

An outbreak of *Mycobacterium marinum* infection associated with handling seabass in China

Qing Zhao¹, Fangfang Bao¹, Zihao Mi¹, Zhenzhen Wang¹, Pengcheng Huai¹, Qing Pan¹, Zheng Pang¹, Yaoming Li², Nan Cao¹, Xiaotong Xue¹, Buyan Li¹, Xuechao Chen¹, Jinliang Wang¹, Yanxia Cui³, Wenqian Chang¹, Yuan Zhang¹, Zhenhua Yue¹, Yongxia Liu¹, Zhenhua Wang⁴, Weiguo Yan⁵, Jinyong Li⁶, Hongqing Tian¹, Xianmei Lu¹, Guizhi Zhou¹, Jianjun Liu⁷, Hong Liu¹, Furen Zhang¹

¹Shandong Provincial Hospital for Skin Diseases & Shandong Provincial Institute of Dermatology and Venereology, Shandong First Medical University & Shandong Academy of Medical Sciences, Jinan, Shandong 250022, China;

²Shangkou Hospital, Shouguang, Shandong 262732, China;

³Shouguang People's Hospital, Shouguang, Shandong 261000, China;

⁴Weifang People's Hospital, Weifang, Shandong 261000, China;

⁵Shouguang Hospital for Skin Diseases, Shouguang, Shandong 261000, China;

⁶Weifang Hospital for Skin Diseases, Weifang, Shandong 261000, China;

⁷Human Genetics, Genome Institute of Singapore, A*STAR, Republic of Singapore.

To the Editor: *Mycobacterium marinum* is a nontuberculous mycobacterium that can cause opportunistic infections in humans, ranging from a single cutaneous lesion to disseminated disease.^[1] It was first isolated from a fish in 1926 and identified as a cause of human infection in 1951.^[1] The estimated annual incidence ranges from 0.04 to 0.27 per 100,000 persons in different countries. Outbreaks of *M. marinum* infections related to handling fish are not common, but have also been reported.

On December 20, 2019, a dermatologist in Shouguang, Shandong Province, China, reported seven patients presenting with similar chronic plaques and nodules on their hands and forearms with a common history of being stabbed while handling fish through the infection surveillance system to Shandong Provincial Institute of Dermatology and Venereology (SPIDV). An outbreak of *M. marinum* infections was suspected based on the history of being injured by handling seabass and the clinical presentation. Thus, on December 23, 2019, investigators from SPIDV went to the township hospital in Shangkou, Shouguang, and initiated an investigation to identify additional cases and examine the etiological agent causing the disease.

Four interviews were conducted from December 2019 to April 2020. To determine the extent of this outbreak, all the rural doctors from 65 villages in Shangkou were notified of a potential outbreak of mycobacterial infection.

They were asked to inform people to visit the township hospital in Shangkou if they had been stabbed or handled fish with an open skin wound on their fingers or hands. Those individuals with skin or soft tissue infections (SSTIs) characterized by plaques, subcutaneous nodules, and ulcers, as well as deep tissue injuries to tendons, synovia, and joints were interviewed. With the approval of Ethical Committee of SPIDV (No. 20191221KYKTKS001) and written informed consent of each patient, the patients' demographic information, clinical data, and skin specimens were collected. We also interviewed the retailer who sold the fish to the villagers and collected suspected contaminated fish from patients and similar fish from six different markets in Shouguang. Laboratory testing included histopathology, acid-fast bacilli (AFB) staining, cultures, mycobacterial quantitative PCR (qPCR) analysis, and whole-genome sequencing (WGS) [Supplementary Figure 1, <http://links.lww.com/CM9/A996>].

A total of 217 patients presenting with SSTIs were interviewed and documented. Among them, 80% (173 patients) were women with a median age of 57 years (range: 26–82 years). Out of 180 samples, 161 (89%) showed infective granulomas, and 62 (34%) were positive for AFB staining. Furthermore, 149 (83%) out of 179 samples tested positive for mycobacterium qPCR, and 64 (36%) culture specimens were positive.

Correspondence to: Furen Zhang, Shandong Provincial Hospital for Skin Diseases & Shandong Provincial Institute of Dermatology and Venereology, Shandong First Medical University & Shandong Academy of Medical Sciences, 27397 Jingshi Road, Jinan, Shandong 250022, China
E-Mail: zhangfuren@hotmail.com

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According to the diagnostic criteria [Supplementary Appendix, <http://links.lww.com/CM9/A996>], 157 confirmed, 56 probable, and 4 suspected cases were identified [Supplementary Table 1, <http://links.lww.com/CM9/A996> and Supplementary Figure 2, <http://links.lww.com/CM9/A996>].

