

Human cardiovirus / Saffold virus

- a cause of serious invasive infections in children

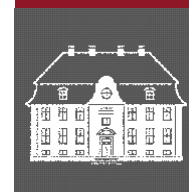
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Conclusion

Saffold virus was detected in the cerebrospinal fluid of two children. It is very likely that saffold virus was the cause of the neurological symptoms in the first patient, and was the direct cause of death in the second patient. The detection of saffold virus in invasive sample materials demonstrates the potential invasive nature of this virus in humans.

Introduction

In 2007 Jones et al discovered the first human cardiovirus, provisionally named saffold virus, by sequence-independent genomic amplification on virus isolated from a stool sample from an 8-months-old child with fever. Previously, cardioviruses were known to cause serious intracerebral infections in rodents. Subsequent attempts to find a correlation between saffold virus and various diseases have, until now, been unfruitful.

Objective

To investigate if saffold virus is an invasive pathogen in humans.

Methods

Diagnostic test: A newly developed real-time RT-PCR assay based on the alignment of available 5' UTR saffold virus sequences in GenBank - table 1.

Molecular typing: Newly developed nested VP2 and nested type 2 specific VP1 PCR assays were used prior to sequencing on an ABI automated sequencer using BigDye v1.1 (Applied Biosystems) chemistry - table 1.

Sample material

Cerebrospinal fluid (CSF) samples (n=332) from 319 patients ≤ 4 years-of-age submitted to Statens Serum Institut, Copenhagen, between January 2006 and December 2009 for viral diagnostics were selected for testing.

Results

Saffold virus was detected in CSF from 2 of the 319 children (spf268 and spf520) - table 2.

Both patients were found to contain saffold virus type 2 upon sequencing – figure 1.

Table 1 – Primer/ probe table

Assay	Sequence (5' -> 3')
Diagnostic RT-PCR	CTA WCA TGC CTC CCC GAT T
	GYT TAG ACC GGG GGA ACC
	TTT CTG CCC TGC TGG GCG G - Probe
VP2 typing	GAR ATG ACY AAY CTB TCW GAY AGA GT
	CCR TTR AAN ACS GGY TTN AC
	CGG CYA YAA ACA CKC AAT C
	TTD GCR TGY TGN GTC CA
VP1 typing - type 2 specific	GCA GAA AAA GGA AAG GTT GC
	GCA GAA AAA GGC AAA GTT GC
	TCT TGG RCA AAA CAC TCT CA
	CYA TAG CTC TTC CTG AAA AYC A
	TGR ACC GAA AAY CTG TCT GC

Table 2 – Patient information

Patient	SPF268	SPF520
Age	16 months	27 months
Sex	Male	Female
Prior medical history	None	None
Symptoms	Monosymptomatic ataxia preceded by fever	Found dead in her bed
Additional samples	Stool sample: Positive for saffold virus & human parechovirus type 3. Acute serum sample: Negative for saffold virus.	Acute serum sample & Myocardial biopsy: Positive for saffold virus.
Miscellaneous	MRI: A small venous malformation in the left frontal lobe. No signs of tumour, haemorrhage or inflammation.	Autopsy: Signs of cerebral incarceration. No signs of cerebral infection. Routine culture: No significant bacteriae.

Figure 1 – Phylogenetic tree

