

Impact and Utility of Whole Genome Sequencing on a Cluster Investigation in Northeast Texas

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Background

A large cluster of tuberculosis (TB) was identified in northeast Texas, with cases diagnosed between January 2014 and January 2017. A total of 21 cases were identified, with 15 genotyped isolates. The particular strain was identified as G00617, a genotype associated with a prior outbreak in the same area in 2012.

The Texas Department of State Health Services Tuberculosis (TB) and Hansen's Disease Branch began a cluster investigation in October of 2016. A cluster investigation was initiated to determine whether these new cases were infected during the 2012 outbreak, or if these cases represented a new chain of transmission. However, the regional health department found this investigation was limited by cases outside the jurisdiction. Additionally, several cases in this cluster were poor historians. Whole Genome Sequencing (WGS) results were explored to refute or confirm suspected links both within this current cluster and the prior 2012 outbreak.

Methods

- Between January 2014 and January 2017, 15 genotyped cases were identified.
- After notification that G00617 was identified as a Large Outbreak of TB in the US (LOTUS) cluster in 2016 via the Tuberculosis Genotyping Information Management System (TB GIMS), G00617 was determined a high priority for cluster investigation.
- A LOTUS cluster is defined as 10 or more cases with matching genotypes in a 3 year window related by recent transmission.
- A conference call was held to collect readily available epidemiological data on cases and discuss any known association with 2012 outbreak.
- Data collected by the program, including infectious periods, known epi-links, and contact investigation findings were analyzed.
- After identifying commonalities, cases were re-interviewed to establish missing epi-links and assess for potential sites of transmission.
- Other jurisdictions with similar clustered cases were contacted for epidemiological data.
- WGS results for G00617 were provided by the Centers for Disease Control and Prevention to the state program and shared with jurisdictions to discuss findings and determine where to focus investigative resources.

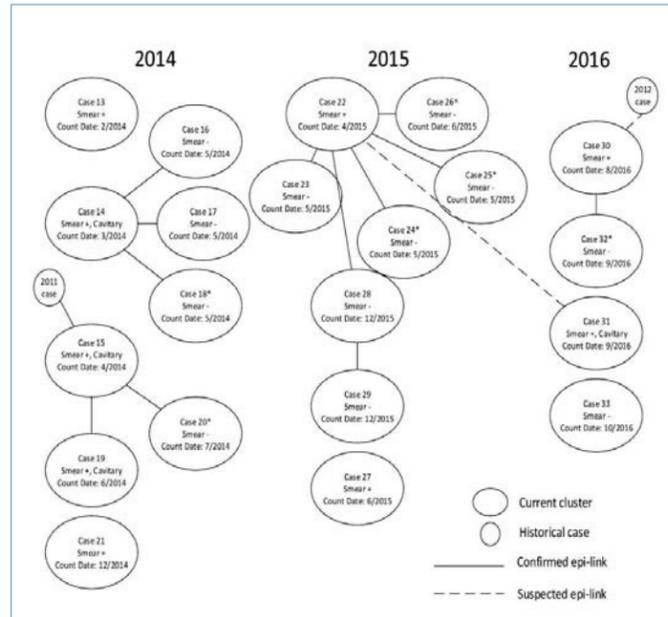


Figure 1: Confirmed and suspected epi-links prior to WGS
 ^ Single Locus Variant GENType, *Clinical case

