Int J Clin Exp Pathol 2015;8(9):11835-11836
www.ijcep.com /ISSN:1936-2625/IJCEP0013455

Medical Hypothesis

Oral bacteria in pancreatic cancer: mutagenesis of the p53 tumour suppressor gene

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Received July 26, 2015; Accepted August 26, 2015; Epub September 1, 2015; Published September 15, 2015

Abstract: Carcinoma of exocrine pancreas is the fourth leading cause of cancer deaths, worldwide. The prevalence of this disease is very high in patients with chronic pancreatitis. Orodigestive cancers are frequently seen in patients with periodontitis. These findings suggest that this type of cancer may have some bacterial origins. This study hypothesizes that the peptidyl arginine deaminase (PAD) enzymes found in oral bacteria may be responsible for the p53 point mutations that occur in patients with pancreatic cancer. Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythia, and Treponema denticola possess the PAD enzyme, and p53 arginine mutations have been detected in patients with pancreatic cancer. Moreover, the Pro allele p53Arg72-Pro is a risk factor for the development of this cancer. Anti-P. gingivalis antibody titers have been found to be higher in patients with pancreatic cancer as compared to healthy controls. The hypothesis in question can be tested if the DNA of P. gingivalis or the antibodies against P. gingivalis can be detected in patients with the p53 arginine mutation.If this hypothesis is true, it could reveal the real cause of pancreatic cancer, which is a fatal disease. Further studies are necessary in order to confirm this hypothesis.

Keywords: Pancreatic cancer, oral bacteria, p53 mutation, arginine

Inroduction

Carcinoma of exocrine pancreas is the fourth leading cause of cancer-related deaths, worldwide [1]. This cancer is responsible of 8000 deaths annually in England [2]. Furthermore, its incidence is increasing in Western countries [3].

The prevalence of pancreatic cancer is very high in patients with chronic pancreatitis, with an incidence that is 160% greater than what is seen in healthy individuals [4].

Periodontitis is chronic inflammatory disease of the gingiva and the surrounding tissues [5]. It occurs if gingivitis, which is caused by bacterial plaque, is left untreated [5]. It is quite common in the general population, and it is generally observed after the age of 35. Orodigestive cancers are more frequent in patients with periodontitis [6].

Approximately 20 types of bacteria that could cause periodontitis have been isolated from the oral cavity, including *Porphyromonas gingivalis, Prevotella intermedia, Tannerella forsythia*, and *Treponema denticola* [7]. These bacteria are Gram-negative anaerobic bacilli, which are generally present as saprophytes in the human gastrointestinal system and in the female reproductive system [7]. While these bacteria mainly cause periodontitis, they may also be responsible for tonsillitis, pharyngitis, gastritis, colitis, and genital infections [7]. These bacteria possess many virulent factors. *P. gingivalis*, *T. forsythia, and T. denticola* also possess arginine protease [7].

Presentation of the hypothesis

This study hypothesizes that the peptidyl arginine deaminase (PAD) enzymes found in oral bacteria may be responsible for the p53 point mutations that occur in patients with pancreatic cancer.

Testing the hypothesis

In a 2013 study conducted by Michaud et al., the levels of ATTC 53978 antibodies against P. *gingivalis* were found to be higher in the 405

patients with pancreatic cancer as compared to the healthy volunteers (OR 2.14; 95% CI 1.05 to 4.36; > 200 ng/ml vs ≤ 200 ng/ml) [8].

In another study, Barton et al. observed that patients with pancreatic cancer have higher mutation rates for the tumour suppressor gene p53 [9]. Moreover, Barton et al. observed p53 arginine mutations in those patients [9].

Several studies have documented the relationship between p53Arg72-Pro and cancers of the gastrointestinal system [10]. The Pro allele p53Arg72-Pro is a risk factor for the development of pancreatic cancer [10]. In conclusion, the hypothesis in question can be tested if the DNA of P. *gingivalis* or the antibodies against P. *gingivalis* can be detected in patients with the p53 arginine mutation.

Implications of the hypothesis

If this hypothesis is true, it could reveal the real cause of pancreatic cancer, which is a fatal disease.

Disclosure of conflict of interest

None.

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