



Review

Myxomatosis in Australia and Europe: A model for emerging infectious diseases

Peter J Kerr*

CSIRO Ecosystem Sciences, GPO Box 1700, Canberra, ACT 2601, Australia

ARTICLE INFO

Article history:

Received 18 November 2011

Revised 20 January 2012

Accepted 26 January 2012

Available online 8 February 2012

Keywords:

Myxoma virus

Myxomatosis

Poxvirus

Rabbit

Coevolution

Virulence

ABSTRACT

Myxoma virus is a poxvirus naturally found in two American leporid (rabbit) species (*Sylvilagus brasiliensis* and *Sylvilagus bachmani*) in which it causes an innocuous localised cutaneous fibroma. However, in European rabbits (*Oryctolagus cuniculus*) the same virus causes the lethal disseminated disease myxomatosis. The introduction of myxoma virus into the European rabbit population in Australia in 1950 initiated the best known example of what happens when a novel pathogen jumps into a completely naïve new mammalian host species. The short generation time of the rabbit and their vast numbers in Australia meant evolution could be studied in real time. The carefully documented emergence of attenuated strains of virus that were more effectively transmitted by the mosquito vector and the subsequent selection of rabbits with genetic resistance to myxomatosis is the paradigm for pathogen virulence and host–pathogen coevolution. This natural experiment was repeated with the release of a separate strain of myxoma virus in France in 1952. The subsequent spread of the virus throughout Europe and its coevolution with the rabbit essentially paralleled what occurred in Australia. Detailed molecular studies on myxoma virus have dissected the role of virulence genes in the pathogenesis of myxomatosis and when combined with genomic data and reverse genetics should in future enable the understanding of the molecular evolution of the virus as it adapted to its new host. This review describes the natural history and evolution of myxoma virus together with the molecular biology and experimental pathogenesis studies that are informing our understanding of evolution of emerging diseases.

Crown Copyright © 2012 Published by Elsevier B.V. All rights reserved.

Contents

1. Introduction	388
2. Natural history of myxoma virus	388
2.1. Myxomatosis	388
2.2. Virus properties	389
2.3. Natural hosts, geographic range and related leporipoxviruses	389
3. Myxoma virus and biological control of the European rabbit	390
3.1. Natural history of the European rabbit	390
3.2. History of introduction of myxoma virus into Australia	390
3.3. The first epizootic of myxomatosis in Australia	390
4. Host pathogen coevolution of myxoma virus and the European rabbit	391
4.1. Attenuation of the virus	391
4.2. Genetic resistance in wild rabbits	394
5. Enhancing biological control by myxomatosis in Australia	395
5.1. Release of virulent strains of myxoma virus	395
5.2. Novel vectors: Introduction of rabbit fleas to Australia	395
5.3. Success or failure of biological control?	395
6. Repeating the experiment: Myxomatosis in Europe	395
6.1. Introduction in France and subsequent spread	395
6.2. Impact of myxomatosis in Europe and Britain	396
6.3. Host–pathogen coevolution: Changes in virulence of MYXV in Europe	396
6.4. Genetic resistance in rabbits in Europe	397
6.5. Amyxomatous myxoma virus strains	397

* Tel.: +61 2 62464334; fax: +61 2 62464094.

E-mail address: peter.kerr@csiro.au

7.	Similarities and differences between Australia and Europe	397
8.	Pathogenesis of myxomatosis	398
8.1.	Pathogenesis in laboratory rabbits	398
8.2.	Infections with attenuated virus	401
8.3.	Immune responses	401
8.4.	Clearance of virus – Does persistent infection play any role in epidemiology?	401
8.5.	Vaccination against myxomatosis	402
8.6.	Drug therapy for myxomatosis	403
8.7.	Pathogenesis studies in resistant rabbits	403
9.	Genetics of resistance	404
9.1.	Selection studies	404
9.2.	Sire effect	404
10.	Molecular basis of pathogenesis	404
10.1.	Virulence and host-range genes	404
10.2.	Replication, assembly and exit from infected cells	406
10.3.	Poxvirus entry into cells	406
10.4.	Subversion of the host-antiviral response by MYXV	406
10.4.1.	Subversion of pattern recognition receptor signalling	406
10.4.2.	Inhibition of IFN activity	407
10.4.3.	Inhibition of caspase 1 activation and IL-1 β and IL-18	407
10.5.	Regulation of cell death	407
10.6.	Inhibition of effector cells of the innate and adaptive immune response	408
10.7.	Cell and host permissivity for MYXV replication	408
11.	Pathways of host–pathogen evolution	409
12.	Conclusions and further work	410
	Acknowledgements	410
	References	410