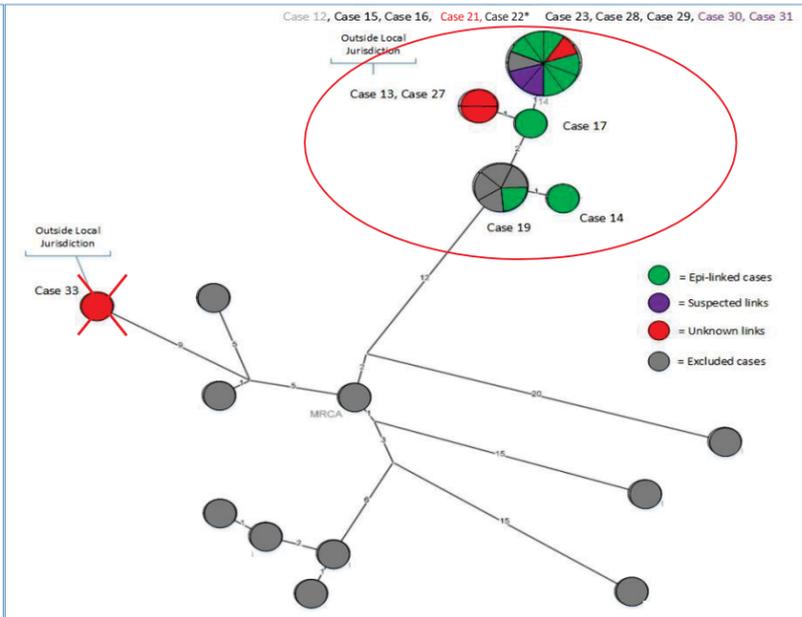
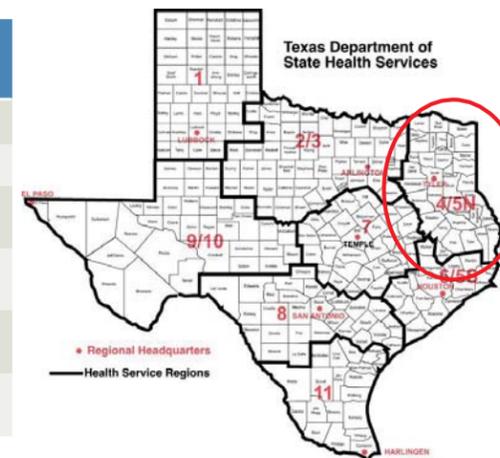


Figure 2: Phylogenetic tree representing WGS results of G00617
 *Index of current cluster

Case #	Epi-links before WGS	Epi-links after WGS	Outbreak Case before WGS?	Outbreak Case after WGS?
33	Unknown: Mentioned family in outbreak jurisdiction	N/A	UNK	N
31	Suspected	Contact to case is twin sister of contact to Case 22	UNK	Y
30	Unknown	Case was a poor historian and could not indicate contacts even after re-interview	UNK	Y
27	Unknown	Case was a poor historian and could not indicate contacts even after re-interview	UNK	Y
21	Unknown	Case was a poor historian and could not indicate contacts even after re-interview	UNK	Y
13	Suspected	Case was diagnosed in another jurisdiction, but mentioned being from the northeast TX region	UNK	Y

Figure 3: G00617 cases with unknown or suspected links before and after WGS



Findings

- Cases with similar characteristics to 2012 outbreak associated with poor treatment outcomes and recent transmission, including: homelessness, substance abuse, and a number of cases under five-years of age.
- Before WGS, 14 of 21 cases in current cluster had confirmed epi-links
 - 5 additional clinical cases identified via contact investigation
 - 1 Single Locus Variant (SLV) case identified with strong epi-links to cluster (ex-girlfriend of index case)
 - 2 suspected epi-links from patient interviews
 - 4 unknown links
- Of the four remaining cases with unknown epi-links, homelessness and substance abuse were identified as common risk factors
- Two of the 4 unknown cases lived outside the regional jurisdiction but indicated family ties to the regional jurisdiction
- After WGS, links were confirmed for 20 of 21 cases, an increase of 43 percent
 - The two suspected links were confirmed
 - Three unknown cases were nearly identical to other outbreak cases
 - The last unknown case, who indicated family in the northeast Texas area, was not closely related genetically

Conclusion

WGS confirmed familial transmission with an extended social network. One case outside the jurisdiction was ruled out of this outbreak. WGS was also able to confirm relatedness to the 2012 outbreak. The discriminatory power of WGS in TB control is far greater than traditional genotyping methods in that it can refute or confirm suspected epi-links. As evidenced by G00617, there is potential to focus investigations within a genotyped cluster to save limited resources, especially when dealing with large, cross-jurisdictional outbreaks.



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