Astroviruses as causative agents of gastroenteritis

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Astroviruses were first identified over 30 years ago and the virus was soon established as an important cause of gastroenteritis, particularly in young children. Human astrovirus disease was thought to result from infection by a limited number of serotypes. However, recent studies have indicated that the extent of genetic diversity is greater than previously assumed. In addition, the widespread occurrence among animals and reports of recombination and possible cross-species transmission suggest that astroviruses have zoonotic potential.

Astroviruses are small (28–30 nm), non-enveloped viruses belonging to the family *Astroviridae*. The viral genome comprises a single-stranded RNA of positive sense. The genome length is between 6.8 and 7.9 kb and includes a 50 bp untranslated region (UTR), followed by three open reading frames, ORF1a, ORF1b, and ORF2, a 30 bp UTR and a poly-A tail[1]. Figure 1 shows the genome structure of a typical astrovirus. ORF1a/1b encodes the viral non-structural proteins (protease and RNA-dependent RNA polymerase) while ORF2, expressed from a subgenomic RNA, encodes the viral capsid protein.

Symptoms of disease

Human astrovirus infection results in a mild, self-limiting gastroenteritis, generally indistinguishable from other causes of viral gastroenteritis, which sometimes requires hospitalisation. Diarrhoea is the predominant clinical symptom; however, disease can be accompanied by fever, nausea and occasionally vomiting, headache and abdominal discomfort. Co-infections with other enteric pathogens, especially rotaviruses, are known. Most infections in adults are asymptomatic. In other mammalian species, infection results in diarrhoea and gastroenteritis, while infection in birds leads to extraintestinal diseases, including interstitial nephritis in young chicks and acute hepatitis in ducklings[2].

Epidemiology

The first description of astrovirus came in 1975 after electron microscopic analysis of diarrhoeal stool samples from infants[3,4]. The unusual appearance of the virion particles (10% show a characteristic five- or six-pointed star pattern on their surface) indicated a previously unrecognised virus. Astroviruses have since been reported worldwide in samples from infants and young children with gastroenteritis. Soon after the first report in humans, astrovirus-like particles were observed in domesticated animals. There is now abundant evidence that astroviruses are widespread among domestic, synanthropic and wild animals, avian and mammalian species in terrestrial and aquatic environments[1]. The list of animal species from which astroviruses have been identified (chronologically) includes sheep, cattle, chickens, pigs, dogs, cats, deer, ducks, mice, turkeys, mink, guinea fowl, cheetahs, bats, sea lions, dolphins and rats. Reports of unusual astroviruses that have possibly arisen through recombination events indicate that co-infections within and between species are possible.

By convention, the naming of astroviruses has been according to species of origin (for example, human astroviruses are referred to as HAstV). The family *Astroviridae* is divided into two genera: *Mamastroviruses* (MAstVs) which infect mammals and *Avastroviruses* (AAstVs) which are known to infect avian species. HAstV are classified into eight 'classic' serotypes (HAstV 1-8). In recent years, new highly divergent human astroviruses (MLB1, VA1, VA2 and VA3) have been described[5-9], some of which are genetically related to rat astroviruses. However, a case-control study has questioned the role of one of these new viruses, MBL1, in human disease[10].