The interviews revealed that all 217 patients had purchased seabass from the same retailer in Shangkou in August 2019. Of these patients, 212 (98%) recalled being stabbed with seabass spines or handling whole seabass with an open skin wound. Symptom onset in 212 patients (98%) was between August 2019 and March 2020 and a peak of 35% (75 patients) was seen in October 2019 [Supplementary Figure 3, <http://links.lww.com/CM9/A996>]. The median length of the incubation period was 10 days (range: 0–140 days).

The fish retailer reported purchasing 2854.5 kg seabass from a fishing vessel in Yangkou, Shouguang, which

caught the fish from the Bohai Sea. All the seabass were sold to villagers of Shangkou for the Mid-Autumn Festival, 2019. We checked 14 suspected contaminated seabass provided by patients and six fish bought from markets. No lesions were observed on the body surface or in internal organs. However, they were significantly shorter and thinner than the healthy control fish, and the gills of the 14 seabass were khaki whereas the gills of healthy controls were bright red [Supplementary Figure 4, <http://links.lww.com/CM9/A996>]. Twelve (86%) fish obtained from patients were positive by qPCR analysis for *M. marinum* and six (43%) were positive by culture. Water from the Bohai Sea, ice from the refrigerator in the fish shop, and six control fish were free of *M. marinum* by qPCR and culture analysis.

WGS and the analysis of average nucleotide identity were performed using 71 isolates (57 from patients in this outbreak, two from sporadic unrelated patients, and 12 from six infected fishes) and nine published strains,

