Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 114; No. 5; P365

Genomic Evidence of SARS-CoV-2 Reinfection in Ireland

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Abstract

Presentation
A 40-year-old healthcare worker (HCW) presented with cough, headache, sore throat, fatigue and myalgia seven months after primary infection with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Symptoms were milder and recovery was faster on the second episode.

Diagnosis
Reinfection with phylogenetically distinct SARS-CoV-2 was confirmed by whole-genome sequencing (WGS).

Treatment
Management involved symptomatic treatment and self-isolation.

Discussion
The incidence of SARS-CoV-2 reinfection is not well characterised. Infection control precautions may still be required in healthcare facilities, even in previously infected and possibly in vaccinated individuals while SARS-CoV-2 remains in circulation. Further research on the nature and duration of immunity is required to inform public health and infection control policy.

Introduction

SARS-CoV-2 reinfection has been reported in a number of countries since June 2020. Hall *et a*l report a reinfection incidence density in UK healthcare workers (HCWs) of 3.3 per 100,000 person days.[1] To our knowledge, this is the first report of reinfection from Ireland.

Case Report

A 40 year-old female HCW presented with fever, headache, sore throat, shortness of breath and dysgeusia in April 2020. Her past medical history included mild asthma, with no known immunocompromise. Real-time reverse transcription polymerase chain reaction (qRT-PCR) analysis of a nasopharyngeal sample detected SARS-CoV-2 RNA (Table 1). While never hospitalised, she was unfit for work for four weeks due to significant headaches and persistent fatigue lasting four months. She reported no further sequelae. One of two household contacts also developed COVID-19.

Seven months later, she represented with cough, headache, sore throat, fatigue and myalgia. Symptoms were milder and she experienced a quicker recovery, remaining off work for the two-week period of self-isolation. She reports a post viral wheeze controlled with low dose inhaler. Of note, she had an asymptomatic screening test (nasopharyngeal swab qRT-PCR) 15 days prior to this episode in which SARS-CoV-2 RNA was not detected (Table 1).[2] SARS-CoV-2 was again detected by qRT-PCR in nasopharyngeal specimens, while other respiratory pathogens were not detected on further molecular analysis (Table 1). Viral RNA from both presentations was referred to the National Virus Reference Laboratory (NVRL) for WGS using the ARTIC v3 sequencing protocol.[3] Sequence data were acquired using the MinION platform (Oxford Nanopore Technologies, ONT). Raw sequences were assembled with the artic-ncov2019 pipeline and lineage identification was according to the PANGOLIN nomenclature.[4,5] Maximum-likelihood phylogenetic trees were built with RAxML (Figure 1). Nucleotide differences between the specimens and the Wuhan reference sequence identified by pairwise comparison locate both samples in differentiable lineages with high confidence.

Table 1. *Nasopharyngeal qRT-PCR results of a Healthcare Worker with SARS-CoV-2 Reinfection.*

	Specimen Date	Test Platform	SARS-CoV-2 Result
	19/03/2020	Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Roche	Not detected
Episode 1	04/04/2020$	Altona RealStar® SARS-CoV-2 RT-PCR Kit 1.0 (Roche	**Detected**
	29/10/2020	CerTest VIASURE SARS-CoV-2 (Roche Flow System)	Not detected
Episode 2	16/11/2020	CerTest VIASURE SARS-CoV-2, Flu & RSV (Roche Flow	**Detected***
	16/11/2020	ePlex RP2 (GenMark Diagnostics, Inc)	**Detected^**
	18/11/2020$	CerTest VIASURE SARS-CoV-2 (Roche Flow System)	**Detected**

***** *Flu A, Flu B and RSV not detected*

^ Adenovirus, Coronavirus (229E, HKU1, NL63, OC43), MERS Coronavirus, Human Bocavirus, Human Metapneumovirus, Human Rhinovirus/Enterovirus, Influenza A, Influenza A H1, Influenza A H1-2009, Influenza A H3, Influenza B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Parainfluenza 4, Respiratory Syncytial Virus A, Respiratory Syncytial Virus B, Bordetella pertussis, Legionella pneumophila and Mycoplasma pneumonia not detected
$- specimens referred for whole genome sequencing

