Risk Factors for GA

It is generally thought the causes of GA are multifactorial, caused by the complex interaction of metabolic, genetic and environmental factors. Several risk factors have been strongly associated with the development of GA, most of which are also risk factors for other forms of AMD. These include:

Age: Epidemiological studies show the prevalence of GA increases exponentially with age; some studies have found that GA can affect as many as 1 in 5 people aged >90 years. (See also PREVALENCE DATA - LATE AMD.PDF and INCIDENCE DATA - LATE AMD.PDF for further details of studies reporting prevalence and incidence data for GA.)

Smoking: Smokers are at greater risk factor of developing advanced AMD than non-smokers. A case-control study of 715 white patients found that smoking >40 pack-years of cigarettes was associated with a 3.5-fold greater risk for GA, compared with non-smokers.

Ethnicity: A higher prevalence of GA has been reported in white Europeans, compared with other ethnic groups including Africans, Hispanics and Asians.

Genetic risk factors: Genetic factors play a major role in determining the risk of susceptibility to AMD and progression to late-AMD (GA or neovascular AMD). Large genome-wide association studies have identified over 30 genetic variants associated with the risk of developing AMD. It should be noted that the presence of these genes does not mean that one will inevitably develop AMD, rather one is at higher risk of developing AMD.

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Risk Factors for GA

Of these, genetic variants located at 2 loci – genes associated with the complement cascade on chromosome 1, and the ARMS2/HTRA genes on chromosome 10 – are associated with significantly increased susceptibility to AMD.\(^8\)

The complement cascade is part of the innate immune system that regulates cell death and inflammation. Dysregulation of the complement pathway is believed to play an important role in the development and progression of AMD.\(^1\) Genetic variants in 5 key genes associated with regulation of complement cascade account for 57% of the contribution to disease risk. These include: complement factor H (CFH), complement component 2 and factor B gene (C2/CFB); complement component 3 (C3) and complement factor I (CFI).\(^9\)

In addition to determining the risk of developing AMD or GA, variants of these genes have also been linked to GA progression rates.

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