Multifocal Tuberculosis in Immunocompetent Patients
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Abstract
Multifocal tuberculosis is defined as the involvement of two non-contiguous extra-pulmonary sites with or without pulmonary involvement. It is a rare but serious form that occurs mainly in immunocompromised patients. The aim of our work was to analyze the epidemiological, clinical and evolutionary features of multifocal tuberculosis in immunocompetent patients. For this we conducted a retrospective study of 67 cases of multifocal tuberculosis in immunocompetent patients, collected at the service of respiratory diseases of Ibn Rochd University Hospital of Casablanca over a period of 17 years. There are 45 women and 22 men. The average age was 32 years old. The average consultation time was 72 days. Recent tuberculosis was found in 33% of cases. The field assessment performed on all patients for possible immunosuppression was negative. Our patients had at least three associated disorders. Pulmonary tuberculosis was found in all cases. It was associated mainly with pleural involvement in 38.8% of cases, mediastinal lymph node in 23.8% of cases, peritoneal in 19.4% of cases and peripheral lymph node in 16.4% of cases. Patients were treated according to the recommendations of the national program against tuberculosis in Morocco. The evolution was favorable in 68.6% of the cases. We insist on the possibility of the occurrence of multifocal tuberculosis even in immunocompetent subjects. TB treatment should be started as soon as possible to avoid sometimes disastrous complications.

Keywords: Tuberculosis multifocal; immunocompetent; adult; extra pulmonary tuberculosis.

INTRODUCTION
Tuberculosis remains a public health problem, especially in developing countries such as Morocco. According to estimates by the World Health Organization, the number of all forms of tuberculosis cases in Morocco was about 31,542 in 2016 [1]. Multifocal lesions of tuberculosis are rare and represent 10% of cases [2,3] and occur most often in immunocompromised patients, especially those with HIV. However, this form of tuberculosis may be of interest even to immunocompetent individuals as is the case in our series. The objective of our study was to identify the epidemiological, clinical and evolutionary peculiarities of this form of tuberculosis.

PATIENTS AND METHODS
We report a descriptive retrospective study of 67 cases of immunocompetent patients followed in the pneumology department for multifocal tuberculosis over a period of 17 years from January 2002 to September 2019. The patients had no field of immunosuppression. They all benefited from an assessment comprising an HIV, hepatitis B and C serology as well as a renal, hepatic assessment and a primary immunodeficiency assessment. All of our patients also had good nutritional status.

The diagnosis of tuberculosis has been made in the presence of bacteriological and / or histological confirmation or a set of epidemiological, clinical, radiological and evolutionary arguments.

For each patient, we filled in a form that allowed us to collect epidemiological, clinical, radiological, bacteriological and pathological data as well as the treatments received and the evolution. Data was processed and analyzed using SPSS software.

RESULTS
In our series of 67 cases of multifocal tuberculosis, there was a female predominance of 67%. The average age of the patients was 32 years old with extremes ranging from 17 to 82 years old. All our patients were vaccinated with BCG. A recent tuberculous contagion was found in 22 (33%) patients. No history of tuberculosis has been found. Seventy-five percent of the patients were of low socio-economic status.
status and nine patients were smokers. The average time between onset of symptoms and first visit was 72 days with extremes ranging from 2 weeks to 4 months. Fever and alteration of the general condition were found in all cases. Tuberculin intradermal reaction (TDI) in all patients was positive in 48 (71%) patients.

All patients had at least three associated disorders. Pulmonary tuberculosis was found in all cases. The pulmonary lesions were of miliary type in 56.7% of cases, pneumonia in 17.9%, atelectasis in 14.9% and cavern in 10.4% of cases. It was associated with pleural involvement in 38.8% of cases, mediastinal lymph node in 23.8% of cases, peritoneal in 19.4% of cases, peripheral lymph node in 16.4% of cases. Splenic tuberculosis involved ten patients. Eight patients had tuberculous cold abscess from the wall, a surgical flattening of the abscess with bank biopsy performed in 7 patients. Seven patients had uro-genital tuberculosis. Cerebro-meningeal tuberculosis (Figure 1) was observed in six patients, five of whom had tuberculous miliary disease. Six patients had tuberculous pericarditis (Figure 2) confirmed by pericardial biopsy in 2 cases. The osteoarticular tuberculosis concerned 5 patients, it is a spondylodiscite in four cases. The cavum involvement involved two patients in our series. Psoas abscess associated with spinal involvement was noted in a single patient with percutaneous drainage (Figure 3).

Patients were treated according to the recommendations of the national tuberculosis control program in Morocco which is based on a poly-antituberculosis chemotherapy combining streptomycin, rifampicin, isoniazid, pyrazinamide and ethambutol according to the 2SRHZ / 7RH regimen. for cases diagnosed before 2011 and 2RHZE / 7RH for those diagnosed after. This follows the changes made on this program on this date. Oral corticosteroid therapy at a dose of 1 mg / kg / day for 4 to 6 weeks has been prescribed in patients with neuro-meningeal, pericardial or miliary hypoxemic disease with gradual dose depression. The evolution was clinically, bacteriologically and radiologically favorable in 68.6% of cases. One patient had a relapsing tuberculosis two years later, undergoing relapse treatment (2SRHEZ / 1RHEZ / 5RHE). We deplored two deaths, one in a respiratory distress chart secondary to pneumothorax complicating tuberculosis miliary, the other following multi-visceral failure secondary to disseminated intravascular coagulation (DIC) and eighteen patients were lost. of view.