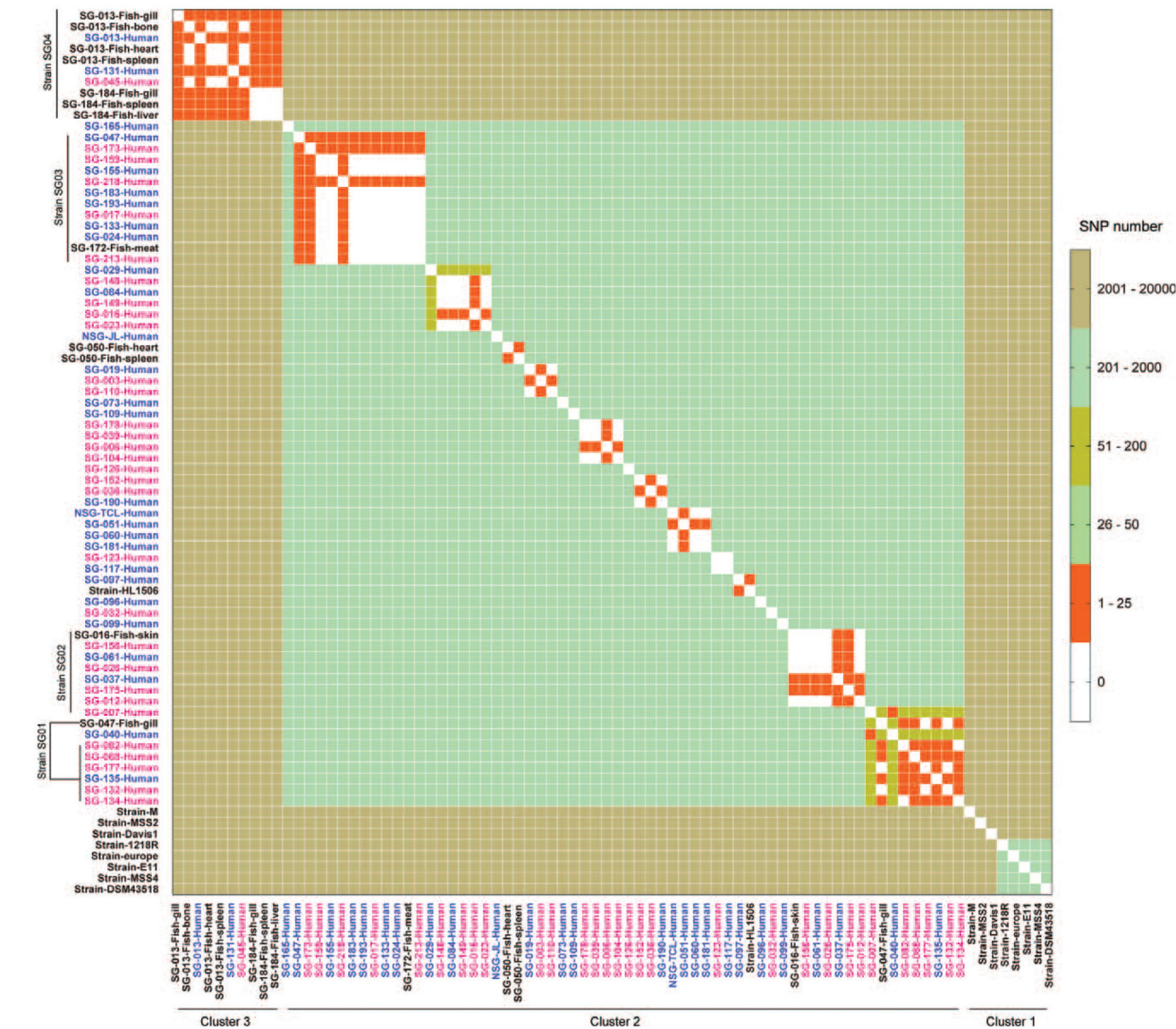


Figure 1: Core SNP between each pair of strains. Four strains (SG01, SG02, SG03, and SG04) were shared by both patients and fish. SNP: Single nucleotide polymorphism.

including strain HL1506 isolated from farmed seabass from China.

We identified that all the isolates could be classified into three clusters [Supplementary Figure 5, <http://links.lww.com/CM9/A996>]. Cluster 1 consisted of five “Aronson”-type subspecies and three “M”-type subspecies, which were isolated from the USA, Europe, and Israel.^[2] Cluster 2 contained 54 isolates from the patients in this outbreak, two from sporadic unrelated patients, five from infected fish, and the strain HL1506. Cluster 3 only contained three isolates from patients and seven from fish. The result of online blasting using the EzBioCloud database indicated that all isolates were *M. marinum* [Supplementary Figure 6, <http://links.lww.com/CM9/A996>].

To further analyze the genetic similarity among individual isolates, we performed a single nucleotide polymorphism (SNP) analysis. According to the established methods for SNP comparison,^[3] all isolates in cluster 3 were the same strain [Figure 1]. In contrast, isolates in cluster 2 originated from 22 strains, and the isolate SG_097_Human and the reference isolate HL1506 were the same strain. Four strains (SG01, SG02, SG03, and SG04) were shared by both patients and their fish, providing strong evidence for transmission from seabass to patients.

M. marinum was first recognized in humans as swimming pool granuloma due to infection in swimmers. With the rapid development of fish farming and the ornamental fish industry, the risk of infections from handling fish has increased. Two outbreaks related to handling fish, involving 18 and 98 patients,^[4,5] were reported in the past two decades. However, the fish that caused these two outbreaks were not identified or investigated.

Our study has identified a polyclonal outbreak of *M. marinum* infections involving 217 patients in China. Integrating WGS data with focused epidemiological investigations confirmed transmission from seabass to patients. However, the total number of patients in this outbreak could be undervalued due to individuals with asymptomatic or mild infections.

Our findings have implications for clinical and public health responses to outbreaks and prevention of *M. marinum* and the management of this disease. Individuals should wear puncture-resistant gloves or avoid handling seafood with an open skin wound.

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Conflicts of interest

None.

References

1. Bhatti MA, Turner DP, Chamberlain ST. Mycobacterium marinum hand infection: case reports and review of literature. Br J Plast Surg 2000;53:161–165. doi: 10.1054/bjps.1999.3245.
2. Das S, Pettersson BMF, Behra PRK, Mallick A, Cheramie M, Ramesh M, et al. Extensive genomic diversity among Mycobacterium marinum strains revealed by whole genome sequencing. Sci Rep 2018;8:12040. doi: 10.1038/s41598-018-30152-y.
3. Bryant JM, Grogono DM, Greaves D, Foweraker J, Roddick I, Inns T, et al. Whole-genome sequencing to identify transmission of Mycobacterium abscessus between patients with cystic fibrosis: a retrospective cohort study. Lancet 2013;381:1551–1560. doi: 10.1016/S0140-6736(13)60632-7.
4. Feng Y, Xu H, Wang H, Zhang C, Zong W, Wu Q. Outbreak of a cutaneous Mycobacterium marinum infection in Jiangsu Haian, China. Diagn Microbiol Infect Dis 2011;71:267–272. doi: 10.1016/j.diagmicrobio.2011.07.003.
5. Yacisin K, Hsieh JL, Weiss D, Ackelsberg J, Lee E, Jones L, et al. Outbreak of non-tuberculous mycobacteria skin or soft tissue infections associated with handling fish - New York City, 2013–2014. Epidemiol Infect 2017;145:2269–2279. doi: 10.1017/S0950268817001066.

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