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EPIDEMIO CLINICAL PRESENTATION AND THERAPEUTIC RESULTS OF ENT TUBERCULOSIS IN A MALAGASY HOSPITAL

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ABSTRACT

Introduction: Tuberculosis is a public health problem in endemic areas like Madagascar. Our objectives are to report the clinical, the epidemiological profile and the therapeutic results of the ENT localizations of tuberculosis. **Materials and Methods:** This is a prospective study carried out in the otorhinolaryngology and pneumo-phtisiology departments of the Professor ZAFISAONA Gabriel's University hospital of Mahajanga, Madagascar, from January 2016 to January 2019. It focused on patients aged 15 and over, who presented with otolaryngology and cervical tuberculosis. The parameters studied were the epidemiological, clinical, and therapeutic outcome variables. **Results:** We included 53 patients representing 13.9% of all tuberculosis patients, with a sex ratio of 1.3. The mean age (± standard deviation) was 33.01 (± 14.3) years. Promiscuity was found in 88.6% of cases, and the concept of contact with tuberculosis was present in all patients. Lymph nodes location was the most common (69.8%) followed by laryngeal location (13.2%). Other ENT locations were rare and tuberculosis of the salivary glands was absent. The evolution at 6 months of treatment was favorable in 75.4% of cases, while 18.8% were lost to follow-up. **Discussion:** ENT tuberculosis is not uncommon in our Tuberculosis endemic area. The clinical signs are misleading and borrowing those of tumor pathologies or

other infections of the ENT sphere. Educating patients about the treatment would have a better therapeutic outcome.

KEYWORDS: Lymphadenopathy, extra pulmonary, Madagascar, ENT, Tuberculosis.

INTRODUCTION

Tuberculosis is one of the most common causes of morbidity and mortality in the world. The number of new cases in 2018 per year is estimated to be 10 million worldwide, of which 1.2 million die from this disease (1). Most cases of tuberculosis are found mainly in Southeast Asia (44%) and Africa (24%). However, in recent years, thanks to the fight against tuberculosis, a reduction of 27% compared to deaths due to tuberculosis has been reported in HIV negative. But more than 95% of mortality and morbidity occurs in developing countries (2).

In Madagascar, out of the 26 million general population, tuberculosis reaches 233 people per 100,000 inhabitants with a mortality of 13,000 in 2018.

Pulmonary tuberculosis is the most frequently encountered clinical presentation. Out of a total of 1.68 million cases of tuberculosis identified, extra pulmonary tuberculosis represented approximately 16.36% of cases (1). They are responsible for 25% of the morbidity of tuberculosis in general (3). Among these extra pulmonary tuberculosis, the most frequent ENT manifestations are cervical lymphadenopathy and chronic laryngitis (4). Their prevalence is little known in Madagascar. Due to their unusual clinical presentation, the diagnosis can be difficult and their discoveries fortuitous, yet the delay in diagnosis contributes to the delay in treatment which darkens the prognosis of this pathology. The objective of this study is therefore to report the epidemiological and the clinical profile, and show the therapeutic results of the ENT localizations of tuberculosis.

MATERIALS AND METHODS

This is a prospective study carried out in the otorhinolaryngology and pneumo-phtisiology departments, treatment center for tuberculosis of all forms at the University Hospital Professor ZAFISAONA Gabriel (PZAGa) of Mahajanga, Madagascar. It was carried out over a period of 3 years from January 2016 to January 2019. Were included, male or female patients aged 15 and over, who presented with tuberculosis with Ear noise and throat (ENT) and cervical localization, confirmed by cyto or histological examination and who agreed to

participate in the study through consent. A survey based on a pre-established card was carried out in the presence of signs which pointed towards tuberculosis: chronic cough, weight loss, appetite disorder, fever, associated with ENT signs: swallowing disorders, chronic dysphonia, chronic otorrhea recurrent, suspicious swellings either during a fortuitous discovery of tuberculosis on histological examination.

The parameters studied were the epidemiological (age, gender, socioeconomic profile), clinical, and therapeutic outcome at 30 days, 60 days and 6 months of treatment. A complete ENT examination was performed. A histological or cytological sample confirmed the diagnosis. A chest X-ray with sputum test was systematically performed to look for associated pulmonary locations, as well as a biological assessment consisting of a hemogram, a hepatic and renal assessment, an HIV serology. The treatment of the patients followed the protocol of the national tuberculosis control program: the patients started a 2-month attack treatment with ethambutol (15mg / Kg), Rifampicin (10mg / kg), Isoniazide (5mg / kg), Pyrazinamide (25mg / kg), followed by a 4-month maintenance treatment of rifampicin and isoniazid at the same dose. The data was processed using Epi info 7.2 software.

