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Review Article

Epidemiology of vasculitis – Lessons learnt from the differences in different geographical areas

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ABSTRACT

The epidemiology of the vasculitides has been increasingly investigated over the past 30 years and we have now gathered significant knowledge about the occurrence of vasculitis in many populations. There is however still a lack of reliable data from the Indian subcontinent. For most types of vasculitis it is not known if differences in occurrence represent variation in genes, environment, or ascertainment. Giant cell arteritis is most common in populations of Northern Europe or Scandinavian origin and is rarer in the far East, whilst Takayasu arteritis is apparently commoner in Asia. The ANCA vasculitides have an overall occurrence that is similar in most populations, but in China and Japan microscopic polyangiitis is more common than granulomatosis with polyangiitis, whilst in Northern Europe the opposite occurs. Kawasaki disease is markedly more common in South East Asian populations than Caucasians. Behcet's disease is most common along the ancient silk route between the Mediterranean and China. Increasing genetic knowledge is beginning to explain these differences. Behcet's disease is strongly associated with HLA-B*51, Takayasu arteritis with HLA-B*52 and granulomatosis wit polyangiitis with the HLA-DPB1*0401 allele. Variations in allelic frequency might partially explain the global variation in occurrence.

1. Introduction

The epidemiology of the vasculitides has been increasingly investigated over the past 30 years and we have now gathered significant knowledge about the occurrence of vasculitis in many populations. There is however still a lack of reliable data from the Indian subcontinent. For most types of vasculitis it is not known if differences in occurrence represent variation in genes, environment, or ascertainment.

The aim of this review is to describe what is known about the occurrence of the various types of vasculitis in different populations with a focus on Indian populations.

2. Background

Epidemiological studies in rare diseases are hard to conduct even in well resourced and stable Western populations. A successful epidemiological study requires a well defined denominator population, comprehensive case ascertainment and good case classification. In a health care system based on comprehensive coverage, the definition of a denominator population for a common condition is not very difficult. For rare diseases it is harder because in order to study a large enough number of cases either a large population is needed or a long timescale, both of which may be difficult. In health care

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systems based on insurance and with a lack of comprehensive cover, the definition of a reliable denominator population may prove to be impossible. Accurate case ascertainment is the second key component again in health care systems with comprehensive coverage and centralized registry of patients this can be achieved, systems without comprehensive case coverage will lack the ability to accurately identify all cases in a given population. Case classification for many types of vasculitis remains a problem despite the promulgation of the revised Chapel Hill Consensus Conference definitions.[1] There are still no validated classification criteria for microscopic polyangiitis (MPA), and for many of the rarer types of vasculitis.

2.1. *Large vessel vasculitis*

2.1.1. *Takayasu arteritis*

Takayasu arteritis (TAK) is a large vessel vasculitis, which is well recognized worldwide. It predominantly occurs in those aged <40 years. The incidence of TAK appears varies in its distribution across the world with an incidence of 0.5–3/million,[2] but is generally considered to be more common in Asia. Cases have been in most ethnic groups including African. There is no accurate data on the occurrence of TAK in India, but large case series have been reported.[3] The clinical phenotype of TAK varies, in Japan, Korea and Japan the aortic arch is mainly affected whilst in India, Thailand and Europe the abdominal aorta appears to be more frequently involved.

There is evidence for a genetic susceptibility to TAK, it has been recorded in monozygotic twins and around 1% of Japanese patients with TAK have an affected relative.[4] Studies from East Asian countries and Turkey suggest that the main HLA association is with HLA-B*52.[5,6] HLA B52 is slightly more common in the eastern part of the Indian subcontinent than other parts of India or Europe.[7]

2.1.2. *Giant cell arteritis*

Giant cell arteritis (GCA) is a large vessel vasculitis with a predilection for those aged >65 years. The occurrence of GCA across the world appears not to be uniform with the highest incidence and prevalence rates occurring in Scandinavia, UK and Northern Europe. Prospective studies from Scandinavia have reported annual incidence figures for biopsy-proven GCA of 15–35 per 100,000 individuals aged over 50 years (reviewed in).[2]

Giant cell arteritis appears to be most common in Caucasian populations and is uncommon in non-Caucasians. The incidence is highest in Scandinavians and in populations descended from them, and is less common in southern European populations.

There are few studies directly comparing different populations. A study from Tennessee (USA) reported a low incidence in African–Americans (0.36/100,000 aged >50 years) compared with 2.24/100,000 in the white population.[8] A retrospective review from the Texas Gulf Coast reported that 13/27 patients were black women, but that the disease was rare in Hispanics.[9] No incidence figures are available from either study. In contrast a survey from Florida showed a difference in occurrence between Hispanics and non-Hispanics.[10] Referral bias might account for their results. Two studies from California have suggested that GCA is much less common in Asians than Caucasians.[11,12]

There is a low prevalence in Japan compared with Europe.[13] A study from Saskatoon (Canada) suggested a higher frequency in the Aboriginal population (16/100,000) compared with 7.7/100,000 in the Caucasian population. The numbers of subjects was very small (2 non-Caucasians).[14]

GCA is recognized in the Indian subcontinent but appears to be relatively uncommon this may reflect the age distribution of the Indian population.[15] The presentation of GCA appears to be similar.

The relative contribution of genetic and environmental factors as an explanation for geographical differences in GCA incidence remains disputed. GCA appears to be more common in higher latitudes. *HLA-DRB1*04* is the strongest HLA marker for GCA.[16] When genetic diversity within Europe is subjected to principle component analysis, *HLA* is one of several genetic regions that are strongly associated with a component that runs along a north-south gradient from Norway and Sweden to Spain and this could explain the relatively lower incidence in Southern Europe.[17] The HLA-DRB1*0401 and HLA-DRB1*0404 alleles are very much less common in the Japanese population than in Northern European populations and this may explain the rarity of GCA in Japan.[13] These alleles are also uncommon in India and GCA may therefore be relatively uncommon.

2.2. *Medium vessel vasculitis*

2.2.1. *Polyarteritis nodosa (HBV and nonHBV)*

The original description of periarteritis nodosa by Kussmaul and Maier in1866 was of a patient with inflammation and necrosis of medium-sized arteries leading to aneurysm formation and organ infarction. The dominant feature of PAN is organ infarction (gut, nerve) due to involvement of medium-sized arteries. PAN is now considered to be an ANCA negative vasculitis.[1] The literature on the epidemiology of PAN and MPA has to be carefully interpreted, because many older studies used the term polyarteritis nodosa as a generic term for any form of necrotizing vasculitis.

In Europe and the USA the estimated annual incidence of PAN ranges from 2.0 to 9.0/million. Overall, the European and American studies of PAN do not suggest a change over time, but differences in classification make direct comparison difficult. Use of the CHCC definitions makes classical PAN a much rarer disease. A prevalence study from France suggests that improved public health control of HBV infection by vaccination is producing a fall in the prevalence of PAN (Mahr et al 2004).

The highest incidence of PAN recorded was 77/million in Alaskan Indians.[18] The population was, however, small (14,000) and all the cases were positive for hepatitis B surface and e antigen at diagnosis. Detailed hepatitis serology is not available in most other studies. Whether these data reflect geographical and ethnic differences or the high infection rate with hepatitis B virus is unclear as no other comparable study has been reported. A study from Paris reported a prevalence of classical PAN of 30.7/million,[19] similar to Sweden 31/million.[20] Of the French PAN patients, 30% were HBV positive.