

Human Papilloma Virus in Progressive Pterygium and Stationary Pterygium

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ABSTRACT

The purpose of this study is to compare the proportion of HPV between progressive and stationary pterygium. This study used a cross-sectional research design. The subject of this study was patients with primary pterygium presenting to the teaching hospital of Faculty of Medicine Gadjah Mada University in Yogyakarta and its networking hospitals. Examination was performed to 62 pterygium tissues, 31 of which were progressive pterygia and 31 were of stationary pterygia. All pterygium tissues were examined by a Polymerase Chain Reaction (PCR) technique with a primer DNA of a single strand HPV Hela. An HPV-positive was present in 66.7% of cases of progressive pterygium and only 22.6% of cases of stationary pterygium with $p < 0.05$ ($p = 0.001$). The result of this study showed that the proportion of HPV-positive in progressive pterygium was greater than stationary pterygium.

Key words: progressive pterygium, stationary pterygium, human papillomavirus, polymerase chain reaction

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INTRODUCTION

Pterygium is a fibrovascular growth tissue of the conjunctiva and bulbar subconjunctiva which radiates and infiltrates corneal surface with the head advancing towards the pupil. Pterygium occurs in the interpalpebral fissure and consists of the same epithelia as that in the conjunctiva which covers vascular structures and loose fibrous connective tissue with an abundant vascularization. Pterygium is usually located on the nasal side of the eyes and often bilateral.¹

Duke Elder et al divided pterygium clinically into: progressive pterygium which is characterized by a very thick body and abundant vascularization, stationary pterygium which has a thin and pale body with scanty vascularization and, atrophic pterygium, characterized by a very thin body resembling a healthy conjunctiva with very scanty vascularization. Progressive pterygium has a recurrence rate 6 times higher than that of stationary pterygium. In the elderly group, the recurrence rate for progressive pterygium is 2.7 times higher than stationary

pterygium. The earliest recurrence emerged at the second week following the surgery and reaching its peak at the third week.¹ Up to present time, the cause of pterygium has not yet been clear. A lot of theories have been developing to explain the pathogenesis which is generally multifactorial. The developing theories comprise: inflammation theory, pinguecula theory, degenerative theory, tropical theory, ultraviolet beam theory, and stem cell deficiency of the limbus conjunctiva theory.^{2,3,4,5}

Dushku et al. (1997) proposed that there was a high p 53 expression on the epithelia of the pterygium. P 53 is a tumor suppressor gene, which has an important role in regulating cell cycle and acts as a guardian of the genome. Mutations occurs on p 53 due to chemical substances and radiation, hence p 53 will loss its function as a tumor suppressor gene, therefore the cell cycle will keep on going despite the existence of defective DNAs. This will lead to the development of cancer cells.⁴ With the discovery of p53, the pathogenesis of pterygium which was previously believed as a degenerative lesion has changed nowadays into tumor characteristics, due to its histological properties,

in which there are mild dysplasia, local invasion and a high recurrence rate.^{3,5} *Human Papilloma Virus* (HPV) is classified as Papovavirus, a DNA virus which can trigger genetic mutations. This virus also has the characteristic of being epitheliotrophic which dominantly infect the skin and muocus membrane with a feature of proliferating epithelia on the infection site. The structure of HPV consists of 3 subparts; an Upstein Regulatory Region (URR), an Early Region (ER), and a Late Region (LR). Early Region plays its part in coding the proteins needed for the work of E1, E2, E4, E5, E6, and E7 proteins. The main mechanism of E6 HPV protein is to engage in some reactions with p53 protein from the target cell leading to the trigger of a cancer development process.⁶ In this time being, the involvement of HPV in a pterygium growth is still controversial, as what has been reported by several researchers that HPV was found in up to 50% cases, meanwhile some other researchers were not succeeded in detecting HPV in pterygium.

MATERIAL AND METHOD

This study used a cross-sectional research design. The subject of this study was patients with primary pterygium presenting to the ophthalmology clinic of the teaching hospital of Faculty of Medicine Universitas Gadjah Mada in Yogyakarta and its networking hospitals, who met the inclusion and exclusion criteria. After the operations had been performed, the pterygium tissues were brought to the Biomolecular Laboratory in Faculty of Medicine, Universitas Gadjah Mada for being examined by a PCR using a primer DNA of a single strand HPV Hela.

RESULT

The study took place in the clinic of Dr. Sardjito Hospital and its networking hospitals. After applying the inclusion and exclusion criteria, 62 pterygia tissues were obtained, all of which were eligible to be examined for the existence of HPV by using a PCR technique in the biomolecular laboratory in Faculty of Medicine, Gadjah

Mada University; those included in the progressive pterygia group (n = 31) and those in the stationary pterygia group (n = 31). All subjects were under 60-year old age (between 30 and 60 years old with mean of 46.61 ± 5.80 years old). The characteristics of subjects consist of distribution of age, sex, sunlight exposure and the use of sun protectors are listed on Table 1.

