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Profile of Extra-Pulmonary Tuberculosis in Internal Medicine

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Abstract

Introduction: Tuberculosis is an infectious disease that mainly affects the lung. Extra-pulmonary localizations are a reason for hospitalization in our health facilities. The objective of this study was to describe the epidemiological, clinical, paraclinical and evolutionary aspects of extra pulmonary tuberculosis (EPT) at the Abass Ndao Hospital Center. **Patients and Methods:** This was a descriptive cross-sectional study conducted over a period of 11 years (January 1, 2010 to December 30, 2021). All patients with extrapulmonary tuberculosis hospitalized in the department of internal medicine during the recruitment period were included. **Results:** Fifty-two (52) patients were collected. The year 2019 recorded the most cases 23.08% (n = 20). The mean age of the patients was 40.56 ± 18.24 years. The age group 20 - 34 years 42.31% (n = 22) was the most represented. Females were in the majority 61.54% (n = 32) with a sex ratio (M/F) was 0.63. Housewives were in the majority 40.38% (n = 21). 60.87% of the cases (n = 14) came from a health facility. 38.46% of the cases had been infected. 21.74% (n = 9) were smokers. The reasons for consultation were dominated by fever (67.44%), AEG (62.79%) and cough (41.86%). Eighteen patients (40.91%) had fever. The mean time to consultation was 77.37 ± 90.3 days with extremes of 3 and 365 days. The median was 45 days. More than half of the patients 61.90% (n = 26) had anemia. Positive retroviral serology was noted in 21.43% of cases. All patients had a CRP greater than 6. More than half of the patients 51.92% (n = 27) had multifocal tuberculosis. The peritoneum 44.23% (n = 23) was the main organ affected. The average hospital stay was 9.8 ± 4.9 days with extremes of 1 and 19 days. All patients had received the protocol in force at the national level. Death was noted in 4 patients (9.52%). **Conclusion:** EPT is characterized in our context by a notorious diagnostic difficulty due to the multiplicity of clinical presentations, the complexity of explorations, and the problems of

differential diagnosis notably with other granulomatosis, systemic lupus and cancers. This difficulty is reflected in the low rate of diagnosis with a paraclinical argument of certainty and in the long diagnostic delays.

Keywords

Extrapulmonary Tuberculosis, Epidemiology, Diagnosis, Senegal

1. Introduction

Tuberculosis is a contagious infectious disease of human-to-human transmission due to the pathogenic effects of bacteria of the Mycobacterium Tuberculosis complex [1] [2]. It is the most frequent specific bacterial infection with a preferential pulmonary location [3]. In Senegal, the national tuberculosis control programme has estimated the annual incidence at 117 per 100,000 inhabitants for the year 2020 [4]. The treatment success rate for new cases of bacilloscopy-positive tuberculosis is stationary around the target set at 90%. There is an upsurge in multidrug-resistant tuberculosis. Its prevalence was 11% among 128,836 cases of all forms of tuberculosis [5].

In addition to these pulmonary forms, extra-pulmonary tuberculosis (EPT) is a real diagnostic challenge. The diagnosis of extra-pulmonary tuberculosis is less easy, depending on the difficulty of obtaining material through invasive procedures (bone biopsy, cerebrospinal fluid, liver biopsy, etc.), and sometimes on the difficulty of bacteriological documentation (lesser bacterial inoculum). The diagnosis is most often presumptive, based on a range of clinical, radiological, histological and biological arguments, or even on a favourable evolution under anti-tuberculosis treatment, cultures sometimes remaining negative [6].

In sub-Saharan Africa, their prevalence varies according to the series and the country. Thus, Nganda *et al.* [7] in the Congo estimated it at 51.8% of all forms of tuberculosis. In Senegal, Diop *et al.* [8] reported 12.7% of extra-pulmonary forms among 824 cases of tuberculosis collected in the Thiès health district. Senegalese epidemiological data from 2009 and 2018 reported extra-pulmonary forms in 14% of 12,836 cases of tuberculosis. They require a search for a particular underlying terrain. This was mainly HIV infection [5].

In internal medicine, the EPT profile, sometimes atypical or even misleading, is a source of diagnostic error. Thus, the objective of this work was to describe the epidemiological, clinical, paraclinical and evolutionary aspects of extra-pulmonary localisations of tuberculosis in the Internal Medicine Department of the Abass Ndao Hospital.

