

痤疮丙酸杆菌感染与椎间盘退变的研究进展

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【摘要】 椎间盘退变的机制十分复杂, 可能与椎间盘机械应力损伤、营养缺乏、炎症因子刺激等多种因素有关。近年来, 不少学者在退变椎间盘组织内检测到痤疮丙酸杆菌, 认为痤疮丙酸杆菌可引起椎间盘退变。笔者就痤疮丙酸杆菌感染与椎间盘退变相关文献作一综述, 并归纳总结痤疮丙酸杆菌进入椎间盘途径以及引起椎间盘退变的机制, 旨在为临床治疗椎间盘退变提供参考。

【关键词】 痤疮丙酸杆菌; 椎间盘退变; 综述文献

DOI: 10.3969/j.issn.1003-0034.2017.05.018

Progress on propionibacterium acnes and degenerative intervertebral disc XU Si-qi, DAI Jia-ping, and HU Xu-qi^{*,*}

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ABSTRACT The mechanism of degenerative intervertebral disc is very complex, which may be associated with multiple factors such as the mechanical stress force injury of intervertebral disc, nutritional deficiency, inflammatory stimulation, etc. Recently, many studies detected propionibacterium acnes (*P. acnes*) in degenerative intervertebral disc and supposed *P. acnes* was associated with degenerative intervertebral disc. Here, the papers related to *P. acnes* and degenerative intervertebral disc were reviewed. Further, we deduced the approach of *P. acnes* entering into the intervertebral disc as well as the mechanism of *P. acnes* aggravating the disc degeneration. These may provide suggestions for treating degenerative intervertebral disc.

KEYWORDS Propionibacterium acnes; Degenerative intervertebral disc; Review literature

Zhongguo Gu Shang/China J Orthop Trauma, 2017, 30(5):481-483 www.zggszz.com

慢性腰痛是临床常见的疾病, 目前研究认为椎间盘退变是引起慢性腰痛的主要原因^[1-2]。椎间盘退变的机制十分复杂, 可能与椎间盘机械应力损伤^[3]、营养缺乏^[4-5]、炎症因子刺激^[6]等多种因素有关。痤疮丙酸杆菌(*Propionibacterium acnes*, *P. acnes*)是革兰阳性(G⁺)兼性厌氧菌, 广泛存在于人体皮肤及黏膜。Stirling 等^[7]在《Lancet》杂志上首次报道了在退变椎间盘组织内检测到痤疮丙酸杆菌并认为痤疮丙酸杆菌是引起椎间盘退变原因之一, 引起众多学者广泛关注。现笔者结合国内外最新研究进展对痤疮丙酸杆菌感染与椎间盘退变的研究进展综述如下。

1 痤疮丙酸杆菌特性

痤疮丙酸杆菌, 又称痤疮丙酸杆菌, 属于放线菌目, 丙酸杆菌科, 属痤疮丙酸杆菌种, 广泛定植于人体皮肤和黏膜上^[8-9]。它是一类 G⁺兼性厌氧菌, 不产芽孢, 生长较为缓慢, 分裂一代时间约为 5.1 h^[10]。痤疮丙酸杆菌可产生许多细胞外酶, 如脂肪酶、蛋白

酶、透明质酸酶和特异的炎前因子。富含多种类脂成分, 油脂的酶解产物被认为是痤疮丙酸杆菌的主要营养来源。磷脂酶可以水解磷脂酰胆碱和乙醇胺使组织产生损伤^[11]。透明质酸酶能裂解硫酸软骨素等间质成分, 有助于痤疮丙酸杆菌的扩散^[12]。因油脂含有较多脂肪酸成分可为痤疮丙酸杆菌提供营养, 因此痤疮丙酸杆菌常定植于皮肤。

虽然痤疮丙酸杆菌本身的致病力较低, 但是其除了可以引起痤疮外, 还可引起其他类型的内源性感染。有报道称心脏植入起搏器后引起痤疮丙酸杆菌感染性心内膜炎^[13], 青光眼术后玻璃体内可检出痤疮丙酸杆菌感染^[14], 部分骨髓炎也可由痤疮丙酸杆菌感染引起^[15-16]。由于痤疮丙酸杆菌繁殖很大程度受到 pH 和氧分压的影响, 因此常规培养很难检测到痤疮丙酸杆菌。

2 椎间盘内痤疮丙酸杆菌检测

Stirling 等^[7]在柳叶刀杂志发表研究显示对 36 例椎间盘突出患者术中切除的椎间盘组织检测发现 19 例细菌培养阳性, 其中 16 例为痤疮丙酸杆菌。由此提出了腰椎间盘退变与低毒性细菌感染具有一定相关性, 引发众多学者的关注与研究。但是有许多学者对上述结果提出质疑。Carricajo 等^[17]对 54 例腰椎

基金项目: 浙江省医药卫生一般研究计划 A 类(编号: 2016142166)

Found program: Supported by the General Research Plan of Medicine and Health of Zhejiang Province for Class A (No. 2016142166)

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间盘组织检测仅发现 2 例痤疮丙酸杆菌感染,但在手术室空气、黄韧带、肌肉作为对照组的样本中痤疮丙酸杆菌检出率却高达 29.6%。由此提出椎间盘组织标本内痤疮丙酸杆菌来源于皮肤、空气等污染。Rigal 等^[18]为了减少污染可能采取前路手术获取椎间盘组织,对 379 例样本行细菌培养检测仅 6 例细菌培养阳性,其中痤疮丙酸杆菌 2 例。

