

13例伴印戒细胞分化的原发性乳腺癌临床分析

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摘要 目的:探讨伴印戒细胞分化的原发性乳腺癌的临床特点及预后。方法:回顾性分析天津医科大学附属肿瘤医院1999年2月至2011年6月收治的13例伴印戒细胞分化的原发性乳腺癌患者的临床资料,所有患者均为女性,年龄38~84岁,中位年龄53岁。首发症状多为乳腺肿物。治疗以乳腺癌改良根治术为主,术后辅助放疗、化疗及内分泌治疗。结果:本组13例术后经组织病理学检查均证实为伴印戒细胞分化的原发性乳腺癌,其中临床分期Ⅰ期患者1例,Ⅱ期8例,Ⅲ期4例。术后平均随访53.8个月。3年生存率为46.2%(6/13),5年生存率为30.8%(4/13),10年生存率为7.7%(1/13)。结论:与常见的乳腺浸润性导管癌相比,伴印戒细胞分化的原发性乳腺癌发病率低,侵袭性强,确诊后应积极行手术、放化疗、内分泌等综合治疗。目前尚无可推荐的最佳特异治疗模式,有关研究应继续进行。

关键词 伴印戒细胞分化的癌 乳腺癌 临床特征

doi:10.3969/j.issn.1000-8179.2013.11.011

Clinical analysis of 13 cases of primary breast carcinoma with signet-ring cell differentiation

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Abstract Objective: This study aims to analyze the clinical characteristics of primary breast carcinoma with signet-ring cell differentiation. **Methods:** Clinical data of 13 patients were analyzed retrospectively. These patients were suffering from primary breast carcinoma with signet-ring cell differentiation and admitted to Tianjin Medical University Cancer Institute and Hospital between 1999 and 2011. All patients were female with ages ranging from 38 years to 84 years; the median age was 53. The initial symptom in nearly all cases was a single breast mass. Modified radical mastectomy was identified as the treatment of choice. Radiation therapy, chemotherapy and endocrine therapy consisted the postoperative adjuvant therapy. **Results:** Histopathological examination after surgery confirmed the diagnosis for 13 cases of primary breast carcinoma with signet-ring cell differentiation. From this group, 1 case was in Stage I, 8 were in Stage II, and 4 were in Stage III. Follow-ups were conducted for an average of 53.8 months, in which 6 patients were shown to have survived for more than 3 years, 5 for more than 4 years, and only 1 for more than 10 years. The 3-, 5- and 10-year survival rates were 46.2%, 30.8%, and 7.7%, respectively. **Conclusion:** Compared with the commonly observed infiltrating mammary duct carcinoma, primary carcinoma with signet-ring cell differentiation exhibits a lower incidence and higher invasiveness. Surgery, radiotherapy, endocrine and other comprehensive treatments should be administered actively after diagnosis. To date, no standard specific guideline has been recommended for clinical practice. Further clinical research relevant to this study should be conducted in the future.

Keywords: carcinoma with signet-ring cell differentiation, breast cancer, clinical characteristics

乳腺癌是我国女性发病率较高的恶性肿瘤之一,其病理分型较为复杂。伴印戒细胞分化的乳腺癌极为罕见^[1-2],文献报道其发病率占乳腺癌的1%~4.5%^[3],有原发性和继发性之分,伴印戒细胞分化的原发性类型约占乳腺癌的0.75%,继发性多为胃肠道肿瘤转移到乳腺所致。本研究对天津医科大学附属肿瘤医院收治的13例伴印戒细胞分化的原发性乳腺癌进行临床分析。

1 材料与方法

1.1 研究对象

收集天津医科大学附属肿瘤医院1999年2月至2011年6月收治的13例伴印戒细胞分化的原发性乳腺癌患者的临床病理资料,所有患者均进行手术治疗并诊断明确。患者均为女性,年龄38~84岁,中位年龄53岁。13例患者中,12例(92.3%)以肿物为首发症状,1例(7.7%)为乳头凹陷伴肿物;6例(46.2%)

为绝经前,7例(53.8%)为绝经后。

1.2 病程及确诊

患者自发现到就诊时间:最短为1d,最长为6年,平均时间为18个月。13例患者均经病理检查确诊:1例(7.7%)在外院行肿物切检术,经本院病理科会诊后确诊;12例(92.3%)于本院手术治疗,术后病理确诊。

2 结果

2.1 TNM分期、病理及激素受体检测

本组患者肿物直径为1.5~9 cm,6例(46.2%)淋巴结未见转移,其余7例(53.8%)均有淋巴结转移,阳性淋巴结数目分别为2、2、2、3、11、30、32枚。临床分期Ⅰ期1例(7.7%),Ⅱ期8例(61.5%),Ⅲ期4例(30.8%)。11例(84.6%)患者术后病理类型为单纯型伴印戒细胞分化的乳腺癌,1例(7.7%)伴有浸润性导管癌(浸润性导管癌成分占30%),1例(7.7%)伴有淋巴结结核(结核病灶成分占20%)。本组病例12例行激素检测,1例未进行。行激素检测者中ER、PR均为阳性者10例(83.3%),阴性者2例(16.7%),12例HER-2均阴性。