2. Patients and Méthods

This was a cross-sectional, descriptive study, conducted over a period of 11 years

(from 01 January 2010 to 30 December 2021). We systematically recorded all cases of tuberculosis diagnosed in the internal medicine department of Medical Clinic II during the study period study. Among them, only cases meeting the criteria of EPT were included in our study. We used the WHO Definitions and Reporting Framework for Tuberculosis - 2013 Revision manual for case definition [9].

EPT represented any bacteriologically confirmed or clinically diagnosed TB case in which organs other than the lungs are affected (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges, etc.).

In our study, EPT was retained on the basis of definite proof of disease by demonstration of Mycobacterium Tuberculosis on bacteriological tests or by identification of a giganto-epitheliocellular granuloma with caseous necrosis. The presumptive diagnosis of EPT was made in cases where only indirect markers of high sensitivity were increased. These included GeneXpert, adenosine deaminase > 55 IU/L, tuberculin intradermal test (TID) and interferon-gamma release assay (IGRA) [10]. In these cases, the therapeutic argument was used to retain the diagnosis a posteriori.

A pre-established investigation form allowed us to collect data from direct questioning, a complete clinical examination and complementary explorations. The data required for the study were as follows.

- Epidemiological data: age, sex, history and terrain;

- Clinical and paraclinical data: reasons for consultation, consultation delays, inflammatory markers, renal and hepatic functional explorations, glycaemia and glycated haemoglobin, retroviral serology. The exploration of the topographical form of tuberculosis, as well as the assessment of extension, were carried out according to the profile. These included bacilloscopy, culture on Loweinstein Jensen medium, GeneXpert, adenosine deaminase (ADA) assay, IDRT > 15 mm, interferon-gamma release test (IGRA), tissue biopsies, morphological investigations (standard radiography, ultrasound, CT scan).

- Therapeutic data: we evaluated the type of anti-tuberculosis treatment, the duration of treatment and the evolutionary modalities.

Data analysis was performed with the following software: Excel 2016 and R version 4.1.1. In the descriptive analysis, categorical variables were described by their frequency. Quantitative variables were described by their position (mean) and dispersion (extreme) parameters.

3. Results

3.1. Epidemiological Data

During the study period, 114 cases of all forms of tuberculosis were recorded. Among these patients, extrapulmonary localization was found in 52 patients, *i.e.* a prevalence of 45.61%. The average age of the patients was 40.56 years with extremes of 16 and 84 years. The 20 - 34 age group was the most represented with 42.31% (22 cases). Females accounted for 61.54% of the cases with a sex ratio

(M/F) of 0.63. A history of tuberculosis infection was found in 38.46% of cases (20 cases) and 17.30% (9 patients) of patients were smokers. Positive retroviral (HIV) serology was noted in 21.15% of cases (11 cases) and diabetes mellitus in 5 patients (9.61%). Table 1 shows the epidemiological profile of our study population.

3.2. Clinical Data

The mean delay of consultation was 77.37 days with extremes of 3 and 365 days. The reasons for consultation were dominated by fever (75.00%), weight loss (71.15%), cough (38.46%) and abdominal pain (46.15%). More than half of the patients (61.53%) had clinical anaemia. Table 2 shows the distribution of clinical signs in our population.

Table 1. Shows the epidemiological profile of our study population.

Epidemiological data	Results
Number	52 cases
Prevalence among all cases of TB	45.61%
Mean age of patients	40.56 years
Women	32 cases (61.54%)
Sex ratio	0.63
Tuberculosis contact	20 cases (38.46%)
Diabete mellitus	5 cases (9.61%)
Tobacco use	9 cases (17.30%)
HIV positif	11 cases (21.15%)

Table 2. Distribution of clinical signs in our population.

Manifestations cliniques	Effective (n = 52)	Pourcentage
Fever	39	75.00%
Weight loss	37	71.15%
Cough	20	38.46%
Dyspnea	9	17.30%
Chest pain	7	13.46%
Abdominal pain	24	46.15%
Ascites	22	42.30%
Uncotrolable vomiting	6	11.53%
Anemia syndrom	32	61.53%
Adénopathy	10	19.23%
Headache	3	5.76%
Lumbago	1	01.92%

3.3. Paraclinical Data

All patients presented a biological inflammatory syndrome with an average C-reactive protein at 9.57 mg/l and a white blood cell count of 8254/mm^3. We found microcytic anaemia, mainly inflammatory (increased ferritinemia) in 44 patients (84.61%). Bacilloscopy was performed in 39 patients and found an acid-fast bacillus (Koch's bacillus) in 27 cases (51.92%).