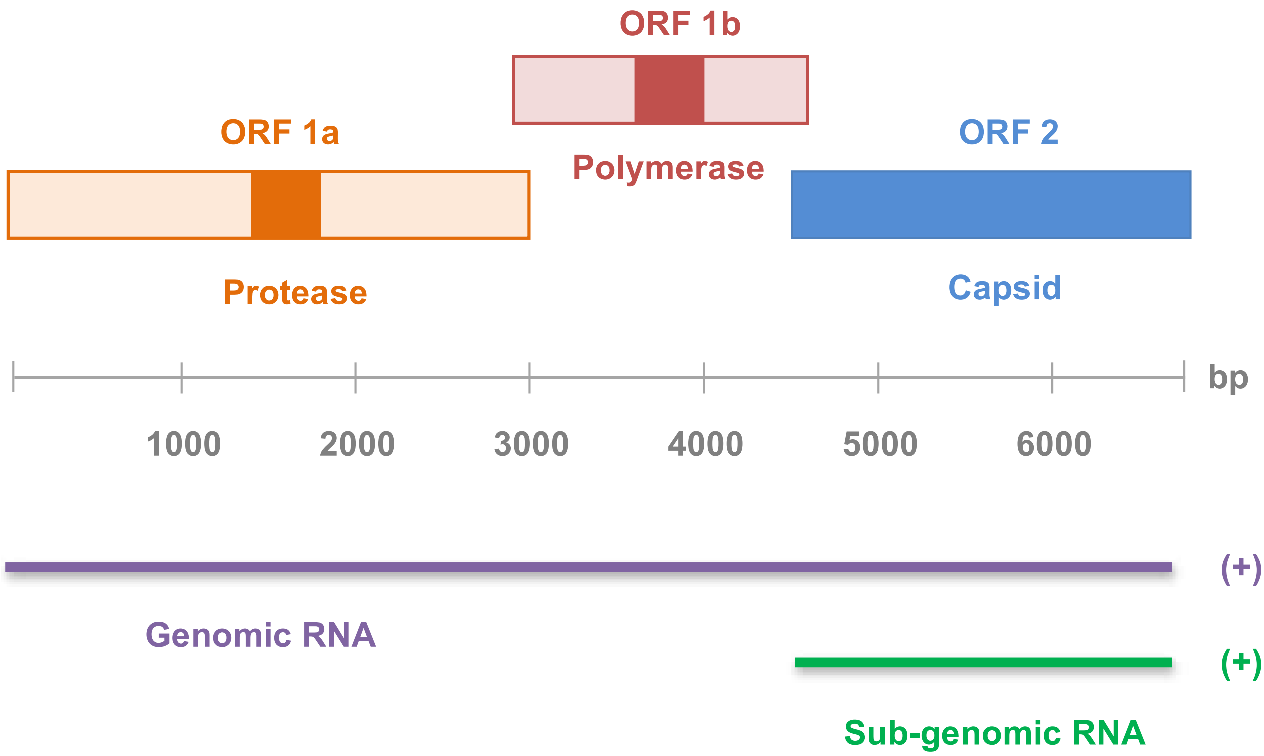

Figure 1. Genomic organisation of astroviruses. ORF indicates open reading frame. A sub-genomic RNA co-linear with ORF2 is found within infected cells.

In humans, astroviruses commonly infect young children with seropositivity rates reaching 80% by the age of 10[2]. Infection (at least with common types) is then infrequent until later in life when infection rates rise in the elderly due to natural immune suppression. Of the classic human serotypes, most infections involve HAstV-1 (up to 94%) with HAstV-2 – 6 contributing to most of the remainder. HAstV-7 and HAstV-8 are uncommon. The prevalence of the new human types is not known but recent studies indicate that these viruses are geographically widespread[11].

Infection control

Given that (i) there are no astrovirus vaccines, (ii) the virus is spread by the faecal–oral route and (iii) viruses can contaminate the environment (for example, astroviruses are detected in drinking and recreational waters[12]), disease control is achieved by a combination of normal public health measures (sewage treatment and disposal, and the provision of safe drinking water) and good hygiene practices[2]. Efficient diagnosis of infection can help to contain outbreaks, although testing of the virus is not routinely performed in most diagnostic laboratories. Astroviruses are physically robust and can tolerate exposure to conditions from pH 2-11, chloroform and heating up to 60°C for five minutes with little loss of infectivity. The viruses are also relatively resistant to chlorine inactivation.

Astroviruses in Australia

There have been few studies of astrovirus epidemiology in Australia and the majority have focused on paediatric populations. The first epidemiological study of Australian astroviruses was performed using molecular techniques to identify viruses in stool samples from children hospitalised with gastroenteritis over a single year in Melbourne[13]. This study indicated that astroviruses were responsible for about 4% of admissions (greater than adenovirus and all bacterial pathogens) and that the peak of infections occurred during the winter months. HAstV-1 was the most frequently isolated type (supporting global tends) although some HAstV-4 isolates were detected. A prospective analysis of historical faecal samples also identified HAstV-5 from a patient who was likely to have acquired the virus nosocomially. A follow-up study conducted over a four-year period supported the earlier observations that HAstV-1 was the dominant serotype, with HAstV-2, -4 and the rare -8 identified sporadically. The seasonal winter peak was not consistent and was only observed in two of the four years[14].

A similar survey conducted in Alice Springs found similar overall trends to the earlier studies with incidence rates ranging from 1.6% to 6.6%[15]. The incidence of astrovirus detection was greater than "Norwalk-like" viruses but considerably lower than rotavirus. This study also found that the monthly distribution of astrovirus detection was not consistent over the four years of the survey; positive cases were detected in the colder months in three of the four years. HAstV-1 was dominant in three years but absent in one of the years, while HAstV-2, -3 and -4 were found in two, two and three of the four years of the survey, respectively.

A further study performed in Sydney compared the rates of detection of astroviruses and other enteric pathogens in a cohort of children who attended an outpatient clinic or were admitted for diarrhoea over a 12-month period[16]. Astroviruses were detected in 12% of the 137 samples in which a pathogen was present. Only four of the 17 astroviruses were detected in children admitted to the isolation ward and the majority of astroviruses were detected in June–October. No information about serotype distribution was obtained.

There has been a single study that implicated astroviruses as the causative agents of an outbreak of gastroenteritis in an aged-care facility. In this study, astrovirus was identified as the cause of only one of the 53 outbreaks investigated[17]. Further analysis indicated that the strain involved in the outbreak belonged to HAstV-1[18].

With respect to animal astroviruses, a recent study identified avian nephritis virus (ANV) in young chickens with clinical signs of dehydration and diarrhoea for the first time in Australia, thus indicating the circulation of this pathogen in Australian poultry[19].

Conclusions

Although astroviruses were first identified over 30 years ago, the difficulty in propagating the virus in cell culture limited their investigation to electron microscopic analysis. With the development of DNA-based technologies, detection and characterisation allowed the virus to be established as an important cause of gastroenteritis, particularly in young children. The extent of genetic diversity, the widespread occurrence among animals, together with evidence of recombination and possible cross-species transmission suggest that astroviruses have zoonotic potential[1]. Increasing our understanding of the genetic features and pathogenesis of this virus will provide new insights relevant to the design of specific and accurate diagnostic assays.

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Biography

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