Influenza Virus Infections in Cats

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In the past, cats were considered resistant to influenza. Today, we know that they are susceptible to some influenza A viruses (IAVs) originating in other species. Usually, the outcome is only subclinical infection or a mild fever. However, outbreaks of feline disease caused by canine H3N2 IAV with fever, tachypnoea, sneezing, coughing, dyspnoea and lethargy are occasionally noted in shelters. In one such outbreak, the morbidity rate was 100% and the mortality rate was 40%. Recently, avian H7N2 IAV infection occurred in cats in some shelters in the USA, inducing mostly mild respiratory disease. Furthermore, cats are susceptible to experimental infection with the human H3N2 IAV that caused the pandemic in 1968. Several studies indicated that cats worldwide could be infected by H1N1 IAV during the subsequent human pandemic in 2009. In one shelter, severe cases with fatalities were noted. Finally, the highly pathogenic avian H5N1 IAV can induce a severe, fatal disease in cats, and can spread via cat-to-cat contact.

Keywords: cats ; influenza A virus ; low pathogenic ; highly pathogenic

1. Introduction

Influenza is a highly contagious, acute infection, usually of the upper respiratory tract, and has been detected worldwide in many vertebrate hosts [1]. Feline respiratory diseases caused by influenza viruses appear to be rather rare and usually self-limiting; however, secondary bacterial infections can lead to complications, and can be associated with fatalities. Very rarely, highly pathogenic influenza viruses can induce a severe, generalised viral disease with a high fatality rate in cats [2].

2. Aetiology

The virus is a member of the *Orthomyxoviridae* family. Four types (A, B, C and D) of this agent are known. Influenza virus type A (IAV) is the most important and induces mass disease in humans worldwide, as well as animals, including birds, horses, pigs, minks, ferrets, bats and marine mammals. Dogs and cats may also be affected.

The IAV types are further classified as subtypes based on the antigenicity of the two viral surface proteins, haemagglutinin (H) and neuraminidase (N). There are 16 H and 9 N antigens [1], and their different combinations result in 144 IAV subtypes (e.g., H1N1, H3N8, H5N2, etc.). In addition, further subtypes (H17N10 and H18N11) of influenza-like viruses have been found in bats, but they appear to be distinct from conventional IAVs in multiple aspects [3].

IAVs are genetically highly variable, rapidly changing their antigens, virulence, and ability to replicate in novel host species [4]. Two mechanisms are responsible for this: genetic drift and genetic shift. Genetic drift results from mutations in the genes encoding N or H, producing a new antigenic variant of a given subtype. If the replication of such a variant is less effectively inhibited by the host immunity that eliminated the infection caused by the original strain, the mutated virus can infect the same population again. In contrast, antigenic shift leads to the sudden emergence of a new subtype resulting from the exchange (reassortment) of RNA fragments between two or more IAV subtypes replicating at the same time in a host [4]. Well-recognised “mixing vessel” hosts for human IAVs include pigs and birds, but recent data suggest that dogs and cats might also potentially play such a role [5][6]. These new subtypes, which share pathogenic properties with their parental lineages and have a mixture of the surface antigens of the original strains, can be highly dangerous. As the target host population is often immunologically naïve to the new subtype, epidemics, or even pandemics, in different animal species and humans have arisen in the past [1]. Due to further selection pressure (genetic drift), a new subtype can evolve into multiple antigenic variants, grouped into sublineages or clades [7]. All of these genetic variability mechanisms contribute to the permanent circulation of IAVs in avian and mammalian populations.

IAVs are quickly inactivated by UV light, detergents and disinfectants. However, in water, IAV remains infectious for weeks or months depending on the pH, salinity, and temperature [8][9].

3. Epidemiology of IAV Infections in Cats

For a long time, it was believed that cats were resistant to influenza. Today, it is clear, that cats, dogs, ferrets and other carnivores are involved in the worldwide circulation of IAVs [10].