GeneXpert was performed in 7 patients with 02 positive cases. Adenosine deaminase (ADA) was measured in 25 patients. A level higher than 55 IU/l was found in all cases (48.07%). Adenograms were performed in 10 patients. It found 7 cases of caseum and 03 cases of necrotizing adenitis. All were in favour of epithelial-gigantocellular granuloma with caseous necrosis. Table 3 shows the distribution of investigations performed in our patients.

3.4. Topographical Data of Lesions

Thus, 27 patients (51.92%) had both pulmonary and extra-pulmonary tuberculosis and the other 25 (48.08%) had an isolated extra-pulmonary form. Among the pure extra-pulmonary forms of tuberculosis, there were 11 cases (21.15%) of unifocal extra-pulmonary involvement and 14 cases (26.92%) of multifocal involvement. In the latter cases, tuberculosis mainly involved 02 organs (12 cases, 23.07%), 03 organs (2 cases, 3.84%). The predominant locations were peritoneal (44.23%, 23 cases), pleural (21.15%, 11 cases), lymph node (19.23%, 10 cases), neuro-meningeal (5.77%, 3 cases), pericardial (3.84%, 2 cases), hepatic (1.92%, 1 case), cutaneous (scrofuloderma) (1.92%, 1 case), disco-vertebral (Pott's disease) (1.92%, 1 case) (see Table 4).

3.5. Therapeutic Data

The average length of hospital stay was 9.8 days with extremes of 1 and 19 days. All patients had received the protocol in force at the national level. This treatment, developed in the 1980s, lasts 6 months for pulmonary forms. It comprises an attack phase combining RMP + INH + PZA + EMB for 2 months, followed by a maintenance phase using RMP + INH dual therapy for 4 months (2 RHZE/4RH regimen). The required dosages were rifampicin (10 mg/kg/day), isoniazid (4 - 5 mg/kg/day), pyrazinamide (20 mg/kg/day) and ethambutol (15 mg/kg/day). To improve compliance and accessibility of the drugs, a fixed combination of tablets is given to patients according to their weight. Vitamin B6 supplementation (10 - 25 mg/d) is indicated for pregnant women, malnourished patients, alcoholics, patients with pre-existing neuropathy, HIV-infected patients, diabetics, or patients with chronic liver or kidney disease. This treatment prevents neuropathy secondary to INH. In cases of extra-pulmonary tuberculosis, this duration of treatment must be continued beyond 6 months. Thus, it will be between 6 to 9 months in the case of lymph node tuberculosis and 9 to 12 months in the case of other extra-pulmonary forms. Death was noted in 4 patients (9.52%).

Table 3. Distribution of investigations performed in our patients.

Further investigations	Number (%)	Positive result (%)
Biologiques		
Blood count	52 (100%)	44 (84.61%)
C-réactive protein	52 (100%)	52 (100%)
Bacilloscopy	39 (75%)	27 (51.92%)
Tuberculin intradermal test	52 (100%)	40 (76.92%)
IGRA	03 (05.76%)	03 (100%)
GeneXpert	07 (13.46%)	02 (03.84%)
Adénosine déaminase (ADA)	25 (48.07%)	25 (48.08%)
Serum puncture	34 (65.38%)	34 (65.38%)
Histology		
Adénogram	10 (19.23%)	10 (19.23%)
Skin biopsy	01 (01.92%)	01 (01.92%)
Bone biopsy	01 (01.92%)	01 (01.92%)
Morphology		
Chest X-ray	52 (100%)	27 (51.92%)
Abdominal ultrasound	30 (57.69%)	22 (42.30%)
Lymph nodes ultrasound	10 (19.23%)	10 (19.23%)
Cardiac ultrasound	3 (05.76%)	2 (03.84%)
CT scan	20 (38.46%)	20 (38.46%)

Table 4. Topographical distribution of the different forms of tuberculosis.

