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非哺乳期乳腺炎发病高危因素的病例-对照研究

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摘要 目的:分析非哺乳期乳腺炎的临床特点及发病高危因素。**方法:**回顾性分析 2011 年 1 月至 2016 年 1 月秦皇岛市第一医院乳腺外科就诊,经病理确诊的非哺乳期乳腺炎患者 110 例(病例组)资料,另选取秦皇岛市第一医院体检中心的健康人群 110 例作为对照组。比较两组研究对象临床特征,并进行单因素及多因素分析。**结果:**病例组病人临床分型以肿块型(46.36%)为主,初诊主要症状为单纯肿块 39 例(35.45%),乳房红肿伴肿块 37 例(33.64%)。两组在生育次数、肥胖、初育年龄、平均哺乳时间、主动/被动吸烟、乳头内陷、失眠/焦虑、服用避孕药、乳头溢液病史方面比较差异有统计学意义($P<0.05$)。多因素分析显示乳头内陷($OR=5.29$, 95%CI 2.12~13.25, $P=0.000$)、失眠/焦虑($OR=4.20$, 95%CI 1.68~10.48, $P=0.002$)为非哺乳期乳腺炎发病高危因素,而生育次数($OR=0.42$, 95%CI 0.27~0.64, $P=0.001$)为该病的保护因素。**结论:**失眠、焦虑及乳头内陷增加该病发病风险,生育次数多可降低该病的发病风险。

关键词:非哺乳期乳腺炎;浆细胞性乳腺炎;肉芽肿性乳腺炎;危险因素

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Case Control Study on Risk Factors of Non Puerperal Mastitis

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ABSTRACT Objective: To analyze the clinical characteristics and risk factors for non-puerperal mastitis. **Methods:** A total of 110 cases of non-puerperal mastitis, who were confirmed by pathology (case group) during January 2011 to January 2016 in Breast Surgery Department of Qinhuangdao First Hospital, were retrospectively analyzed. In addition, 110 healthy people in the physical examination center of Qinhuangdao First Hospital were selected as control group. The clinical features of the two groups were compared and analyzed by univariate and multivariate analysis. **Results:** The main clinical symptoms of the patients in the case group was mass type (46.36%), in which, there were 39 cases of simple mass (35.45%) and 37 cases of breast swelling and mass (33.64%). There was statistical significance in the number of births, obesity, age at first child bearing, the average long duration of breast feeding, active/passive smoking, nipple, insomnia/anxiety, oral contraceptive use, nipple discharge disease between the two groups ($P<0.05$). Multivariate analysis showed that the nipple ($OR=5.29$, 95%CI 2.12~13.25, $P=0.000$) and insomnia/anxiety ($OR=4.20$, 95%CI 1.68~10.48, $P=0.002$) were the risk factors of non-puerperal mastitis, but the number of births ($OR=0.42$, 95%CI 0.27~0.64, $P=0.001$) was the protective factors of the disease. **Conclusion:** Insomnia, anxiety and nipple increase the risk of the disease, the number of birth can reduce the risk of the disease.

Key words: Non-puerperal mastitis; Plasma cell mastitis; Granulomatous lobular mastitis; Risk factor

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前言

非哺乳期乳腺炎(NPM)是发生在女性非哺乳期的炎症性疾病,其发病率近年来有逐渐升高的趋势^[1-3]。非哺乳期乳腺炎在发病期上包括婴儿期、青春期、绝经期和老年期,类型上主要包括乳腺导管扩张症(MDE)、导管周围乳腺炎(PDM)、肉芽肿性小叶性乳腺炎(GLM)^[4-6]。该病虽是良性疾病,但一般药物治疗效果不佳,且行手术后易复发,严重影响女性患者的身心健康。目前,非哺乳期乳腺炎的发病机制尚无明确结论,有学者研

究发现,其发病高危因素与先天性乳头凹陷或畸形、外伤、吸烟、肥胖等有关^[7,8]。本研究利用非哺乳期乳腺炎患者的病例特点进行分析,与健康人群进行对照,探讨其发病高危因素,为预防及早期诊断提供依据。

1 资料与方法

1.1 一般资料

选取 2011 年 1 月至 2016 年 1 月秦皇岛市第一医院乳腺外科诊治的 110 例非哺乳期乳腺炎患者临床及病理资料作为

实验组, 中位年龄为 38 (22~62) 岁。其中乳腺导管扩张症(MDE)/ 导管周围乳腺炎(PDM)96 例、肉芽肿性小叶性乳腺炎(GLM)54 例, 入组标准: (1)汉族女性; (2)病理学确诊为肉芽肿性小叶性乳腺炎、乳腺导管扩张症(MDE)/ 导管周围乳腺炎(PDM); (3)临床资料可获取, 并签订知情同意书。排除标准: (1)诊断为其他乳腺良恶性肿瘤(2)病理学诊断不明确; (3)资料不完整; (4)拒绝知情同意书签字、不合作或不能完成者。对照组选取秦皇岛市第一医院体检中心的健康人群。入组标准: (1)汉族女性; (2)乳腺查体及超声未见异常; (3)签署知情同意书。对照组纳入 110 名, 中位年龄 36(25~67)岁。

