Cardiomyopathy Syndrome (CMS) in Atlantic salmon

WP4. Literature review
WP 4. Deliverables

- Report in Norwegian
- Fact sheet in Norwegian
- Scientific review
- PP-presentation
Overview of review

- CMS - Cardiomyopathy syndrome
- PMCV - piscine myocarditis virus

Epidemiology
- Occurrence
- Reservoirs
- Transmission
- Risk factors

Prevention and control

Economy

Knowledge gaps
CMS - cardiomyopathy syndrome

- Severe cardiac disease affecting Atlantic salmon

- Occurrence
  - Norway
  - Faroe Islands
  - Scotland
  - Ireland
CMS - cardiomyopathy syndrome

- Onset and course of disease:
  - Typically second year of sea phase, but also earlier
  - Acute: Sudden high mortality
  - Chronic: Prolonged period of moderate mortality

Photo: Trygve Poppe
CMS – clinical signs

- None or signs of lethargy
- Signs of circulatory failure
  - Protruding eyes (Exophthalmia)
  - Ventral skin bleedings
  - Raised scales
- Internal findings
  - Ascites
  - Blood clots in the pericardial cavity.
  - Enlarged or ruptured atrium and/or sinus venosus = «Hjertesprekk»
  - Discoloured liver with fibrinous casts

Photo: Per Anton Sæther, MarinHelse AS

Photo: Brit Tørud, Norwegian Veterinary Institute
PMCV – piscine myocarditis virus

- **Similarities with Totiviridae family**
  - A family that infects protozoan parasites and fungi
  - Transmission during cell division, sporogenesis or cell fusion

- **Recently several more complex “toti-like” viruses**

- **Structure PMCV:**
  - *First toti-like virus found vertebrate host*
  - *Spherical ~50nm*
  - *Non-segmented ds RNA-genome*
  - *Non-enveloped (naked) → resistant (?)*

- **Biophysical properties:**
  - Unknown

*Totiviridae*

Swiss Institute of Bioinformatics (SIB) used with permission
PMCV – genome

- 6.688bp
- Three open reading frames (ORF1, ORF2 and ORF3)
  - ORF3: Exclusive for viruses infecting vertebrate hosts
    - Research is focused on the ORF3

Illustration: Aase B. Mikaelsen
NMBU
PMCV – genetic variation

- Homogenous population in Norway (one genogroup)
- Most divergent: 98.6% nucleotide identity
- Atlantic argentine 86% nucleotide identity
- Virulence factors:
  - Three positions on the ORF3 have been suggested

Illustration: Åse Helen Garseth, NVI
CMS & PMCV – diagnostic tools

- The CMS diagnosis is based on:
  - Clinical observations and autopsy
  - Histopathology
  - Differential diagnosis: PD and HSMI

- PMCV specific real-time PCR:
  - High correlation between virus load and pathological changes
  - Widely used for screening
  - Patent by Pharmaq Analytiq
In situ hybridization:
- Detects virus specific nucleic acids in fish tissue with histopathological changes
- Not used for routine diagnostics

ImmunHistoChemistry (IHC):
- Detects PMCV specific proteins
- Not available for routine use due to lack of antibodies

Cell culture:
- PMCV replicates in fish cell lines, but at too low levels, and too weak CPE.

Immunhistochemistry detects PMCV specific proteins by the use of labelled antibodies
Photo: Gulla et al. 2012
Reservoir PMCV:

- Farmed Atlantic salmon
- Farmed escapees
- Found in a few wild salmon*
- PMCV found in cleaner fish in Ireland
- Not found in environmental samples, but in mucus, faeces and salmon lice in infected cage

*A virus sharing 86 % nucleotide identity with PMCV has been found in Atlantic Argentine. Photo: Wikipedia
Transmission routes:

- Horizontal transmission
- Vertical transmission is under investigation
Risk factors

- Time in sea
- Size of population
- Infection pressure
  - CMS in neighbouring farms and distance
- CMS in previous cohorts
- HSMI in same cohort
CMS - prevention and control

- **Biosecurity**
  - Pathogen free stock
  - All-in all-out, fallowing
  - Infection pressure from neighbours
  - Time at sea
  - Cleaning and disinfection (robust)

- **Screening for PMCV (or CMS)**
  - Early detection
  - Before the fish is moved
Husbandry and Animal welfare

- Affected fish are fragile

- General advice:
  - Know your fish!
  - Avoid stress!
  - Early slaughter
  - On-site harvesting

- Delousing - mechanical methods - mortality
  crowding-pumping-flushing-brushing-elevated temperatures
Modulating host response

- Vaccination
  - Pharmaq is working on a vaccine
  - Lack of a cell line

- Selective breeding
  - Cardiovascular capacity
  - High heritability for resistance
  - QTL-selected eggs are available

- Feed
  - Lower lipid content and higher $\Omega-3/\Omega-6$ ratio (PUFAs)
  - Effect demonstrated in trials
Legislative control

- Not a notifiable disease

- The challenge:
  - CMS 1985
    - Limited occurrence
    - Unknown cause
  - Transmissible disease 2009
  - PMCV 2010
    - Disease and virus ubiquitous
CMS - economic impact

- > 100 cases per year

- 2000:
  - ~4.5-8.8 million €

- 2007:
  - ~25 million €

Not including costs for prevention and extra labour

Photo: Per Anton Sæther, MarinHelse
Knowledge gaps

- **PMCV:**
  - Characterize proteins that are coded for by the virus RNA
  - Understand mechanisms for infection and replication in the host
  - Develop cell culture

- **CMS:**
  - Pathogenesis
  - Factors that trigger disease development in infected fish
  - Can infected fish get rid of virus?

- **Transmission, prevention and control**
  - Can PMCV be transmitted vertically?
  - Virus reservoir (beyond the farmed salmon)
  - The importance of smolt from freshwater phase?
Read more about CMS and the project

http://www.fhf.no/prosjektdetaljer/?projectNumber=901118


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