2.2 治疗方法

13例患者均进行手术治疗,其中1例(7.7%)行单纯乳房切除术,2例(15.4%)行乳腺癌根治术,10例(76.9%)行乳腺癌改良根治术。13例患者中只行手术治疗者2例(15.4%),其余11例(84.6%)均行手术联合化疗;行术后放疗5例(38.5%),未行放疗8例(61.5%);行内分泌治疗7例(53.8%),未行内分泌治疗6例(46.2%)。联合化疗、放疗、内分泌治疗中的两种或两种以上辅助治疗者8例(61.5%)。化疗所用方案主要为TE、CMF及CEF,放疗部位为内乳区、锁骨上、胸壁,内分泌治疗主要应用三苯氧胺和芳香化酶抑制剂。

2.3 预后及随访

所有病例均随访至2011年12月,术后平均随访53.8个月,无瘤生存期2~144个月。6例(46.2%)患者发生远处转移,主要为多发性骨转移,4例(30.8%)患者死亡(1例发生多发性骨转移后死于呼吸循环衰竭,1例发生同侧胸壁转移后死于冠心病,1例死于脑转移,1例死于脑出血)。生存时间>3年者6例(46.2%),生存时间>5年者4例(30.8%),生存时间>10年者1例(7.7%)(表1)。

表1 13例伴印戒细胞分化的原发性乳腺癌患者临床资料

Table 1 Clinical data of 13 patients suffering from primary breast carcinoma with signet-ring cell differentiation

Case number	Age (years)	Onset (month)	Breast tumor size (cm ²)	Clinical stage	Treatment	Axillary lymph nodes (metastasis/resection)	Follow-up result
1	46	12	1.5×1.5	Ⅲ B	Modified radical mastectomy + chemotherapy + endocrinotherapy	2/27	Lived and well for 29 months after the operation
2	53	1/30	3.0×3.0	Ⅱ A	Modified radical mastectomy + chemotherapy + endocrinotherapy	0/22	Alived and well for 32 months after operation
3	38	3	2.5×2.0	Ⅱ B	Modified radical mastectomy + chemotherapy	2/17	Suffered bone metastasis 2 months after the operation,and lived and well for a 6-month follow-up
4	50	72	4.5×4.5	Ⅲ C	Modified radical mastectomy + chemotherapy + endocrinotherapy + radiotherapy	32/34	Suffered bone metastasis in the third month after operation,and lived and well for an 8-month follow-up
5	53	2	2.5×2.0	Ⅱ A	Modified radical mastectomy + chemotherapy	0/20	Alive and well for 35 months after the operation
6	38	12	9.0×7.0	Ⅲ B	Modified radical mastectomy + chemotherapy + endocrinotherapy	30/34	Suffered bone metastasis 24th months after operation,and lived and well for 68 months following the surgery
7	63	24	3.0×2.0	Ⅱ A	modified radical mastectomy + chemotherapy	2/23	Alive and well for 56 months after the operation
8	66	1	2.0×1.5	Ⅱ A	Modified radical mastectomy + chemotherapy + radiotherapy	3/19	Suffered bone metastasis in the 72nd month after operation,and died of respiratory failure in the 84th month
9	56	48	5.0×7.0	Ⅲ B	Radical mastectomy + chemotherapy + endocrinotherapy + radiotherapy	11/35	Sufferred bone metastasis 12 months after the operation,and died of brain metastasis 24 months after surgery

表1 13例伴印戒细胞分化的原发性乳腺癌患者临床资料 (续表1)

Table 1 Clinical data of 13 patients suffering from primary breast carcinoma with signet-ring cell differentiation (Continue table 1)

Case number	Age (years)	Onset (xmonth)	Breast tumor size (cm ²)	Clinical stage	Treatment	Axillary lymph nodes (metastasis/resection)	Follow-up result
10	44	48	2.5×2.0	II A	Modified radical mastectomy + chemotherapy + endocrinotherapy + radiotherapy	0/10	Alive and well for 144 months after the operation
11	38	1/4	5.0×4.0	II A	Modified radical mastectomy + chemotherapy + endocrinotherapy + radiotherapy	0/20	Suffered by left chest wall metastasis 24 months after operation, and died of coronary heart disease 72 months following the surgery
12	84	3/4	3.0×2.5	II A	Mamectomy	No lymph node dissection	Died of cerebral hemorrhage 24 months after surgery
13	75	1/4	1.5×1.5	I	Modified radical mastectomy	0/28	Alive and well for 117 months after surgery