3.1. Low Pathogenic IAVs

Early experiments revealed that cats are susceptible to some IAVs isolated from humans, birds and seals, which usually only induce subclinical infections or a mild fever [11][12][13].

Additionally, canine IAV can occasionally be transmitted to cats. The first outbreak of severe influenza in dogs occurred in 2002 in English foxhounds and was caused by equine H3N8 IAV [14]. Serological studies revealed that this agent, adapted to dogs as canine IAV, was circulating among racing greyhounds in the USA from the early 2000s [15]. After an outbreak in Florida, this virus spread to other breeds and regions of the USA, particularly to shelters [16][17][18]. Another cross-species transmission of the H3N8 IAV to dogs was documented during an epidemic of equine influenza in Australia in 2007 [19]. Natural equine H3N8 IAV infection has not been found in cats thus far, but after experimental inoculation, cats do develop the disease, shed the virus, and transmit the infection to other cats via contact [20].

In South Korea and China, around 2004–2005, a H3N2 IAV emerged in dogs, most probably of avian origin, and became enzootic there [21][22]. Since 2015, this agent has been repeatedly introduced to the USA and Canada by dogs rescued from Asian meat production farms, resulting in several outbreaks [10][23]. Cross-species transmission of this virus is possible as, after experimental inoculations, ferrets, guinea pigs and cats have all been infected [24]. Furthermore, natural feline outbreaks with fever, tachypnoea, sneezing, coughing, dyspnoea and lethargy were noted in two shelters [25][26]. In one of these shelters, the morbidity rate was 100% and the mortality rate was 40%. Although cats can be infected via direct dog-to-cat or cat-to-cat transfer, this virus obviously replicates less efficiently in cats than in dogs, as natural feline outbreaks appear to be very rare. Such outbreaks were largely confined to shelters, and the virus does not appear to undergo prolonged transmission in household cats [23].

From 2016 to 2017, an avian H7N2 IAV infected cats in a New York shelter, and quickly spread to other shelters in New York and Pennsylvania, likely via the movement of cats between the shelters [27][28]. The virus was easily transmitted between cats, but not amongst dogs, chickens, or rabbits housed in the same facilities [29]. In total, approximately 500 cats were found to be infected and most experienced mild respiratory illness [30]. One elderly cat with underlying conditions developed severe pneumonia and was euthanised. Additionally, a veterinarian and a shelter worker, both of whom had multiple direct periods of exposure to the cats without using personal protective equipment, became infected and exhibited mild, transient respiratory disease [31].

Experimental inoculations confirmed that cats were susceptible to the human H3N2 IAV that induced the “Hong-Kong” influenza pandemic in 1968 [11]. Furthermore, several studies indicated that, in 2009, cats (and dogs) worldwide could be infected by the H1N1 IAV during the subsequent human influenza pandemic, probably by direct transmission from their owners [6][32][33][34][35][36][37][38]. In Italy, this virus caused an outbreak of respiratory and gastrointestinal disease in a colony of 90 cats, resulting in 25 deaths [39]. Cat-to-cat transmission was suspected [39][40].

There are also reports of occasional influenza cases in cats caused by other IAVs [10][41][42]. A recent study confirmed that the presence of antibodies to IAVs of both avian and human origin is not uncommon in European shelter cats [6]. Antibodies against H1, H3, H5, H7 and H9 were found in their sera.

3.2. Highly Pathogenic H5N1 IAV

In Asia, a highly pathogenic H5N1 virus emerged in 1996, which caused a substantial epidemic of “avian flu” with a high mortality rate in poultry at the beginning of the 21st century. Hundreds of millions of poultry were destroyed [43]. Mammals were sporadically affected, including over 860 humans, with a fatality rate of more than 50% [44]. Severe cases in domestic cats were also noted [2][45], as well as in wild felids [46] that were fed, or had other contact with, infected chickens. In one outbreak, tiger-to-tiger transmission was suspected [47]. As this epidemic reached Europe and Africa, incidental feline cases were also seen there [2], as well as subclinical infections [48]. Usually, these were connected to infected wild birds or poultry. Nevertheless, even in areas in which birds are infected with H5N1 IAV, cats are rarely positive by serology or PCR [49][50]. Experimental infections have confirmed that the highly pathogenic H5N1 IAV may induce a severe, fatal disease in domestic cats, and can spread via cat-to-cat contact [45][51][52]. The virus is excreted not only via the respiratory tract, but also in faeces. It should be stressed that the highly pathogenic H5N1 IAV is still circulating in many parts of the world, including Europe. In the first half of 2021, several outbreaks in wild birds or poultry were noted in Finland, Germany, Denmark, Slovakia, Hungary, France, Latvia, and Estonia [53].

