Mycobacterium Chimaera

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Mycobacterium Chimaera (MC) in recent years has shown a high infectious capacity via the aerosol by operating room equipment and represent a new frontier of medico legal aspect of nosocomila infections

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1. Introduction

Mycobacterium chimaera (MC) belongs to the large family of non-tuberculous mycobacteria (NTM), which are commonly found in the environment, especially in water. This particular type of mycobacterium was only identified in 2004, when Tortoli et al [1] carried out molecular tests and identified particularly aggressive, epidemiological characteristics that led to the proposal of a new taxonomic classification, *Mycobacterium chimaera*. The term *chimaera* is used due to its hybrid characteristics as compared with the more widely known mycobacteria [2][3] and similarity to *M. avium* and *M. intracellulare*; the name refers to the creature described in Greek mythology composed of the parts of different animals.

In subsequent years, references to MC in the literature from many parts of the world have increased; the mycobacterium has often been found in patients affected by respiratory problems among others, indicating rising dissemination on a global level [4][5][6][7][8][9][10][11][12].

The clinical manifestations of an MC infection can be varied and may include systemic and aspecific signs and symptoms, such as fever, asthenia, easy fatigue, and other more specific symptoms, such as the formation of emboli on cardiac valves or structures involved in surgery. These formations can then embolize and cause neurological, ocular and auditory damage [13][14]. The infection has a long latent period that can extend even beyond 70 months. On average, patients present with no symptoms until approximately 20 months [15][16], which makes diagnosis complex. To date, treatment with antimycobacterial drugs [17][18][19] is still uncertain and the mortality rate remains above 50% [20][21][22].

Although MC in water [23] is generally not dangerous to immunocompetent humans, since 2014 it has been indicated as a cause of infection in patients who have undergone heart surgery with exposure to contaminated heater–cooler units (HCU) [24]. Several patients have been affected by MC with a long incubation period following cardio-surgical operations, despite the small surgical opening in the chest [25][26][27][28][29][30].

Epidemiological studies have demonstrated a clear link between the infection and a specific HCU model: the 3T device manufactured by LivaNova/Sorin. In particular, the tests conducted at the manufacturing site revealed that the HCU water tanks and water present in the system pump assembly area were contaminated. Genetic investigations on the strains of MC on environmental and clinical isolates from patients from three different European countries showed almost identical genome sequences [31]. One study on the whole genome sequence of clinical isolates from patients infected with MC who had undergone open-heart surgery in hospitals in the USA showed few single nucleotide polymorphism differences [32]. Apart from this, there are no references in the literature to cases of infection associated with HCU devices produced by manufacturers other than LivaNova. These factors show the high probability that contamination occurs at the manufacturing site before the devices are dispatched to hospitals. The characteristics of MC enable it to lodge on the device and form a biofilm that is particularly resistant to the disinfection protocols in place. The assumption that contamination first begins in the production stage is supported by the fact that no other operating room equipment such as extracorporeal membrane oxygenation (ECMO) devices, though considered a potential source of infection, has been shown to have caused a patient to contract MC, and none of the studies has detected any contamination of the air in the environment [33]. This confirms the hypothesis that HCU contamination occurs during the manufacturing process.

In order to comprehend the infection mechanism, several studies have been conducted, the results of which show that the exhaust vent from contaminated HCUs can transmit contaminated aerosol to the surgical field by laminar airflow [34]. It has been demonstrated that the probability of NTM infection increases in proportion to the time the patient spends connected to a running HCU; surgeries that exceed 5 hours present a significant risk [35]. These findings suggest that the source of

infection is, therefore, the contaminated aerosol that, by means of insufflation, comes into contact with parts of the body exposed during surgery and that MC is able to lodge and create a thin biofilm on body structures, particularly cardiac structures, and manifest over long periods of time [36].