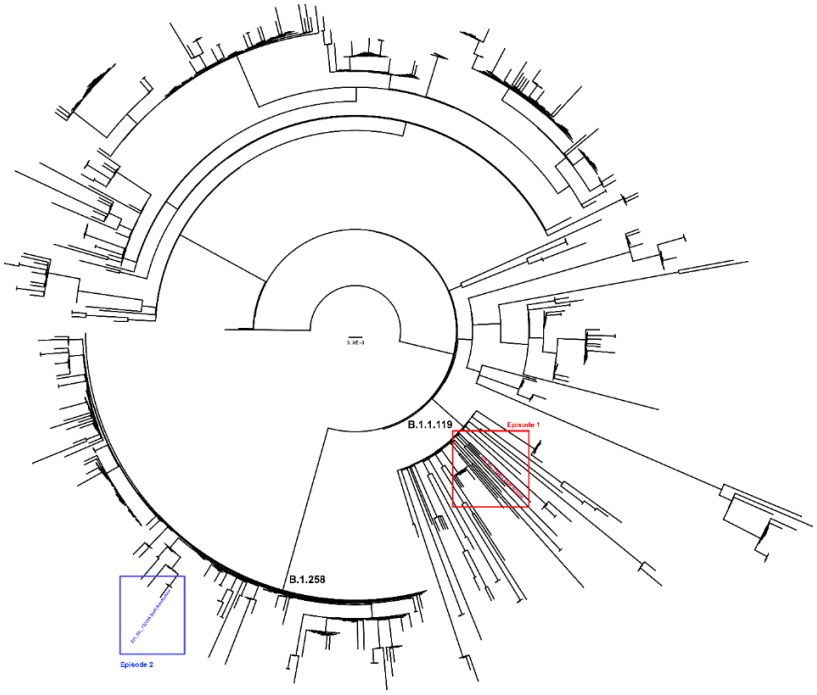

Figure 1: *Maximum likelihood phylogenetic tree drawn with RAxML, indicating where samples from Episode 1 (Red outline: Lineage B.1.1.119) and Episode 2 (Blue outline: Lineage B.1.258.2) fall in relation to other Irish SARS-CoV-2 sequences (n=628) and the Wuhan SARS-CoV-2 reference (MN908947). Sequences corresponding to this case are publicly available in the Global Initiative on Sharing All Influenza Data (GISAID) database and can be found with accession IDs: EPI_ISL_732441, EPI_ISL_732384.*

Discussion

To our knowledge, this is the first reported case of SARS-CoV-2 reinfection in Ireland. The consequences of SARS-CoV-2 reinfection are significant in HCWs due to the impact on service delivery and cross-infection to other HCWs and patients. The race to protect HCWs, prevent further deaths and to return to normal social and economic activity by establishing herd immunity through vaccination has begun worldwide. COVID-19 vaccines have shown efficacy rates of 70-95% in clinical trials; however, the effectiveness in populations overall and the durability of immunity is yet to be evaluated.[6] Lasting immunity to SARS-CoV-2 infection may prove not be universal in those previously infected or vaccinated. Preliminary data from a UK study of HCWs suggests that SARS-CoV-2 infection is associated with an 83% lower risk of reinfection, with the median protective effect lasting up to five months from primary infection.[1] While new variants with increased infectivity are being described; their potential for reinfection is as yet unknown.[7]

A number of publications of asymptomatic or pauci symptomatic reinfection in HCWs suggest that these individuals could potentially act as sources of cross-infection.[8,9] It is also widely accepted that pre-symptomatic transmission occurs. Despite awareness of and vigilance for symptoms, transmission may occur in the pre-symptomatic phase if appropriate precautions are not maintained.[10] This would suggest that current droplet, and where necessary, airborne precautions may need to be continued in healthcare facilities while SARS-CoV-2 remains in circulation. Further study into the level and duration of immunity conferred by both infection with, and vaccination against, SARS-CoV-2 is required to inform future vaccination campaigns and infection prevention and control policy.

Declaration of Conflicts of Interest:

The authors have no conflicts of interest to declare.

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