Report on “Radiation Disaster Recovery Studies”

Course Radiation Disaster Medicine
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○Regarding “Radiation Disaster Recovery Studies”

On March 11, 2011, the Great East Japan Earthquake occurred. This disaster was an unprecedented disaster, combining the aspects of an earthquake, tsunami, and a radiation disaster. Through “Radiation Disaster Recovery Studies”, we have learned many things about radiation disasters. We learned that recovery from a radiation disaster takes a long time and that there are many factors that contribute to this.

First of all, in a radiation disaster, we have a fear of radiation. This fear is exacerbated by the fact that radiation is invisible and that its effects on the body are almost unknown. This has led to people being forced to evacuate due to concerns about their own and their families' health, and has also led to the spread of rumor-based damage that is not based on accurate information. This rumor-based damage has had an impact on important industries in the region, such as agricultural and marine products, and has become an obstacle to recovery. In order to solve this, it is necessary to disseminate accurate information about Fukushima based on science and to spread correct knowledge about the effects of radiation.

Secondly, in order to recover from the radiation disaster, decontamination is necessary before houses and infrastructure can be restored. In fact, the area around the Fukushima Daiichi Nuclear Power Plant had high levels of radiation immediately after the disaster, and was designated as an evacuation zone for a long period of time, making it impossible for residents to return. Recovery requires not only the removal of rubble from the disaster, but also the decontamination of the soil, which takes many years, resulting in the long-term evacuation of residents after the disaster.

As the years went by, decontamination progressed, evacuation orders were lifted one after another, and commercial facilities, transportation infrastructure, and educational facilities were developed, but the problem of residents not returning continued. The areas surrounding the nuclear power plant were often places with a high proportion of elderly people and few young people even before the disaster, but after the disaster, the

number of young people disappeared even more, accelerating the aging of the population. Compared to young people, elderly people have a stronger attachment to their hometowns, a stronger desire to return home, and relatively few health concerns about radiation, so the proportion of elderly people returning is relatively high. On the other hand, young people tend to be hesitant to return because the long recovery period had established a life base in the area they moved to, such as schools and workplaces, and they are concerned about the system of employment, education, commercial facilities, and medical facilities after returning, as well as relatively high concerns about the effects of radiation on their children, which led to them not returning to their original areas even after the evacuation orders were lifted.

Residents also seemed to be concerned about medical care. In February 2021, I had the opportunity to work as a doctor at the Futaba Medical Center Hospital in Tomioka Town, Futaba-Gun. Futaba-Gun is the area closest to the Fukushima Daiichi Nuclear Power Plant, and its population before the disaster was about 73,000, but has since decreased to 13,000, and it is one of the areas where residents have not returned. However, as the area recovers from the disaster, more and more residents are gradually returning, and it is expected that medical needs will increase in the future.

The hospital was well-maintained and well-equipped. However, there were only two full-time doctors, and many nurses and paramedical staff were sent from other areas and prefectures. In addition, there were no hospitals in the Futaba medical district that could perform advanced procedures such as surgery, so patients in this situation had to be transferred to other areas, about 40-50 minutes away by helicopter. There were also no specialists in pediatrics or obstetrics, and there was a shortage of day care services, nursing care services, rehabilitation facilities, and long-term care facilities.

According to a survey posted on the Tomioka Town website, about half of the residents were considering returning. The reason they were not returning was due to concerns about the medical system, which outweighed concerns about radiation levels, commercial facilities, transportation infrastructure, education, and work. This shows that improving the medical system is also an important condition for recovery from the radiation disaster.

In this way, recovery from the radiation disaster requires a multifaceted approach and will take a long time. In order to allow residents to live in peace, many issues need to be resolved, such as improving the environment through decontamination, developing

infrastructure, improving living conditions, and providing medical and welfare services, as well as increasing content that will make it easier for young people to return and spreading accurate information to eliminate harmful rumors.

○Title of Doctoral Thesis

Genomic characterization of *Staphylococcus aureus* isolated from patients admitted to intensive care units of a tertiary care hospital: epidemiological risk of nasal carriage of virulent clone during admission

○Summary of Doctoral Thesis

Background

Methicillin-resistant *Staphylococcus aureus* (MRSA) is often associated with invasive infections, such as ventilator-associated pneumonia (VAP), catheter-related bloodstream infection (CRBSI), surgical site infection (SSI), and wound infection, in trauma patients admitted to intensive care units (ICU).

Furthermore, treatment of *Staphylococcus aureus* (*S. aureus*) infections is also important in emergency radiation medicine. This is because patients exposed to high doses of radiation can develop acute radiation syndrome, and bone marrow suppression can cause the patient to fall into an immunosuppressed state, or damage to the skin and mucous membranes can cause the defense mechanisms to collapse, making it easier for bacteria to invade. *S. aureus* in particular is an important bacterium that is the main target in such cases. Therefore, studying the toxicity of *S. aureus* is very important in emergency radiation medicine.

S. aureus displays diverse genotypes, and the genotypes of major clones differ between countries. Molecular epidemiology studies may be useful for risk assessment or treatment selection, however, few large-scale epidemiological studies on *S. aureus* infection in ICU are available, and no such study has been conducted using whole-genome sequencing data.

