Importance of the reversed halo sign for diagnosis of mucormycosis

We read with interest the Clinical Picture by Timothy Sullivan and Meenakshi Rona,[1] who reported the case of a 62-year-old immunocompromised patient presenting on CT a pulmonary lesion with an appearance compatible with the reversed halo sign. A transbronchial biopsy was done, and the final diagnosis was mucormycosis. The authors reported that the reversed halo sign is a non-specific finding, and that given the broad range of diagnoses associated with it, biopsy is necessary to establish the correct diagnosis. By contrast, other authors[2–4] have concluded that the reversed halo sign in immunocompromised patients is strongly suggestive of mucormycosis, and have even speculated about whether it is pathognomonic of this disease, especially in leukaemic patients with neutropenia.[3]

For more on the **ABCs system** see https://www.cdc.gov/abcs

We do not believe that the reversed halo sign is a pathognomonic sign of mucormycosis; although this disease is the most common cause of the reversed halo sign in immunocompromised patients, we would like to emphasise that other pulmonary diseases, such as invasive aspergillosis, organising pneumonia, and tuberculosis, also need to be considered as possible causes of the reversed halo sign in this population. Publications in the past decade have shown the usefulness of some morphological characteristics of the reversed halo sign for differential diagnosis. For example, the presence of nodular walls or nodules inside the reversed halo sign were found to strongly favour the diagnosis of active pulmonary tuberculosis over organising pneumonia. Another study, which aimed to identify CT findings that differentiate the reversed halo sign caused by invasive fungal infections from that caused by organising pneumonia, showed that the presence of reticulation inside the reversed halo sign, with an outer consolidation rim greater than 1 cm thick, is strongly suggestive of invasive fungal infections, particularly mucormycosis.[4] This concept has been widely accepted and confirmed in the medical literature.[5]

In conclusion, although the reversed halo sign is not pathognomonic of mucormycosis, careful analysis of its morphological characteristics might narrow differential diagnosis. Reticulation inside the reversed halo sign and a thick outer rim in an immunocompromised patient are strongly suggestive of mucormycosis. This conclusion is important because although definitive diagnosis should be biopsy based, the time from symptom onset to microbiological or histopathological assessment can be long. Thus, the presence of the reversed halo sign with these morphological characteristics should be sufficient for the early initiation of appropriate therapy, thereby improving outcome.

We declare no competing interests.

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$M1_{UK}$ lineage in invasive group A streptococcus isolates from the USA

Nicola N Lynskey and colleagues[1] reported that a hypertoxigenic clone of *emm*1 group A streptococcus ($M1_{UK}$), characterised by increased streptococcal pyrogenic exotoxin A (SpeA) production, has rapidly emerged in the UK since 2014. Large-scale genomic examinations of this $M1_{UK}$ clade indicated a single lineage in the global group A streptococcus genomic databases, with only one isolate identified in the USA in 2015.[1,2] We investigated whether the $M1_{UK}$ lineage has expanded in the USA since 2015 using data from the Active Bacterial Core surveillance (ABCs) system of the US Centers for Disease Control and Prevention.

From 2015 to 2018, 7366 cases of invasive group A streptococcus infection were identified by the ABCs system, and 6335 (86·0%) isolates were characterised by whole-genome sequencing.[3] Among the characterised isolates, 1052 (16·6%) were *emm*1. Mapping the sequencing reads against the M1 reference genome MGAS5005[4] identified ten isolates carrying all 27 single-nucleotide polymorphisms (SNPs) unique to the $M1_{UK}$ lineage and one isolate carrying 26 of these SNPs. The 11 isolates ($M1_{UK\_USA}$) clustered together with $M1_{UK}$ isolates randomly selected with R software (version 3.4.3) from a previous molecular mapping study[1] (figure), and their distances to the most recent common ancestor ranged from six to 23 SNPs. Analysis of phylogeny temporal structure suggested the ancestor had originated around June, 2012. Three $M1_{UK\_USA}$ isolates from New York state in 2016 differed from each other by a maximum of three SNPs, consistent with close transmission links within a disease cluster.

Between 2015 and 2018, the numbers of $M1_{UK\_USA}$ group A streptococcus isolates (and proportions