3 讨论

印戒细胞癌胞浆内含有大量的黏液,将细胞核推向细胞的一侧,使其外形酷似戒指,因而得名。印戒细胞癌多发生在胃肠道。据文献报道,与胃非印戒细胞癌相比,在早期胃癌中,胃印戒细胞癌淋巴结转移率低,预后好^[4];而在进展期胃癌中,胃印戒细胞癌肿瘤浸润深、淋巴结及腹膜转移率高、预后差。肿瘤浸润深度、淋巴结及腹膜转移率、手术情况均与预后有关,病理类型并不是唯一影响预后的独立因素^[5]。

伴印戒细胞分化的乳腺癌是一种极为罕见的浸润性乳腺癌类型,多数以乳腺肿块为原发症状,少数以疑似导管内乳头状瘤症状,如乳头溢液为首发症状^[6],极少数以腹部疼痛等转移至骨盆的症状首发^[7]。此类肿瘤转移途径特别,易转移至浆膜表面,如胃肠道组织^[8],偶可见转移至下颌骨^[9]。免疫组织化学检查可用于鉴别原发部位。在伴印戒细胞分化的乳腺癌中,MCU1阳性表达率达100%,ER阳性表达率可达80%以上,而CDX2及Hep Par1阴性;在伴印戒细胞分化的胃癌中,CDX2及Hep Par1阳性表达率可达80%以上,而ER阴性^[10]。因此,ER、CDX2及Hep Par1可用于鉴别伴印戒细胞分化的乳腺癌与胃癌。而在伴印戒细胞分化的结肠癌中,MCU2阳性表达率达100%,CDX2阳性表达率可达80%以上,而ER阴性。ER、CDX2、MCU1、MUC2可用于鉴别乳腺与结肠伴印戒细胞癌^[10]。

关于伴印戒细胞分化的乳腺癌组织起源,文献报道并不一致。1976年Steinbrecher等^[11]将其列为小叶浸润性癌的亚型。1980年Hull等^[1]认为此癌多数起源于小叶上皮细胞,少数亦可来自导管上皮,故常同时伴有小叶癌或导管癌,得到多数学者的认可。WHO乳腺肿瘤组织学分类(2003年)因其特殊生物学行为,将其归为一种特殊亚型。以往临床上将其归类为黏液腺癌。黏液腺癌的病理特征是在癌组织

中有大量的细胞外黏液,黏液间有纤维组织增生,形成粗细不等的纤维间隔,将黏液分隔成大小不等的“黏液湖”,黏液周边也被纤维组织包裹,从而限制了黏液腺癌向周围组织浸润的能力。使黏液腺癌在临床上表现为发展慢、不易转移的特点^[12]。龚西骥^[2]提出伴印戒细胞分化的乳腺癌的诊断标准:1)HE染色片中见典型印戒状癌细胞,AB/PAS染色细胞质阳性,无细胞外黏液池;2)印戒状癌细胞成分至少占肿瘤成分的20%以上;3)按伴有或未伴有其他组织学类型成分,分为纯印戒细胞型和混合型印戒细胞型;4)无胃肠、卵巢等其他部位原发病灶。2012年WHO乳腺肿瘤组织学分类(第4版)已将印戒细胞癌更名为伴印戒细胞分化的乳腺癌^[13]。与黏液腺癌相比,伴印戒细胞分化的乳腺癌在临床上表现为发展快、恶性程度高、易转移、预后差。两者临床表现相差甚远,故应将两者严格区分,区别对待,伴印戒细胞分化的乳腺癌应尽快行手术治疗,并辅以化疗、放疗、内分泌治疗等综合治疗。

浸润性导管癌是乳腺癌最常见的病理类型,80%的乳腺癌都是此种病理类型。据文献报道,1994年至2010年2 455例乳腺浸润性导管癌患者5年无瘤生存率为92.0%,5年总生存率为94.9%^[14],二者均高于本组患者。耶鲁New Haven Medical Center病理科1960年至1979年记录的1 138例原发性乳腺癌患者资料中^[8],有24例(2.1%)为伴印戒细胞分化的乳腺癌,对24例患者进行为期4年的随访,随访结果显示:有1例未进行治疗,接受治疗的23例患者中14例(58.3%)在数月至1年内死亡,8例(33.3%)无瘤生存,2例(8.3%)出现转移。生存率与本组13例患者接近,二者远远低于报道的乳腺浸润性导管癌生存率。

伴印戒细胞分化的乳腺癌发病率低,本组患者随访时间短,生存率与文献报道不尽一致^[15]。因该病理类型罕见,国内乃至国际上从未有过大样本研

为下腹部手术,对患者损伤较小,因此使用氯诺昔康在围术期也要密切观察患者有无出血倾向。

总之,老年癌症患者术后镇痛是十分必要的,氯诺昔康超前镇痛结合心理支持对于老年癌症患者术后镇痛效果较未结合心理支持疗法更为满意,是一种可供选择的安全、有效的术后镇痛方法。

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(2012-12-13收稿)

(2013-05-02修回)

(本文编辑:邢颖)

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究报道,对其病理特点、临床特征、生存率、预后等还需做进一步的分析研究。

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(2012-11-08收稿)

(2013-04-01修回)

(本文编辑:张侃)