化生性鳞状细胞癌的患者, 并回顾相关文献及报道, 以探讨其临床特征, 诊断和治疗。

病例简介: 患者因“发现右乳肿物 1 月”入院。患者于 1 月前无意中发现右侧乳房有 1 枚肿块, 约鹌鹑蛋大小就诊于我院后查体: 右侧乳房 11 点钟距乳头 3 cm 处可触及 1 枚肿物, 大小约 3.5×2 cm, 质硬, 界限欠清, 形态不规则, 无压痛, 未累及皮肤, 未侵及胸壁。双侧腋窝淋巴结未及肿大。双侧锁骨上淋巴结未及肿大。

诊疗经过: 患者入院后完善检查: 乳腺及腋窝超声检查示: 右乳 11 点钟距乳头 3 cm 见低回声肿块, 大小 3.5×1.6 cm, 形态不规则, 边界不清, 内回声不均匀, CDFI: 内见少许血流信号。双侧腋下见多发淋巴结样回声, 均皮质无明显增厚, 皮髓质清。CDFI: 腺体内血流分布未见异常(图 1)。

钼靶示: 右乳外上象限见一不规则形高密度肿块影, 边缘模糊, CC 位示大小约 $46 \text{ mm} \times 32 \text{ mm}$, 前缘距乳头基底部约 25 mm (图 2, 图 3)。

穿刺病理示: 右乳浸润性癌(组织学 II 级)。

诊断为右乳恶性肿瘤, 临床分期: cT1N0M0, 首选手术治疗, 完善各项术前辅助检查、检验, 排除手术禁忌症后行全麻下“右乳单纯切除 + 前哨淋巴结活检 + 腋窝淋巴结清扫术”, 术后恢复良好, 刀口无愈合不良。

术后病理示: (右侧)根治切除乳腺标本外上象限见化生性癌 - 鳞状细胞癌(组织学 II 级, 镜下浸润范围 3.1×1.4 cm), 见导管原位癌(中级别, 筛孔型, 约占 70%) (图 4~6)。