Then, we conducted a molecular epidemiological study using the whole-genome sequences of isolates collected via nasal screening patients admitted to the ICU in a teaching hospital. To highlight high-risk clones in the ICU, we compared the relationship between genotypes and virulence determinants of isolates causing infectious diseases and those from in-patients without infectious diseases.

Result

The nasal carriage rates of MRSA and Methicillin-susceptible *Staphylococcus aureus* (MSSA) in ICU patients were 7.0% and 20.1%, respectively. The carriage rate of community-acquired (CA)-MRSA was 2.3%, accounting for 32.8% of all MRSA isolates.

Whole-genome sequencing analysis of the MRSA isolates indicated that most, including CA-MRSA and healthcare-associated (HA)-MRSA, belonged to clonal complex (CC) 8 [sequence type (ST) 8] and Staphylococcal cassette chromosome (SCC) *mec* type IV.

The predominance strains were similar for all classifications, including infectious strains, non-infectious strains, ICU-acquired strains, CA-MRSA strains, and HA-MRSA strains.

Compared with non-infectious strains, the proportion of ST764 and CC30 was higher in infectious strains, and the proportion of CC8 was higher in ICU-acquired strains. The proportion of SCC*mec* types I and II was higher in infectious strains. On the other hand, clones CC8, CC45, CC188, CC15, and CC30 were predominant in MSSA, and the proportion of CC8 and CC5 was higher in infectious strains compared with non-infectious strains.

We investigated the virulence factor genes (VFG) of the major STs that cause infection. ST8 MRSA mainly possessed *sec*, *tst-1*, *sel*, *sep*, and *se1*. ST8 MSSA possessed many genes, such as *sec*, *tst-1*, *sel*, *sea*, *seb*, and *sep*. MRSA/J and MSSA/J, which are highly virulent clones unique to Japan and possess *sec*, *tst-1*, *sel*, and *sep*, were carried by 37.3% and 20% of ICU patients, respectively. In contrast, the USA300 lineage (ST8-SCC*mec*IVa, *pvl* positive), a highly virulent clone commonly found in other countries, was not detected.

ST5 MRSA mainly possessed *sec*, *tst-1*, *seg*, *sei*, *sel*, *sem*, *sen*, *seo*, and *sep*. All ST764 were MRSA, and most of them possessed *psm-mec*, *seb*, *seg*, *sei*, *sem*, *sen*, and *seo*.
ST30 MRSA and ST30 MSSA possessed *seg*, *sei*, *sem*, *sen*, *seo*, and *seu*. ST30 MSSA isolates from infection sites had *tst-1*, and ST30 MRSA had *pvl*.

Infectious diseases included pneumonia (31.8%); skin and soft tissue infection (SSTI) (25.9%); deep abscesses, including infectious endocarditis and multiple abscesses (37.6%). Meanwhile, foci diseases caused by *S. aureus* included bacteremia (48.2%) and acute respiratory distress syndrome (ARDS; 23.5%), disseminated intravascular coagulation (DIC; 42.4%), and septic shock (42.4%). Multilocus sequence typing (MLST) and virulence gene results from genetic sequence showed that the proportion of ST8 was highest in all infection foci, including pneumonia, SSTI, and deep abscesses. Other notable findings were that the ST764 rate was higher in pneumonia than in other infections, and the ST8 rate was the highest in abscesses, with ST20 mainly seen in abscesses. MRSA/J and MSSA/J were the most prevalent isolates from deep abscesses.

Compared with those from nasal swabs of patients who did not present with *S. aureus* infection during their ICU stay, the isolates from infection foci showed higher rates of *mecA* and *psm-mec*. The isolates from patients with pneumonia showed significantly higher ratios of *psm-mec*, *sem*, and *pvl*. In contrast, isolates from SSTI revealed a statistically higher ratio of *seg*, *sem*, *sen*, *seo*, and *pvl*.

Furthermore, we assessed virulence factor genes associated with infectious diseases caused by *S. aureus*. Bacteremia was significantly associated with isolates positive for *seb*, whereas ARDS was significantly associated with isolates positive for *mecA* and *psm-mec*. In contrast, DIC was significantly associated with isolates positive for *tst-1*. However, no related virulence factor genes were detected during septic shock.

Conclusion

We conducted a molecular epidemiological study using the whole-genome sequences of isolates collected via nasal screening patients admitted to the ICU in Hiroshima university hospital, a teaching hospital. In addition, by comparing the relationship between *S. aureus* genotypes and the virulence factors they possess and clinical symptoms, it was suggested that ST8, especially MRSA/J and MSSA/J possessing *tst-1*, ST764 possessing *seb*, *mecA*, and *psm-mec*, ST5-MRSA possessing *tst-1*, and ST30-MRSA possessing *pvl* may be highly virulent clones. A considerable number of ICU patients were carriers of these high virulent *S. aureus* clones from their admission, and might be at risk of severe infection. Eradication targeting these clones may be a treatment strategy to reduce the risk of *S. aureus* infection after admission to the ICU