Research Article

Duckling Short Beak and Dwarfism Syndrome, A Newly Emerging Disease in China

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Abstract | Short beak and dwarfism syndrome virus (SBDSV) is an emerging distinct duck-origin goose parvovirus causing outbreaks of short beak and dwarfism syndrome duckling in Chinese duck flocks. The aim of this review is to describe the current knowledge on SBDSV with an emphasis on epidemiology, clinical symptoms, laboratory diagnosis, genomic organization and pathogenesis. However, the pathogenesis mechanisms of cross-species transmission, retardation and beak atrophy are still needed to be elucidated.

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Introduction

Waterfowl parvoviruses, the autonomous member within the species *Anseriform dependoparvovirus 1*, are classified into two groups, namely goose parvovirus (GPV) and Muscovy duck parvovirus (MDPV) [1, 2]. Classical GPV is the causative agent of Derzy's disease in goslings and Muscovy ducklings [3]. Peking duck and mule duck are resistant to classical GPV infection. In 1970s, an epidemic named "Short Beak and Dwarfism Syndrome (SBDS)" had occurred in mule duck flocks in France where the causative agent was a distinct lineage of GPV (designated as Short beak and dwarfism syndrome virus (SBDSV) or novel duck-origin goose parvovirus (N-GPV)) [4]. SBDSV infection was subsequently emerged in Poland (1995), Hungary (2008), Taiwan (1989) and mainland China (2015) [4-9]. The unprecedented outbreaks of SBDS disease since 2015 have caused considerable economic losses to Chinese waterfowl industry [2, 7]. In order to better understanding SBDS disease, we summarized the characteristics of this disease including the epidemiology, pathobiology, diagnosis, and possible transmission, which might be useful for future research.

Virus transmission and epidemiology

SBDSV infection spreads rapidly in China and poses a great threat to the production of waterfowl. SBDSV mostly affects 5 to 30 day-old mule ducks and Peking ducks (including Cherry Valley duck) with variable morbidity rate (10% - 100%) and slight mortality (2%- 10%) [7, 9]. SBDS disease was also observed in other waterfowl breeds such as Muscovy duckling, Sheldrake and goose [10, 11]. Mule duckling and Peking duckling are most susceptible to SBDSV, followed by Muscovy duckling, and Sheldrake and

gosling [10]. Viral shedding could be detected in oral and cloacal swabs [12]. SBDSV could vertically transmitted from breeder ducks to offspring ducklings, whereas there is no influence on the fertility and hatchability percentage [13]. Contaminated feed and drinking water are the main source of infection. Poor feeding conditions could aggravate the disease with a high morbidity. Also, ducks reared in ponds or on ground are more likely to develop SBDS than ducks raised in netting bed. Susceptibility of ducks to SBDSV infection is age-related [9], infected ducks did not exhibit clinical disease when infected after 2 weeks of age. Most the infected birds (60% - 80%) developed the antibody against SBDSV at 6 to 7 days post infection, and almost all survival birds at 21 dpi and were seropositive [7, 10, 12]. During the period of raising and slaughter, the legs, wings and sternum are easily fractured, leading to more defect rate and economic losses to commercial meat-type duck farms [9, 14].

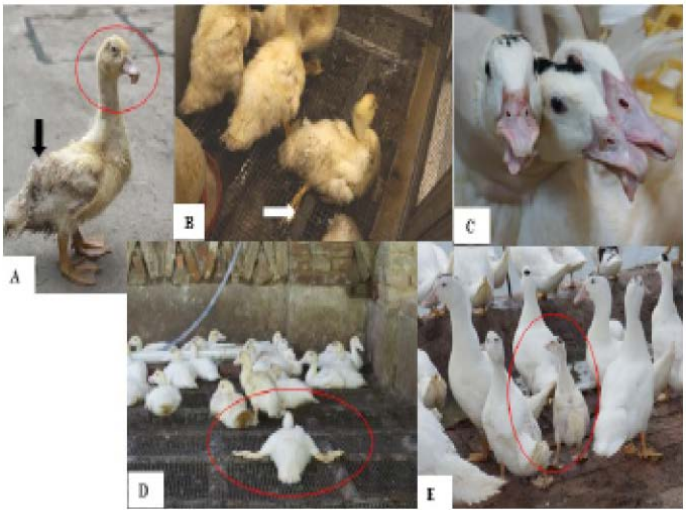

Figure 1: *Typical clinical symptoms of SBDS disease. A. Duckling short beak, protruding tongue and feather disorder. B. Duckling leg fracture. C. Adult ducks' beaks atrophy with protruded tongues. D. Paralysis and dyspraxia. E. Striking growth retardation and dwarfism.*