Figure 1. B ultrasound

图 1. B 超所见

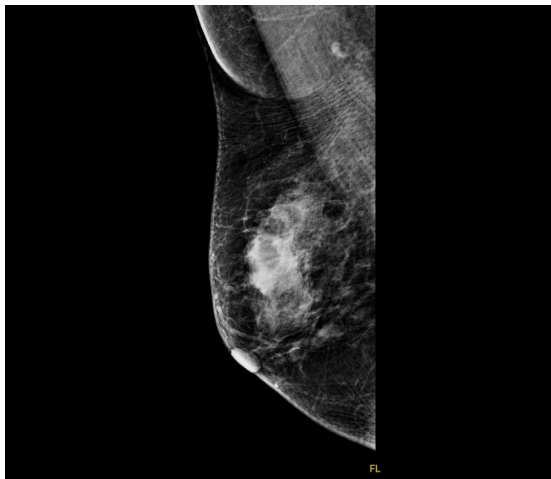


Figure 2. Mamaphic, MLO

图 2. MLO 位钼靶所见

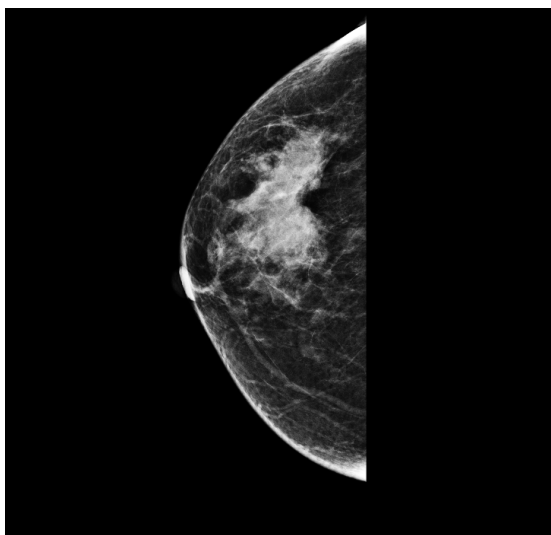


Figure 3. Mamaphic, CC

图 3. CC 位钼靶所见

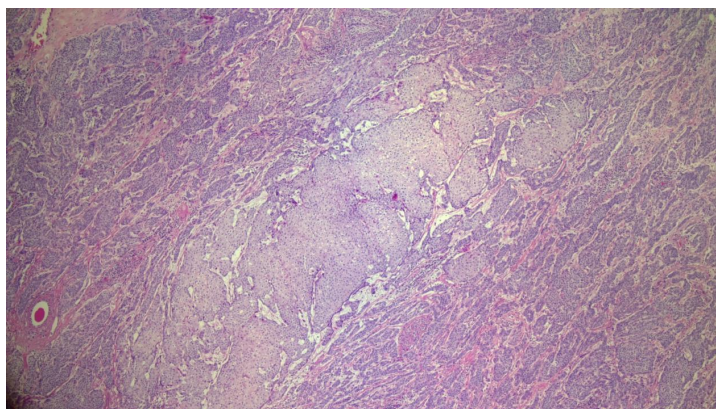


Figure 4. HE 40×

图 4. 肿瘤标本 HE 染色×40 倍镜下所见

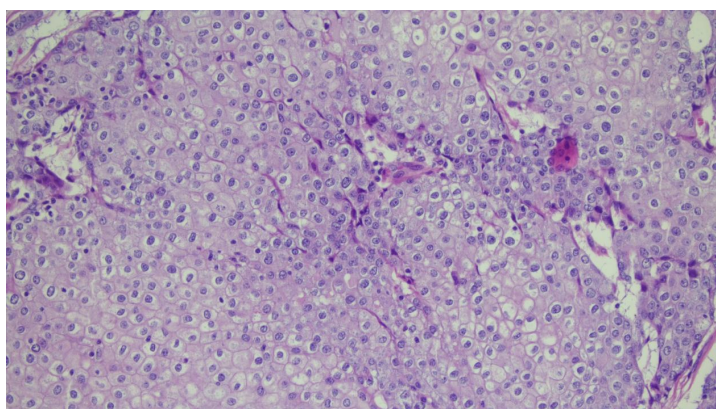


Figure 5. HE 200×

图 5. 肿瘤标本 HE 染色×200 倍镜下所见

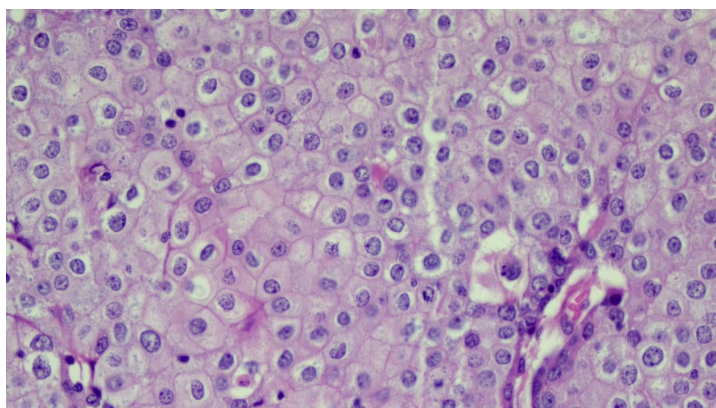


Figure 6. HE 400×

图 6. 肿瘤标本 HE 染色×400 倍镜下所见

区域淋巴结：右侧腋窝淋巴结内见癌转移(1/14)。

病理学分期：ypT2N1aMx。

免疫组化结果：ER(-)，PR(-)，HER2(2+)，Ki-67(+，约 30%)，CK5/6(+)，CK14(-)，P53(弱+)，E-Cadherin(+)，P120Catenin(膜+)，EGFR(+)，D2-40 示脉管癌栓(+)(图 7~9)。

