Tuberculosis and immunosuppression

Abstract

The immunosuppression caused by many factors such as malnutrition, autoimmune disease, HIV infection or immunosuppressive drugs has contributed to the increased incidence of tuberculosis (TB) in the world.

Keywords: tuberculosis, immunosuppression, HIV, transplanted patient, extrapulmonary

Mini review

The natural history of TB shows that most individuals are resistant to infection. Of the people exposed to \textit{M. tuberculosis}, between 10-30\% become infected, and in only 5 to 10\% of these individuals the infection progresses, transforming into active TB. The disease may be disseminated or localized in the pulmonary, lymph, renal, bone, or other organs.\textsuperscript{1} The period of infectivity depends on numerous factors, such as immunological status, age, gender, and location of the disease.\textsuperscript{2} However, in some circumstances, where imbalance occurs in the immune response of the host, there is reactivation of latent infection. This process can occur, for example, through HIV infection, malnutrition, use of steroids or other immunosuppressive medications or old age. Although the estimated risk of reactivation of the disease is between 2\% and 23\%, the risk for individuals immunocompromised by HIV infection is estimated to be high, 5-10\% per year.\textsuperscript{3}

Immunosuppression, whether due to an individual’s health status (malnutrition, autoimmune disease, liver cirrhosis, chronic kidney disease), human immunodeficiency virus (HIV) infection, or use of immunosuppressive drugs has contributed to the increased incidence of tuberculosis in the world. Among the causes of immunosuppression, HIV infection is more important in this context. Raising rates of co-infection with the HIV virus and tuberculosis bacillus poses challenges that prevent the reduction of the incidence of both infections. HIV has not only contributed to a growing number of TB cases, but has also been a major contributor to increased mortality among co-infected patients,\textsuperscript{4} and tuberculosis as the most prevalent opportunistic disease in infected individuals.\textsuperscript{5,6}

In susceptible immunocompetent individuals, the disease exclusively involves the lung in 85\% of cases. Population aging and increased use of immunosuppressive treatments represent risk factors for progression to active tuberculosis.\textsuperscript{7} In immunocompromised individuals, TB can often become a disseminated disease, with a higher frequency of extrapulmonary sites.\textsuperscript{8} Ganglionic TB is the second most common form of extrapulmonary tuberculosis and mainly compromises the cervical chain. The most frequent extrapulmonary sites of tuberculosis in childhood are the ganglion, pleural, bone and meningoencephalic.\textsuperscript{9}

Extrapulmonary tuberculosis is more common in HIV-positive patients, but will occur in about 15\% of immunocompetent patients.\textsuperscript{10} In transplant patients and in patients taking anti-TNF drugs tuberculosis presents in the extrapulmonary form or even disseminated by several sites, in about 25-48\%. It has been observed that asymptomatic patients develop tuberculosis infection during the clinical and laboratory routine of their immunosuppressive disease.\textsuperscript{11} In transplanted patients and in HIV patients with normal CD\textsuperscript{+} levels, radiological findings (focal and miliary infiltrates, nodules and pleural effusion) are characteristic of TB, as well as seen in immunocompetent individuals, but in patients immunocompromised by HIV with CD\textsuperscript{+} radiological exams present atypical and indeterminate.\textsuperscript{12} The clinical form of tuberculosis in patients with HIV usually presents in an unspecified way, and may be confused with other infections that affect this type of patient. Fever is a sign almost always present, much more frequent than in immunocompetent patients. The patient may present acute signs that last for hours to a few days of evolution that are confused with a classic bacetria infection, or present symptoms that last longer such as fever, adynamia, weight loss and anorexia. Symptomatology can affect the urinary system, central nervous system, lymph nodes and liver, although the most commonly affected site is the respiratory tract.\textsuperscript{13}

Immunocompromised people, such as organ recipients, or children under the age of 2 who receive chemotherapy, have a high risk of infectious complications. For example, the incidence of tuberculosis among transplanted patients is 20-74 times higher than in the general population, with a mortality rate of 21-33\%.\textsuperscript{12-14} Few studies report the incidence of TB in transplant patients.\textsuperscript{15-17} The incidence of TB in organ transplant recipients worldwide ranges from 0.35\% to 15\%.\textsuperscript{18} It is estimated that a transplanted patient has a risk of developing TB 50 times higher than the general population.\textsuperscript{19} The chance of developing TB in dialyzed patients is considerably higher due to uremia-induced immunosuppression, this risk is 10-25 times higher in these patients compared to the general population, and is independent of the status of TT (tuberculin test).\textsuperscript{19,20} Furthermore, patients on dialysis are generally the candidates for transplantation and latent disease can progress to the disease during immunosuppression imposed during kidney transplantation, i.e patients on hemodialysis have a high risk of TB reactivation.\textsuperscript{21} Tuberculosis in these patients can be difficult to diagnose and frequently presents in the extrapulmonary form.\textsuperscript{14} Previous studies suggest that there are high rates of PPD energy in patients in the final stage of renal disease,\textsuperscript{21,26} and in dialyses.\textsuperscript{23} The risk is increased between chronic renal failure,\textsuperscript{27,28} and increased even more when these patients undergoing transplantation are placed under immunosuppressive therapy.\textsuperscript{28} Most cases are found in the first year after transplantation,\textsuperscript{29} so they are likely to represent the progression from latent infection to active disease. Identifying these cases has a...
positive impact on the morbidity and mortality associated with this infection.30

Nosocomial transmission of TB has also been reported in long-term dialysis patients.31 Studies report an 8-fold increase in the incidence of tuberculosis in dialysis patients in relation to the general population.32 Detection of latent tuberculosis infection (LTBI) in this population is, thus an important issue, to prevent the progression to active tuberculosis and secondary contamination to other patients and health professionals.

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Conflict of interest

The author declares no conflict of interest.

References