Clinical manifestations and pathological characteristics

The typical clinical symptoms of SBDSV infected Peking ducklings and mule ducklings are striking growth retardation, notable beak atrophy with a protruded tongue, diarrhea, dyspraxia, and fractured feathers, wings and legs (**Figure 1**) [2, 7]. Mostly, the ducklings begin to show the clinical symptoms 4 to 7 days post infection (dpi) including depression, bunching, limping, anorexia, fluffy feathers and diarrhea [10]. The growth retardation and beak atrophy become more and more serious with age. At 14 dpi, the body weight of infected groups was apparently less than those of the control ducks. The beaks of challenged ducks were obviously shorter than those of the uninfected ducks at 21 dpi. The protruded tongues, fractures of legs, wings and sternums, and poor feather growth were mostly observed after 28 dpi. With necropsy, no apparent gross lesions other than enteritis that usually observed in the internal organs of sick or dead ducklings [7, 15]. However, SBDSV could be detected in multiple internal organs including heart, liver, kidney, spleen, lung, pancreas, intestine and bursa of Fabricius, resulting in microscopic lesions. Muscovy ducklings, Sheldrakes and goslings infected with SBDSV also showed remarkable growth retardation, anorexia and diarrhea, whereas no obvious atrophic beaks and or protruded tongues [10].

Laboratory diagnosis

SBDSV is a duck-origin variant GPV, sharing 92.2%–97.5% nucleotide homology with classical GPV in viral genome [8, 16]. It is very difficult to develop a specific method to distinguish SBDSV from classical GPV due to high nucleotide similarity [7]. SBDS infection could be confirmed by traditional diagnosis method along with the clinical characteristics. ELISA assay using recombinant VP3 protein could be used in detection of GPV antibodies in serum [13]. Chen et al., employed GPV MAb labeled with latex agglutination reagent and developed latex agglutination test (LAT) and latex agglutination inhibition (LAI) assay to rapidly detect GPV antigens and antibodies, respectively [7]. Recently, a series of assays for detecting SBDSV had been developed, such as real-time PCR, LAMP, recombinase polymerase amplification (RPA) [16-18]. However, these methods have cross reaction with GPV and not suitable for SBDSV specific detection. Wang et al., developed a real-time PCR assay that could specifically detect SBDSV with no cross-detection with classical GPV and MDPV [19]. A duplex semi-nested PCR assay was also developed for differential detection of SBDSV and classical goose parvovirus [20]. TaqMan-based real-time PCR assay been shown to be effective in specific detection of SBDSV [21]. According the existence of Ssp I restriction site within SBDSV 5' UTR sequence, PCR-RFLP method was established for distinguishing SBDSV from GPV and MDPV [22]. Finally, these specific detection methods play an important role in epidemiological survey and early diagnosis.

Genomic organization

Similar to classical GPV, SBDSV genome is single-

Table 1: *The information of SBDSV strains used in this study.*

Strain name	Geographic origin	Isolation year	Host	Genome size (bp)	GenBank accession No.
M15	Fujian, China,	2015	Mule duck	5030	KU844283
sdlc01	Shandong, China,	2015	Cherry Valley Duck	5006	KT343253.1
AH	Anhui, China	2015	Cherry Valley Duck	5053	MH444513.1
GD	Guangdong, China	2016	Mule duck	5106	MH444514
SD	Shandong, China,	2015	Cherry Valley Duck	5053	KY511124.1
SDHZ1604	Shandong, China	2016	Cherry Valley Duck	5054	MF441223.1
AH1606	Anhui, China,	2016	Cherry Valley Duck	5054	MF441225.1
SDDY1605	Shandong, China,	2016	Cherry Valley Duck	5054	MF441224
AH1605	Anhui, China	2016	Cherry Valley Duck	5054	MF441227
SDLY1512	Shandong, China,	2015	Cherry Valley Duck	5054	MF441221.1
QH15	Shandong, China	2015	Pekin duck	5048	KT751090
GXN45	Guangxi, China	2017	Cherry Valley Duck	5052	MH717783.1
JS1603	Jiangsu, China,	2016	Cherry Valley Duc	5055	MF441226
DS15	Anhui, China	2015	Cherry Valley Duc	5104	KX384726.2
JS1	Jiangsu, China,	2015	Pekin duck	5106	KT935531
SC16	Sichuan, China	2016	Cherry Valley Duc	5109	KY679174
SDLY1602	Shandong, China	2016	Cherry Valley Duc	5110	MF441222
HuN18	Hunan, China	2018	Sheldrake	5110	MK736656
D146/02	France	2002	Mule duck	/	AY496906
D697/3/06	France	2006	Mule duck	/	EU938706
D479/12/04	France	2004	Mule duck	/	EU938702
D518/3/05	France	2005	Mule duck	/	EU938703
D523/2/05	France	2005	Mule duck	/	EU938704
D657/3/06	France	2006	Mule duck	/	EU938705