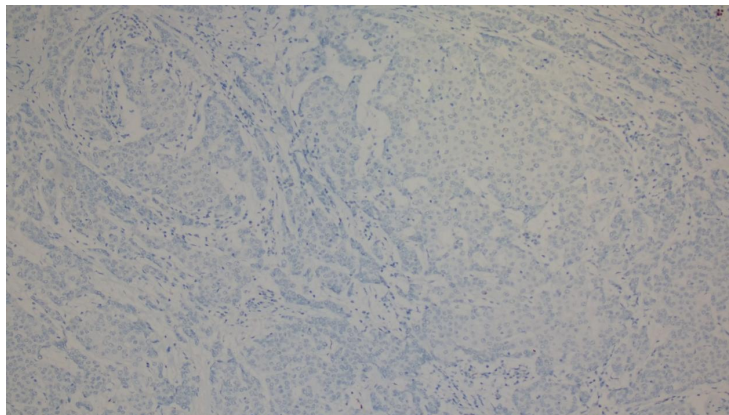


Figure 7. ER 100×
图 7. 免疫组化 ER 染色, ×100 倍镜下所见

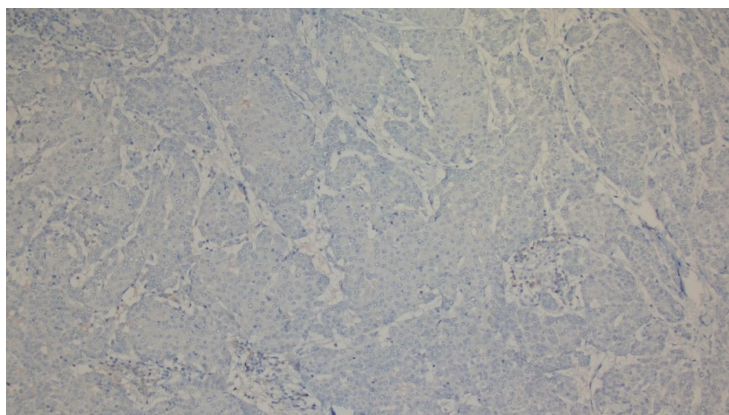


Figure 8. PR 100×
图 8. 免疫组化 PR 染色, ×100 倍镜下所见

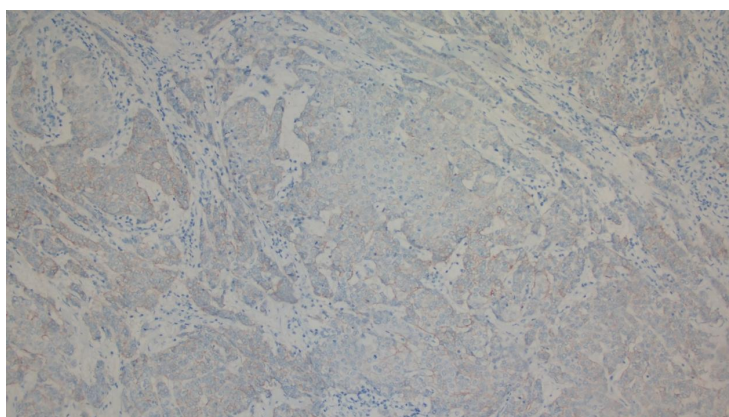


Figure 9. HER-2 100×
图 9. 免疫组化 HER-2 染色, ×100 倍镜下所见

2. 讨论

化生性乳腺癌(Metaplastic Breast Carcinoma, MBC)是一种罕见的乳腺肿瘤, 由 Huvos 在 1973 年首次描述, 占有所有乳腺恶性肿瘤的 1%, 化生性乳腺癌主要分为 5 种亚型, 包括导管起源的鳞状细胞癌、梭形

细胞癌、产生基质的癌、癌肉瘤和伴破骨巨细胞的化生性癌[1] [5]。当 90% 以上的恶性细胞为鳞状细胞时, 诊断为乳腺鳞状细胞癌(squamous cell carcinoma of the breast, SCC), 占有乳腺癌的不到 0.1% [2]。

MBC 患者的年龄范围为 16~90 岁, 但最常受影响的年龄是 50 岁(平均年龄 55~57 岁) [6]。根据 Park 等报道, 10.3% 的 MBC 患者在就诊时为 IV 期疾病, 而 IBC 患者为 0.9% [7]。El Zein *et al.* 的另一项研究包括 46 例 MBC 和 508 例三阴性 IBC, 发现 MBC 患者比 IBC 患者的分期更晚(分别为 34% 和 15.5%) [8]。SCC 好发于绝经后妇女。大多数患者通常表现为临床上可触及的边界清楚的肿块, 偶发皮肤破溃, 很少表现为脓肿[9]。