1.2 研究方法

收集病人一般资料, 包括吸烟、体重指数(BMI)、年龄和生育相关因素(初育年龄、平均哺乳时间、生育次数、流产次数)、既往疾病史(先天性乳头内陷、乳晕区手术史、哺乳期乳腺炎病史、口服避孕药史)等, 对照组以问卷形式收集一般资料及临床相关资料。

1.3 统计学处理

应用 SPSS 19.0 统计软件进行统计学分析, 计量资料采用均数 $\pm$ 标准差表示, 行正态分布检验, 对偏态分布数, 据行对数转换后接近正态分布, 比较采用独立样本 t 检验, 计数资料采用 χ^2 检验, 首先进行临床资料的单因素分析, 将差异有统计学意义的自变量进行 Logistic 回归分析, 得出非哺乳期乳腺炎发病高危因素, 以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 病例组患者临床及病理特征

病例组中临床分型具体为导管扩张型 17 例 (15.45%), 肿块型 51 例 (46.36%), 脓肿型 29 例 (26.37%), 瘻管型 13 例 (11.82%)。病理学分型具体为 MDE/PDM 68 例 (61.82%), GLM 为 31 例 (28.18%), 混合型为 11 例 (10.00%)。初诊以乳房单纯肿块为 39 例 (35.45%), 以乳房红肿伴肿块为 37 例 (33.64%), 以乳房单纯红肿为 9 例 (8.18%), 以乳头溢液为 26 例 (23.64%), 以破溃或窦道形成者 13 例 (11.82%)。初诊时肿块大小(根据超声测量结果)从 0.5-15 cm 不等, 中位长度为 4.2 cm。见表 1。

2.2 非哺乳期乳腺炎病例 - 对照分析结果

病例组与对照组在生育次数、肥胖、初育年龄、平均哺乳时间、主动 / 被动吸烟、乳头内陷、失眠 / 焦虑、服用避孕药、乳头溢液病史方面比较差异有统计学意义 ($P<0.05$)。而年龄、离异、流产史、乳晕区手术史、哺乳期乳腺炎史两组差异无统计学意义 ($P>0.05$)。(见表 2)。通过 Logistic 多因素分析得出: 失眠 / 焦虑、乳头内陷为非哺乳期乳腺炎的独立危险因素, 生育次数多为该病的保护因素(见表 3)。

3 讨论

非哺乳期乳腺炎的病因尚无定论, 治疗方法也是多种多样, 没有统一的治疗标准^[9,10]。这可能与该病的发病机制不明, 疾病的临床特点不清有关。本文通过研究发现, NPM 病例组的年龄范围为 22 岁~62 岁, 中位年龄为 38 岁, 这与国内外的相关研究吻合^[11,12], 根据这些研究可以初步判断 NPM 的发病高

表 1 病例组患者临床及病理特点

Table 1 Clinical and pathological characteristics of patients in the case group

Clinical features		Constituent ratio [n(%)]
Clinical typing	Ductal ectasia	17(15.45%)
	Mass type	51(46.36%)
First symptom	Abscess type	29(26.37%)
	Fistula type	13(11.82%)
	Simple mass	39(35.45%)
	Breast swelling and mass	37(33.64%)
	Simple swelling	9(8.18%)
Pathological type	Burst or sinus formation	13(11.82%)
	MDE/PDM	68(61.82%)
	GLM	31(28.18%)
Tumor size at first visit	Mixed type	11(10.00%)
	0-3 cm	15(13.64%)
	3-6 cm	32(29.10%)
	6-9 cm	18(16.36%)
	9-12 cm	8(7.27%)
	12-15 cm	7(6.36%)

危年龄集中在 33~40 岁这个年龄段, 但仍需大样本的研究证实。在对临床特点的分析中可以看出, 肿块型为主要的临床类型(51 例, 46.36%), 初诊症状以肿块或肿块伴红肿为主, 分别占 35.45% 和 33.64%, 因此 NPM 的初诊症状主要为乳房肿块, 伴或不伴肿块周围红肿。对初诊时乳房肿块大小的统计数据中可以看出, 其大小主要集中在 3-6 cm 这个区间, 分析原因可能与疾病本身特点有关, 非哺乳期乳腺炎虽然病程长, 迁延不愈, 但初起是以肿块迅速生长为主要表现, 因此虽然及时就诊, 但肿块体积仍然很大。