stranded DNA approximately 5.1 kb in length, has two major open reading frames (ORFs). The left ORF encodes two replication (Rep) proteins, Rep1 and Rep2. The right ORF encodes viral capsid proteins named VP1, VP2 and VP3. VP2 and VP3 are included within the C-terminal portion of VP1 and share the same promoter, but have different stop codons [8, 9]. These three capsid proteins constitute the icosahedral capsid in a ratio of approximately 1:1:8 [23]. The genome is flanked with identical inverted terminal repeats (ITR) on both 5' and 3' ends. In China, at least 18 SBDSV strains were genetically characterized and were belonging to the West-European GPV-subgroup [1, 8, 24]. Complete genomes of SBDSV range between 4594- 5110 bp (**Table 1**), sharing 94.66% - 99.9% identity with each other, and 90.26% - 94.37% identity with classical GPV strains. NS1 gene of SBDSV shared 98.99% - 100% nucleotide identity with each other, whereas 93.37% - 97.88% identity with classical GPV. VP1 gene of SBDSV shared 94.95% - 99.95% nucleotide homology with each other, and 91.81% - 95.36% homology with classical GPV. NS gene is more stable than VP gene [9]. In compared to classical GPV, seven coincidental amino acid mutations were found in the C-terminal of Rep protein, and eight synchronous amino acid changes were found in the capsid protein [8]. Among those, two important amino acids changes (Ser489Asn and His650Asn) in the capsid protein that supposed to be responsible for host shift [25]. Two 14-nucleotide-pair deletions in most of SBDSV isolates were found in the stem of ITRs as compared to the classical GPV strains [8, 15].

Pathogenesis and pathobiology

Although duckling SBDS disease was first emerged in Europe, the genomic features of European strains are still not clear. It is difficult to know the detailed relationship and evolutionary mechanisms between Chinese and European SBDSV strains. Until now, there is no commercial vaccine against SBDS disease. Based on the high homology between SBDSV and

classical GPV, it is more likely to employ GPV vaccines or yolk antibodies to prevent and control SBDS infection, however the protective efficacy is low [15]. It is urgent to develop genotype-matched vaccines to effectively control SBDS disease. SBDSV replication and adaptation are not well to host cells and embryos with low viral titers, so it is hard to develop a conventional vaccine. VP3 is the most abundantly expressed protein and could induce host strong immune response [3], development of virus-like particles (VLPs) or recombinant viruses expressing VP3 proteins may give promising vaccine candidates for SBDS control. As compared to classical GPV, some mutations in its encoding proteins and nucleotides deletions in ITRs may be responsible for cross-species transmission and virulence attenuation [8, 9, 15]. The molecular mechanism of SBDSV cross-species transmission needs further investigation. The pathogenesis of the beak atrophy and retardation of bone growth was not clear. However, parvovirus infection might affect the activity of bone morphogenetic protein 4, which in turn can result in the modulation of the beak shape [4, 26]. Most capsid genes of parvoviruses contain phospholipase A2 sequence motif (PLA2) [27, 28] which contain a conserved calcium binding loop (YXGXG motif) [29]. It has been found that the phospholipase activity was increased in serum samples from naturally infected ducks with SBDSV [12]. These data speculate that increased PLA 2 activity in SBDSV infected ducks might compete with calcium absorption, resulting in reduction in blood calcium levels and finally causing bone dysplasia syndrome [12]. This hypothesis needs to be confirmed by further investigation and studies.

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Authors Contribution

Shilong Chen collected the data and wrote original draft; Shifeng Xiao, Shao Wang, Fengqiang Lin, Xiaoxia Cheng, Xiaoli Zhu and Dandan Jiang revised the manuscript; Shaoying Chen and Fusong Yu participated in supervision and coordination

Conflicts of interest

The authors declare no conflict of interest.

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