Topographie des atteintes tuberculeuses	Effectif (n = 52)	Pourcentage
Topographie globale de la tuberculose		
Pulmonary + extra pulmonary	27	51.92%
Isolated extra-pulmonary	25	48.08%
Topographie de localisation extra pulmonaires		
Peritoneal	23	44.23%
Pleural	11	21.15%
Ganglionic	10	19.23%
Cerebro-méningeal	3	5.77%
Pericardial	2	3.84%
Vertebral	1	1.92%
Cutanous	1	1.92%
Hépatic	1	1.92%

4. Discussion

Although primarily considered a pulmonary disease, tuberculosis has the potential to infect almost all organ systems through lymphohematogenous dissemination during the initial infection. Extra-pulmonary tuberculosis represents an increasing percentage, reaching 20% - 40% of tuberculosis cases [1] [11]. We report 52 cases of extrapulmonary forms with a prevalence of 45.61%. This figure is close to the 51.8% reported in the Congo [7]. Extra-pulmonary tuberculosis can occur in isolation or in association with pulmonary involvement [1]. In our study, 51.92% of cases were associated with pulmonary involvement. Senegalese epidemiological data from 2009 and 2018 reported 128836 cases of tuberculosis, an extrapulmonary form in 14% of cases [5]. However, its frequency is assessed differently depending on the country, age group and sex. It appears to be more frequent in blacks, women and immunocompromised patients [1] [6] [11] [12]. We report a female predominance and an age range close to 40 years. This particularity of subjects under 40 years of age on average was already reported by other Senegalese studies [8] [12]. In a Tunisian series of 135 cases of EPT, the sex ratio was 1.7 and the mean age was 66 years. Almost 31% of patients had at least one immunosuppressive factor at the time of diagnosis [13]. The overall importance of diabetes remains to be determined. Studies in Mexico [14] and Indonesia [15] concluded that 18% to 25% of pulmonary TB cases were attributable to diabetes. As in our series, the clinical symptomatology remains diverse and variable. According to Faye *et al.* [12], fever (76.9%) and weight loss (72.5%) were the main clinical manifestations. According to the literature, the most frequent lesions were lymph nodes, pleural or osteoarticular [11] [12]. In the United States, a preponderance of nodal forms (41%) was found [16]. This predominance of lymph node location had already been reported in Tunisian [13] and Senegalese [12] series. However, the predominance of serous localizations, mainly peritoneal in our series and in the Senegalese series of Diop *et al.* [8], could be explained by the predominant gastroenterological orientation of these internal medicine departments.

Extra-pulmonary tuberculosis poses real diagnostic problems, partly because of its similarities with certain conditions such as lymphoma, sarcoidosis and lupus disease. This requires a fine semiological analysis and the justified use of complementary examinations. This has led to the characterisation of this disease as a great simulator. Another diagnostic difficulty concerning tuberculosis in the tropics is to be able to make the diagnosis with certainty. EPT is more difficult to diagnose than respiratory tract disease, as it is less bacillary [1] [11]. This difficulty is also notable in our study, where it was sometimes necessary to resort to therapeutic arguments. If confirmation is essential to comfortably start an anti-bacillary treatment. Among these tests of certainty, the contribution of bacteriology is constantly increasing thanks to technological progress. These include the microscopic observation drug sucesp-tiblity (MODS) technique, the nitrate reductase (NRA) test, and the colorimetric redox indicator (CRI) [17]. Histolog-

ical evidence of epithelioid and giganto-cellular granuloma with caseous necrosis is decisive [18]. Molecular biology with PCR gene amplification, the Xpert MTB/RIF (Gene-Xpert) has an interesting diagnostic contribution [16] [19] [20]. However, this confirmation is only obtained in 67% of cases of extra-pulmonary tuberculosis. This can be explained, in part, by the fact that the site is sometimes difficult to access [21]. In this context, molecular biology techniques can make a valuable contribution, particularly in speeding up the diagnosis, but their sensitivity is usually insufficient to exclude EBC [1] [11]. Immunological tests such as interferon-gamma release assays (IGRA), intradermal tuberculin reaction (IDRT) [22] [23], and adenosine deaminase activity (ADA) assay are often prescribed to support a PET scan. The latter test has a sensitivity of 100% and a specificity of 96%. However, adenosine deaminase activity can be elevated in cancers, and certain inflammatory or infectious diseases [24]. Thus, despite this multiplicity of diagnostic tools, the low rate of proof of the certainty of tuberculosis, particularly extrapulmonary tuberculosis, remains unaffected.

5. Limitations of Our Work

Prospective collection of data at the origin of the missing data.

6. Conclusion

Tuberculosis is a major public health problem in the world. Although pulmonary forms seem to pose fewer diagnostic problems, extra-pulmonary localizations pose 3 major problems: their recrudescence with the advent of HIV infection, the better knowledge of cases of autoimmune diseases and the increase in diabetes, the difficulty of having a paraclinical argument for a diagnosis of certainty, the problems of differential diagnosis with other alternative diagnoses.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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