1. Introduction

The modern world has seen an ever expanding number of novel diseases of humans and animals (Jones et al., 2008; Keesing et al., 2010). Understanding and predicting the outcome of emerging pathogens is not easy and is likely to differ in each case. Infectious diseases such as malaria, smallpox, tuberculosis and bubonic plague have had a major impact on human populations and at least some infectious diseases appear to have influenced human gene frequencies (Dobson and Carper, 1996; Hill, 2006; Vannberg et al., 2011); the outcome of the current AIDS pandemic on human genetics can only be speculated. Good mammalian models for natural selection by pathogens are uncommon but there is one example of a massive biological experiment that was replicated on two continents, this is the release of myxoma virus (MYXV), the cause of myxomatosis, as a biological control for the European rabbit (*Oryctolagus cuniculus*) in Australia and subsequently in Europe (Fenner and Fantini, 1999). The shift in species, initial extreme virulence and subsequent host–pathogen coevolution, in a species with prolific reproduction and short generation time, plus the ability to undertake experimental studies in the same host species, made myxomatosis the classic paradigm for what happens as an emerging pathogen adapts to a new host. In particular, the nexus between virulence and transmission overturned the cosy idea that pathogens should adapt to cause minimal harm to their hosts (Anderson and May, 1982; Massad, 1987; Dwyer et al., 1990). More recently, molecular and genomic studies offer the prospect of understanding the molecular basis of this evolution.

This review firstly describes the natural history of MYXV, its use as a biological control and subsequent host–pathogen coevolution in Australia and Europe. It then turns to the pathogenesis of MYXV and the current knowledge of MYXV genes and the experimentally defined or inferred functions of the encoded proteins for pathogenesis. Finally, the current and future evolution of myxoma virus is briefly examined.

2. Natural history of myxoma virus

2.1. Myxomatosis

Myxomatosis was originally described following an outbreak of a novel lethal disease in laboratory rabbits at the Institute of Hygiene in Montevideo, Uruguay in 1896 (Sanarelli, 1898; Fenner and Ratcliffe, 1965), although the disease was apparently known to rabbit breeders (Aragão, 1927), and subsequently investigated following outbreaks at the Instituto Oswaldo Cruz in Brazil (Moses, 1911; Araújo, 1927; Fenner and Ratcliffe, 1965). These were European rabbits (*O. cuniculus*), the common domestic and laboratory rabbit, which are not native to the Americas. Sanarelli (1898) suggested that the disease was due to a virus, making myxomatosis one of the earliest diseases of animals to be associated with a virus. Sanarelli was unsuccessful at infecting other species, including humans, by inoculation of infectious material from the diseased rabbits although he believed that an inoculated dog developed mammary tumours because of the virus (Hobbs, 1928).

Clinical signs of myxomatosis in rabbits can be observed from about 4 days after infection with virulent virus, initially as conjunctival inflammation accompanied by an elevated rectal temperature; a raised cutaneous lesion at the inoculation site may be visible but in natural infections this may not be noticed. By 6 days, anogenital swelling is present and cutaneous papular secondary lesions can be seen on the face and ears; serous and later mucopurulent discharge from the nostrils and conjunctivae becomes increasingly prominent (Fenner and Ratcliffe, 1965; Best and Kerr, 2000). Rabbits with typical acute late stage myxomatosis 8–10 days after infection have a swollen head and face, swollen drooping ears, mucopurulent blepharoconjunctivitis with swollen, closed eyelids and mucopurulent rhinitis with occlusion of the nasal passages (Fig. 1A). There are multiple discrete cutaneous swellings (sometimes termed tumours or myxomas) ranging from a few millimetres to several centimetres in diameter over the body (Fig. 1B and D). The anogenital region is grossly swollen and

Download English Version:

<https://daneshyari.com/en/article/2510047>

Download Persian Version:

<https://daneshyari.com/article/2510047>

[Daneshyari.com](https://daneshyari.com)