The average age of the subjects in the progressive pterygium group was 45.39 ± 6.45 years old and 47.84 ± 4.87 years old in the stationary pterygium group ($p = 0.097$). The number of male subjects in the progressive pterygium group was 16 (51.6%) and the amount of female subjects was 15 (48.4%), whereas the number of male subjects in the stationary pterygium group was 13 (41.9%) and the number of female subjects was 18 (58.1%) ($p = 0.445$). There was no significant difference between the two groups based on sex.

The history of sunlight exposure in the progressive pterygium group was investigated and showing that the sunlight exposure of more than 5 hours /day was found in 16 subjects (51.6%) and that of less than 5 hours/day in was found in 15 subjects (48.4%). The sunlight exposure in stationary pterygium group which was more than 5 hours/day was found in 16 subjects (51.6%) and that of less than 5 hours/day was found in 15 subjects (48.4%). According to the length of sunlight exposure per day, there was no significant difference between the two pterygium groups ($p = 1.00$). In the progressive pterygium group, 16 subjects (51.6%) did not use any protection and 15 subjects (48.4%) used protection, whereas in the stationary pterygium group, 14 subjects (45.2%) did not use any protection and 17 subjects (54.8%) used protection. No significant difference was found between the two groups based on the use of sunlight protection ($p = 0.611$).

Table 2. The PCR results of the progressive pterygium group and the stationary pterygium group

	Progressive Pterygium (n = 31)	Stationary Pterygium (n = 31)	P score
HPV-positive	21 (67.7%)	7 (22.6%)	0.001
HPV-negative	10 (32.3%)	24 (77.4%)	

Table 1. The characteristics of the subjects

Characteristics	Progressive Pterygium (n = 31)	Stationary Pterygium (n = 31)	P score
Age (year)	45.39 (+ 6.45)	47.84 (+ 4.87)	0.097
Sex: - male	16 (51.6%)	13 (41.9%)	0.445
- female			
Sunlight Exposure			
- > 5 hours/day	16 (51.6%)	16 (51.6%)	1.00
- < 5 hours/day	15 (48.4%)	15 (48.4%)	
Use of sun protectors (hat/sunglasses/helmet)			
- Not using any protections	16 (51.6%)	14 (45.2%)	0.611
- Using protections	15 (48.4%)	17 (54.8%)	

All tissue samples from both of the groups underwent a PCR examination. The PCR results from all tissue samples of the two pterygium groups (62 sample tissues) discovered that 28 (45.2%) sample tissues were proven to be HPV-positive.

This study showed that in the progressive pterygium group, a positive HPV result was found in 21 (67.7%) sample tissues. In the stationary pterygium group, an HPV-positive result was found in 7 (22.6%) sample tissues. Those results indicated that there was a significant difference on the PCR results between progressive pterygium group and stationary pterygium group with $p < 0.05$ ($p = 0.001$)

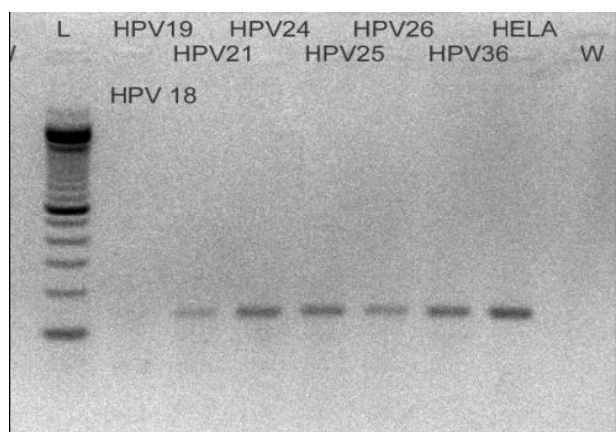


Figure 1. A PCR result on a pterygium.

DISCUSSION

There were two type of HPV infection latent and productive viral. Latent viral infection, viral infection don't produced infectious viral. In Latent infection, the viral was failed to penetrate the membrane cell or capable to penetrate, but they can't multiply because of the failure of particle to be mature. Productive viral phase where virion was formed in this phase. This activity was occurred in the intermediate cell and squamous epithelial cell layer. The virion, multiply and destruct the cells and HPV could be detected by PCR method.^{6,7,8} Pitas et al. on his study entitled the detection of HPV DNA on pterygia collected from several varying geographical areas, wherein all sample tissues of the pterygia were examined using a PCR and resulting in that 22 out of 41 pterygia (54%) had HPVs detected.^{9,10} Gallagher et al. carried out a research on HPV in pterygia by using a PCR which ended up in a result that HPV was

detected in 5 out of 10 (50%) pterygium samples.⁸ Chen et al. was also doing a study on herpes simplex virus and HPV on pterygium, and HPV was detected in 24% pterygium sample tissues.¹¹ In this time being, the involvement of HPV in a pterygium growth is still controversial, as what has been reported by several researchers that HPV was found in up to 50% cases, meanwhile some other researchers were not succeeded in detecting HPV in pterygium.

CONCLUSIONS

The result obtained from this study showed that HPV was present in 66.7% of cases of progressive pterygium and only 22.6% of cases of stationary pterygium with $p < 0.05$ ($p = 0.001$). The study showed that the proportion of HPV-positive in progressive pterygium was greater that that of stationary pterygium.

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