乳腺鳞状细胞癌在影像上没有明确的典型的征象, 这就导致了目前的技术(X 线钼靶摄影、超声检查、MRI)不足以从影像学上对该疾病的患者做出明确诊断[10] [11]。没有特异性的乳腺 x 线检查结果可以帮助诊断该病。在乳腺超声检查中, 某些鳞状细胞癌肿瘤表现为伴有复杂囊性成分的实性低回声肿块[9]。在 X 线钼靶摄影中表现为边界清楚、轮廓分明的高密度肿块, 可能存在毛刺征也可能呈现分叶状[12]。乳腺磁共振检查中, 由于腺体组织, 通常在 T1 上表现为等低信号, 在 T2 加权图像上, 它们通常显示一个高信号的病变, 这取决于这些肿瘤的黏液内容物和坏死成分[13]。术前诊断乳腺鳞状细胞癌具有一定挑战性, 即使是穿刺活检, 都可能无法完全确定鳞状细胞癌的诊断。细针穿刺组织取材较少, 无法确定具体分类。因此, 广泛取材和(或)完整切除并结合详细的免疫组化检查是正确诊断的关键。建立乳腺鳞状细胞癌明确诊断需要几个病理标准, 包括: 1) 肿瘤应独立于肿瘤以上的皮肤和乳头组织; 2) 90% 以上的浸润成分为鳞状细胞型且无其他浸润性肿瘤成分; 3) 排除来源于除乳腺外的其他原发部位的鳞状细胞癌 [3] [4] [14]。

乳腺 SCC 的免疫组化特征主要为雌激素受体/孕激素受体(ER/PR)和 HER-2 受体阴性, CK 阳性。也有一些报道描述了罕见的 ER/PR 阳性病例[15] [16]。HER-2 受体在乳腺鳞状细胞癌中多为阴性, 然而, Karamouzis 等也报道过 1 例 HER-2 受体过表达的鳞状细胞癌[17]。我们的病例免疫组化具备相似特征。由于 ER、PR、HER-2 受体多表现为阴性, 因此大部分乳腺鳞状细胞癌对内分泌治疗及靶向治疗的反应并不灵敏。

乳腺化生性癌的淋巴扩散不常见[18] [19]。据报道, 淋巴结转移的发生率为 0%~63% [18] [20] [21] [22] [23]。本例患者的组织病理并不只是单纯的鳞状细胞癌, 伴有部分乳腺导管原位癌, 存在 1 枚淋巴结转移。

由于 SCC 的罕见性, 目前尚无针对性的诊疗规范, 对于乳腺鳞状细胞癌患者的治疗通常依据患者的临床特点及参考乳腺癌的诊疗指南进行。手术治疗是乳腺鳞状细胞癌的首选治疗, 某些肿瘤范围较小及组织学分级较低的患者也可以选择保乳手术治疗。对于是否要进行腋窝淋巴结的清扫, 各个专家的看法并不相同。有专家认为取前哨淋巴结预测和判断腋窝情况是可行的[24]。本例患者术中取前哨淋巴结示 1 枚淋巴结转移, 清扫腋窝淋巴结后 14 枚淋巴结见 1 枚转移。

强化辅助治疗存在争议。以顺铂为基础的化疗通常用于乳腺以外原发器官的鳞状细胞癌, 乳腺鳞状细胞癌也可考虑使用。根据统计, 化疗显著提高了乳腺鳞状细胞癌患者无病生存率和总生存率[25] [26]。激素治疗的作用有限, 然而, 对于 ER 和/或 PR 阳性的特殊病例, 使用内分泌治疗是合理的[3] [25] [26]。Hennessy 等人的一项研究发现, 疾病分期是无病生存率和总生存率的重要预后因素[26]。Behranwala 等报道肿瘤大和淋巴结转移是预后不良的主要特征[3]。

目前关于 SCC 放疗的报道为稀疏[27]。根据在接受放疗的 580 例(38.6%)患者中, 全因死亡率和乳腺相关死亡率分别降低了 36% 和 26%。此外, 接受乳房切除术的大(>5 cm)肿瘤或腋窝阳性淋巴结(≥ 4)个患者的全因死亡率及乳房相关死亡率分别降低了 47% 和 42%。相反, 肿瘤直径 < 5 cm 且阳性淋巴结少于 4 个的乳房切除术患者并不能从放射治疗中获益[28]。SCC 组织病理大部分表现 EGFR (表皮生长因子受体) 阳性, 提示这部分患者可能会获益于靶向蛋白激酶抑制剂(如吉非替尼) [2]。

总之, 目前对于乳腺化生性癌及原发性乳腺鳞状细胞癌的诊治仍存在较大的困难, 因此加强临床数据的积累及与基础科研相结合, 优化对乳腺鳞状细胞癌的诊断, 增强针对性药物的研发, 对降低乳腺鳞状细胞癌的术后复发风险及死亡率尤为重要。

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