2. Discussion

The dissemination and danger of infections contracted in hospital settings represent a serious public health and medico–legal problem [37][38][39]. In recent decades, there has been an increase in awareness, thereof, due to the social and patient safety implications, an issue that, in Italy, was highlighted by the recent law on the safety of care. This law, no. 24/2017 [40][41], set forth the need to implement clinical risk management programs in all hospital settings to prevent the occurrence of such infections [42][43].

Cases of MC infection are particularly difficult and complex for various reasons: a) the time between infection and manifestation of symptoms is extremely long, and the clinical characteristics can vary greatly and are not yet fully understood and described in the literature; b) the characteristics of this particular mycobacterium, the route of infection and the symptomatological presentation are not widely recognized by doctors, who therefore tend not to suspect infection; c) many diagnostic tests for MC are slow and of low sensitivity; a DNA test is needed to confirm identification; d) the hospital infection route is very specific and occurs through routine processes employed within operating rooms; e) elimination of MC biofilms from surfaces by means of routine disinfection procedures poses significant difficulties.

The study of this specific mycobacterium is complex and further microbiological studies are required to be able to fully identify the transmission characteristics thereof and to measure the efficacy of the prevention measures that have been introduced. For the purposes of risk containment, the evidence considered highlights the need to monitor obsolete devices and arrange for replacements, along with the need to position the device outside the operating room using methods to prevent potentially contaminated aerosol from reaching the patient. In addition to these precautions, the use of safe water only in conjunction with uncontaminated devices can protect the patient. However, there is no significant evidence to warrant routine water and air sampling.

From a training perspective, much can be done. Training for all personnel actively involved in operating rooms is essential for ensuring maximum patient safety. Training healthcare professionals involves providing information, on the methods and presentation of MC infections, to all who work in cardiology and cardiac surgery departments, including cardiovascular perfusion technicians, radiology nurses, and technicians practicing in that department, in addition to primary healthcare and internal medicine physicians.

In order to comprehend the true extent of this silent global epidemic, it is essential to develop an organic preventative monitoring system for at-risk patients undergoing cardiac surgery and to conduct retrospective analyses in order to monitor closely patients who have been exposed to the risk of infection.

Identification of cases of infection cannot be left entirely to the ability of doctors; however, comprehensively and thoroughly trained and informed regarding MC, to arrive at a diagnosis from the symptomatology of an individual patient via laboratory tests. MC is an insidious bacterium because it has an aspecific symptomatology, an extremely late manifestation in relation to contact with the host in addition to a completely asymptomatic latent period. An isolated diagnosis of an individual case by an individual doctor is uncertain and, in any case, late as regards the probability of therapeutic success in the specific patient, the identification of the risk and the consequent prevention of other cases originating from the same source.

Since there is increasing evidence of the possibility of HCU contamination from various non-tuberculous mycobacteria, and other opportunistic pathogens and consequent dissemination via aerosol, it is appropriate that monitoring not be limited to MC infection, but extended to all these additional agents.

The general objective of such monitoring is to make a global contribution to the identification of infectious risks connected to the use of electromedical devices in cardiac surgery.

3. Conclusions

From a medico–legal point of view, MC infection represents a new frontier of hospital infection liability in that, not only are the preventative and diagnostic activities of doctors implicated, but also those of the manufacturer. Given this potential twofold liability, litigation involving MC infections requires careful medico–legal analysis, including an evaluation of the

quality and timeliness of measures the specific hospital has put in place in view of the recommendations issued by the supervisory boards. It would also be necessary to evaluate on a case-by-case basis whether the manufacturers and Ministry of Health's recommendations, if applied, were sufficient to counteract the infection effectively and reliably.

New knowledge on the topic of infections associated with electromedical apparatus has clear repercussions on both clinical risk management in regards to risk identification and elimination, and on medico–legal evaluations on healthcare liability, particularly in the context of reconstructing the causal link of infections with long incubation periods and modest clinical manifestations.

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