In summary, the data presented in this review clearly show that domestic cats are susceptible to natural IAV infections from other species. They result most likely from close contact with infected humans or animals, especially birds. Serological surveys suggest low to moderate rates of seroconversion to low pathogenic seasonal human or animal strains, and sporadic seroconversions to highly pathogenic avian strains. However, IAVs appear to spread inefficiently among feline populations, probably due to their social organisation, which limits the direct cat-to-cat contact that is required for viral transmission. Thus far, feline influenza epidemics have not been recorded, with only rare outbreaks in dense populations such as shelters. Therefore, cats are not considered a reservoir of influenza. In contrast to humans, horses, pigs, bats, dogs and some other species, the adaptation of IAVs to feline hosts has not yet occurred.

4. Diagnosis

In cats showing signs of acute upper respiratory tract inflammation, influenza should be considered if other etiological agents, such as feline herpesvirus and calicivirus, have been excluded. Risk factors include being in a shelter and close contact with humans or animals suffering from influenza. This applies especially when severe acute respiratory disease is seen in a cat that has outdoor access during an outbreak of highly pathogenic avian influenza infections in poultry and/or aquatic wild birds in the region [2].

IAVs can be isolated in tissue culture or embryonated eggs from nasal or oropharyngeal swabs, or—during a post-mortem examination—from pulmonary tissue (and, in the case of highly pathogenic strains, from rectal swabs or faecal samples, affected organs, intestinal content and pleural fluid).

Viral RNA can be detected in nasal swabs by reverse-transcription PCR during the first 4 days of infection.

In subclinical cases, serology (haemagglutination inhibition tests or neutralisation assays) may be useful for the detection of antibodies. A four-fold serum titre increase within 14 days indicates a recent IAV infection. A comparison of serological assays during a screening study for IAV antibodies in cats has been published recently [6].

For dogs and some other animal species, commercial point-of-care tests are offered for the quick detection of IAV antigens in nasal swabs. These assays have not been validated for cats thus far.

5. Control

In the case of an influenza outbreak in a cattery, routine isolation and quarantine procedures should be followed to prevent the spread, as cat-to-cat transmission may occur. The upper respiratory tract disease that occurs as a result is usually mild and self-limiting. In rare, complicated cases, symptomatic medication, combined with the control of secondary bacterial infections, should be implemented alongside other procedures used in cats suffering from other acute viral upper respiratory tract diseases. In humans, oseltamivir is commonly used for the treatment or prevention of IAV infections. This antiviral drug has been given to healthy tigers at risk of highly pathogenic H5N1 IAV infection, but there was no evidence of protection [47].

Though it has been shown that a heterologous avian H5N6 IAV vaccine can protect cats against lethal challenge with the highly pathogenic H5N1 virus [52], no commercial vaccines for cats are available at present. The only prophylaxis is the prevention of any contact with poultry or wild birds infected with H5N1 or other highly pathogenic IAVs. The European Commission has therefore recommended that cats be kept indoors in the areas in which outbreaks of H5N1 IAV infection are recorded in poultry or wild birds [54].

Recently, it was shown that a commercial inactivated H3N2 canine IAV vaccine was well tolerated and induced seroconversion in cats [55]. Even if this vaccine was to be licensed for cats, its usage in Europe is not recommended as this virus has been never detected in Europe, and in regions with canine influenza outbreaks infections in cats are very rare.

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