另外也有不少学者认为痤疮丙酸杆菌感染与椎间盘退变有一定相关性。Albert 等^[19]对 61 例椎间盘突出患者术中切除的椎间盘组织检测发现 46% 细菌培养阳性率,其中痤疮丙酸杆菌的阳性率为 40%,该研究认为痤疮丙酸杆菌可以通过血液进入退变的椎间盘组织。在此基础上,Albert 等^[20]对 162 例盘源性腰痛患者采取随机对照双盲试验,经抗生素阿莫西林-克拉维酸治疗组腰痛缓解显著高于安慰剂组。Rollason 等^[21]对 64 例椎间盘标本检测发现痤疮丙酸杆菌的阳性率为 38%,其中 II 型痤疮丙酸杆菌和 III 型痤疮丙酸杆菌占大多数。由于在皮肤中定植的痤疮丙酸杆菌主要为 I 型,因此他认为椎间盘内检测到痤疮丙酸杆菌不能全归结于标本污染。痤疮丙酸杆菌在人体内可以形成一层生物膜,从而提高耐药性避免被巨噬细胞吞噬^[22]。Capoor 等^[23]认为生物膜可以影响痤疮丙酸杆菌培养检查率。因此该学者利用实时 PCR(破坏了细菌生物膜)对 290 椎间盘切除患者术后标本检测发现 40% 的痤疮丙酸杆菌阳性率。此外痤疮丙酸杆菌为兼性厌氧菌,其存活及繁殖很大程度受到 pH 和氧分压的影响。因此不恰当的标本取材及运输过程也可能是导致痤疮丙酸杆菌检出率下降的原因之一。

3 痤疮丙酸杆菌进入椎间盘途径

椎间盘由髓核、纤维环组成,上下覆盖软骨终板。其中髓核细胞分泌大量 II 型胶原和蛋白聚糖,构成髓核基质。而外层纤维环主要由成纤维细胞构成,分泌 I 型胶原;内层纤维环由类软骨细胞构成,分泌 II 型胶原、蛋白多糖。在胚胎发育 35 周左右血管逐渐延伸入纤维环,但成年人纤维环内血管已基本完全退化只在纤维环周边遗留少量血管,因此成人椎间盘几乎是无血管组织^[24]。椎间盘的营养主要通过两种途径获取:(1)椎体血管内的营养物质通过终板扩散进入椎间盘;(2)外侧纤维环表面血管内营养物质向内层渗透进入椎间盘。

笔者因此推测认为痤疮丙酸杆菌进入椎间盘可能通过以下 3 种途径:(1)通过纤维环破口入侵。有研究报道在年轻椎间盘退变患者中存在纤维环破裂发生率约 50%,而对于老年椎间盘退变患者纤维环破裂的发生率近 100%^[25]。Zhou 等^[26]对 46 例椎间盘

标本检测发现 11 例痤疮丙酸杆菌阳性,排除了标本污染可能,其中 2 例椎旁肌肉标本同时检测出痤疮丙酸杆菌,其余 9 例感染痤疮丙酸杆菌的椎间盘术中均观察到纤维环破裂。由此可知痤疮丙酸杆菌很可能通过破裂的纤维环进入处于低氧状态的髓核并在此适宜的微环境下进一步增殖。(2)通过终板局部蔓延。Albert 等^[19]研究发现厌氧菌培养阳性的椎间盘其邻近终板 Modic 改变的发生率高达 80%,推断椎间盘厌氧菌感染可能导致邻近终板 Modic 改变。椎体靠近终板附近有丰富的毛细血管床,由于骨性终板内含有大量微孔,椎间盘通过这些微孔与椎体间发生渗透转运^[27-28]。因此不能排除血液中的痤疮丙酸杆菌沉积于终板附近的毛细血管床内,从而通过终板渗透感染椎间盘同时引起终板 Modic 改变。(3)医源性感染。有报道称硬膜外麻醉置管可导致痤疮丙酸杆菌感染引起脊柱炎^[29]。由此推测椎间盘造影、神经根阻滞、硬膜外麻醉等操作均可能引起医源性椎间盘痤疮丙酸杆菌感染。

4 痤疮丙酸杆菌引起椎间盘退变的机制

椎间盘退变的病理生理主要表现为:(1)椎间盘细胞外基质合成减少、分解增加;(2)椎间盘细胞凋亡;(3)椎间盘内血管、神经长入^[30]。在退变的椎间盘中 TNF- α 、IL-1 等炎症因子明显升高,炎症因子调控紊乱被认为是椎间盘退变以及下腰痛的重要原因^[31]。研究发现痤疮丙酸杆菌通过上调 NLRP3 和 caspase-1 表达刺激单核细胞分泌 IL-1^[32]。痤疮丙酸杆菌还可通过激活 Toll 样受体刺激单核细胞分泌 TNF- α 、IL-6、IL-8、IL-12,而 IL-1、TNF- α 是退变椎间盘内最重要的炎症因子,可以降低椎间盘细胞的合成代谢同时增加椎间盘细胞的分解代谢导致椎间盘细胞退变^[30]。Studer 等^[33]研究发现 IL-6 可以下调退变椎间盘细胞聚蛋白聚糖及胶原的表达,进一步增强了 IL-1 与 TNF- α 的促分解代谢作用。由此可见,一旦痤疮丙酸杆菌进入椎间盘就可以提高椎间盘内炎症因子表达,从而加快椎间盘退变的病理生理过程。

5 展望

总之,目前退变椎间盘内是否含有痤疮丙酸杆菌仍然存在争议。今后的研究需注意扩大研究的样本量,规范标本的送检过程及检验方法以进一步明确退变椎间盘内是否存在痤疮丙酸杆菌感染。由于痤疮丙酸杆菌可能加快椎间盘退变,因此该领域的研究必将影响和指导临床椎间盘退变的治疗。

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(收稿日期:2016-12-19 本文编辑:王宏)