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Fig-1: Cerebral CT scan showing multiple brain tuberculomas with peri-lesional edema

Fig-2: Chest X-ray showing a miliary appearance with rectitude of the left border of the heart related to tuberculous pericarditis

Fig-3: Lumbar MRI showing L2L3 spondylodiscitis associated with psoas abscess.
**DISCUSSION**

Although the tuberculosis death rate has decreased by 37% between 2000 and 2016, it remains the ninth leading cause of death in the world and the leading cause of death due to a single infectious agent in front of HIV / AIDS [1]. Extrapulmonary forms represent 20 to 40% depending on the series. Among extrapulmonary disorders, multifocal lesions account for 10% [3-5] and occur most often in immunocompromised patients and especially those infected with HIV. Mortality and mortality remain high. The field further aggravates the prognosis with a mortality rate of 16 to 25% [2].

In our series, patients did not present any particular terrain. They all benefited from a report in search of an underlying immunosuppression that proved to be negative. The spread of lesions can be explained by the delay in diagnosis that is often reported in African studies. In our patients the average time between the onset of symptoms and the first consultation was relatively long 72 days, probably related to the low socio-economic and cultural level of the patients. Undernutrition is also a risk factor for multifocal tuberculosis [6,7].

Thus Cathérinot described the syndrome of Mendelian susceptibility to mycobacterial infections (SSMIM) by the existence of a defect of the axis interleukin 12-interferon gamma, responsible for the occurrence of disseminated or recurrent tuberculosis despite the absence of favoring factors [8].

The concept of recent tuberculous contagion is found in 33% of our patients. In an endemic country like Morocco, a source of contagion almost always exists, but is often not reported by the patient.

After pulmonary involvement, the pleural and ganglionic localization were the most frequently observed in our series as well as in the various series of the literature [9,10], easily contributing to the diagnosis by its accessibility to the anatomo-pathological examination. Peritoneal and pericardial involvement were observed respectively in 19.4% and 8.9% of cases. These figures remain lower than those observed in the other series [11, 12]. Splenic tuberculosis involved ten patients. It remains one of the rare aspects of hematopoietic tuberculosis, even in countries with a high TB endemic such as ours [13,14].

The urogenital tuberculosis localization is associated with extrapulmonary disseminated disease in 18% of non-immunocompromised patients [15]. It is characterized by an often insidious but destructive evolution, resulting in irreversible sequelae. Hence the need to systematically search for this location to avoid often daunting complications including kidney failure. Osteoarticular involvement was noted in 7.4% of our patients, which is consistent with figures reported in the literature [16]. It is a location often under-diagnosed especially if it is inaugural sometimes explaining the diagnostic delay. Cerebro-meningeal tuberculosis was observed in six patients, five of whom had tuberculous military disease. This is the most serious form. The diagnostic confirmation is based on a set of epidemiological, clinical, biological and radiological arguments given the lack of sensitivity of the diagnostic means. Direct examination and culture of cerebrospinal fluid are only positive in 10 to 30% of cases [17]. Cutaneous tuberculosis interested two cases in our series. This form represents 2.1% of the localizations in the literature and remains a form with easy diagnosis [18]. Tuberculosis of the cavum is a rare localization, described by GRAFF in 1936 [19]. It concerned two patients in our series. Psoas abscess is a rare but known localization of tuberculosis. It is most often secondary to Pott’s disease, which dissects the surrounding tissues and forms an abscess by flowing along the psoas., more rarely to other intra- or retroperitoneal disorders, particularly digestive and urogenital ones.

Multifocal tuberculosis is usually serious and may involve functional or life-threatening prognosis, requiring early and prolonged treatment in order to avoid sometimes formidable complications. Our patients were treated according to the recommendations of the national program for the fight against tuberculosis in Morocco, which is based on a poly anti-tuberculous chemotherapy. It uses four major anti-bacillary drugs: isoniazid (H), rifampicin (R), pyrazinamide (PZA) and streptomycin (S) which has been replaced by ethambutol (E) from 2011. The evolution under treatment was favorable in the majority of our patients is 68.6% of cases. The mortality rate in our series was 3%. This figure remains lower than that reported in the literature which is 16 to 25% [2]. This difference could be explained by the peculiarity of our patients not presenting immunodeficient ground and also by the introduction of the DOTS strategy. Promiscuity and the low socioeconomic level are the main risk factors favoring the occurrence of tuberculosis in our context. Improvement of the living conditions of people at risk, health education, screening of those with close contact with a contagious case, treatment of sources of contamination and BCG vaccination are the essential means of combating this serious form of tuberculosis.

**CONCLUSION**

Through our study, we emphasize that an immunocompetent subject without risk factors can present a severe and multifocal form of tuberculosis. Also we insist on the systematic search for certain forms such as the urogenital or pericardial attack characterized by an insidious evolution, leading to irreversible long-term sequelae. The prognosis remains relatively good subject to early and prolonged treatment. We insist on prevention based on BCG vaccination and improving living conditions.
REFERENCES