本研究发现在病例组与对照组的比较分析中, 两组在生育次数、肥胖、初育年龄、平均哺乳时间、主动 / 被动吸烟、乳头内陷、失眠 / 焦虑、服用避孕药、乳头溢液病史方面有差异, 而年龄、离异、流产史、乳晕区手术史、哺乳期乳腺炎史两组差异无统计学意义。进一步通过 Logistic 回归分析得出: 失眠 / 焦虑、乳头内陷为非哺乳期乳腺炎发病的独立危险因素, 生育次数多为该病的保护因素。分析本研究结果可能的原因: 非哺乳期乳腺炎的发病基础为乳腺导管和激素的异常, 并与炎症反应有关^[13-16]。乳头内陷的患者乳腺管内容物不能有效排除, 导致导管内类脂质分泌物及其分解产物积累, 积累到一定程度便溢出, 这些溢出物引起导管管壁和导管周围化学性炎症^[17-19], 炎症逐渐扩展累及乳腺组织则形成肿块, 进一步发展形成脓肿^[20-22]。失眠及焦虑是心理表现, 心理因素对 NPM 的影响的相关研究并不多见, 主要集中在术后的护理的心理疏导方面^[23-25]。但心理因素对人体的影响体现在对内分泌系统的影响。失眠、焦虑等精神

表 2 非哺乳期乳腺炎危险因素病例组与对照组比较分析

Table 2 Comparative analysis of risk factors of non-puerperal mastitis Between case group and control group

Indexes	Case group	Control group	t/ χ^2 value	P value
Age (years)	39.34± 8.28	38.65± 6.17	0.587	0.558
Number of births(time)	1.80± 0.85	1.49± 0.79	2.772	0.006
Age at first childbearing (years)	26.41± 3.11	25.26± 3.02	2.770	0.006
Average long duration of breastfeeding (months)	8.35± 6.15	10.31± 6.46	-2.297	0.023
Obesity[n(%)]	46(41.82%)	30(27.31%)	5.150	0.023
Active/passive smoking [n(%)]	51(46.42%)	23(20.91%)	15.960	0.000
Nipple[n(%)]	39(35.45%)	3(2.72%)	38.140	0.000
Divorce[n(%)]	21(19.09%)	11(10.00%)	3.657	0.056
Insomnia/anxiety [n(%)]	56(50.91%)	15(13.64%)	32.110	0.000
Drink wine[n(%)]	20(18.18%)	24(21.82%)	0.460	0.500
Abortion history[n(%)]	25(22.73%)	17(14.45%)	1.880	0.170
Oral contraceptive use[n(%)]	61(55.45%)	39(35.45%)	12.490	0.000
Operation history of areola region[n(%)]	41(37.27%)	32(29.09%)	1.660	0.198
Nipple discharge disease[n(%)]	48(43.64%)	21(19.09%)	15.390	0.000
History of lactation mastitis[n(%)]	38(34.55%)	29(26.36%)	2.450	0.135

表 3 非哺乳期乳腺炎危险因素多因素 logistic 回归分析

Table 3 Multivariate logistic regression analysis of risk factors of non-puerperal mastitis

Factors	B	SE	Wals	P value	OR value	95% confidence interval
Number of births	-0.87	0.21	16.38	0.00	0.42	0.27 0.64
Nipple	1.66	0.46	12.69	0.00	5.29	2.12 13.25
Smoke	0.79	0.47	2.76	0.09	2.21	0.87 5.61
Obesity	0.44	0.68	0.42	0.515	1.56	0.41 5.99
Insomnia/anxiety	1.43	0.46	9.41	0.002	4.20	1.68 10.49
Prophylactic	0.47	0.54	0.77	0.379	1.61	0.56 4.66

心理因素能够影响到女性性激素的分泌,从而导致内分泌系统的紊乱引发相关的疾病^[26]。有研究发现高泌乳素血症与NPM的发病有相关性,并影响疾病的预后^[27]。分析其原因可能是泌乳素水平增高导致乳腺分泌物增加,引起乳管阻塞、分泌物溢出导致局部炎症^[28-30]。本研究的另一个发现在于生育次数是NPM的保护因素,这个结果与刘璐^[12]的研究结果相反,女性在生育过程中体内雌激素、孕激素及泌乳素水平升高,是NPM发病的危险因素。但本研究发现其是该病的保护因素的原因可能是由于生育次数多的女性哺乳次数及时间增加,加强了乳腺导管的疏通,使导管内容物能够充分的排除,由于本文研究病例数较少,其机制尚未明确,需要进一步研究证实。

综上所述,本研究通过对该病的临床特点及发病高危因素的研究,发现非哺乳期乳腺炎有其特征性的临床表现,为NPM的发病机制的研究提供依据,也为该病的预防及早期诊断提供新的思路

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