RESULTS

During the study period, 53 patients among 379 tuberculous patients were included, representing 13.9% of the cases. The mean age (± standard deviation) was 33.01 years (± 14.3). The sex ratio was 1.03, i.e 27 men and 26 women. The location of ENT tuberculosis broken down by age of the patients is shown in Table 1. These patients occupied a profession requiring significant physical effort in 92.45% of the cases, or 49 patients. Patients living with more than 4 people under one roof represented 88.6% or 47 patients.

Table 1: Distribution of patients by age and location.

	Nodes	Oro pharynx	Naso pharynx	sinus	Larynx	Thyroid	Ear	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
15- 24 years	25 (85.3)	1 (3.5)	0	2 (7.1)	0	0	0	28(100)
25-39 years	7 (53.8)	0	3 (23.1)	0	3 (23.1)	0	0	13(100)
40- 49 years	5 (62.5)	0	0	0	0	1 (12.5)	2 (25)	8 (100)
≥ 50 years	0	0	0	0	4 (100)	0	0	4 (100)
Total	37 (69.8)	1 (1.9)	3 (5.6)	2 (3.7)	7 (13.2)	1 (1.9)	2 (3.7)	53(100)

A notion of contact with tuberculosis (contage, previous or in progress) was found in all patients. Table 2 represents the distribution of the medical history of the patients according to

the localizations of tuberculosis. A history of childhood BCG vaccination was reported in 44 patients (83.01%).

Table 2: Medical history of patients according to the location of ENT tuberculosis.

	Number of cases	Tuberculosis story	Smoking	HIV Infection	Anterior Tuberculosis	Tuberculosis in progress
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Cervical nodes	37 (69.8)	25 (67.5)	2 (5.4)	2 (5.4)	9 (24.3)	5 (13.5)
oropharynx	1 (1.9)	1 (100)	0	0	0	0
nasopharynx	3 (5.6)	2 (66.5)	1 (33.3)	0	1 (33.3)	1 (33.3)
nasosinus	2 (3.7)	2 (100)	0	0	0	0
Larynx	7 (13.2)	7 (100)	4 (57.1)	0	4 (57.1)	5 (71.4)
Thyroid	1 (1.9)	1 (100)	1 (100)	0	0	0
Ear	2 (3.7)	2 (100)	0	0	0	2 (100)
Total	53 (100)	39 (73.5)	8 (15.1)	2 (3.7)	14 (26.4)	13 (24.5)

Dysphagia and dysphonia were specific signs of damage to the larynx. The general condition was altered in patients with cervical lymphadenopathy (67.6%) followed by laryngeal locations in 17.6% of cases. Cough was mainly present in the forms of ENT tuberculosis associated with pulmonary tuberculosis. The distribution of physical signs according to the ENT localizations of tuberculosis is shown in Table 3. Lymphadenopathy was unilateral in 27 patients (92.9%). They were soft in 8 patients (21.6%), fistulised in 2 patients (Figure 1, 2). Laryngeal tuberculosis presented as ulcerative inflammatory lesions in 6 patients, and inflammatory budding in 1 patient. Oropharyngeal tuberculosis presented with chronic tonsillitis not responding to the usual treatment on an inflammatory lesion of the tonsillary mucosa. While nasosinus and nasopharyngeal tuberculosis were budding and inflammatory tumor lesions.

Table 3: Distribution of the physical signs of the patients according to the ENT localizations of tuberculosis.

	cervical nodes	Oro pharynx	Naso pharynx	Naso sinus	Larynx	Thyroid	Ear	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General condition deteriored	23 (67.6)	1 (2.9)	2 (5.8)	0	6 (17.6)	0	2 (5.8)	34 (100)
Lymphadenopathy	37 (92.5)	0	1 (2.5)	0	2 (5)	0	0	40 (100)
dysphagia	3 (10)	1 (10)	0	0	6 (60)	0	0	10 (100)
dysphonia	0	0	0	0	7 (100)	0	0	7 (100)
Nasal Obstruction	0	0	2 (100)	2 (100)	0	0	0	4 (100)
Localised swelling	0	1 (7.1)	3 (21.4)	2 (14.2)	7 (50)	1 (7.1)	0	14 (100)
otorrhea	0	0	1 (33.3)	0	0	0	2 (66.6)	3 (100)
Cough	5 (33.3)	0	1 (6.6)	0	7(46.6)	0	2 (13.3)	15 (100)
dyspnea	0	0	0	0	3 (100)	0	0	3 (100)
hemoptysis	2 (40)	0	0	0	3 (60)	0	0	5(100)

Figure 1: Fistulised adenitis of tuberculous lymphadenopathy.

Figure 2: Patient with ear tuberculosis associated with pulmonary tuberculosis.

A: Mastoid fistula

B: Chest x-ray showing his pulmonary tuberculosis

After 6 months of treatment, 40 patients (75.4%) saw their main clinical signs disappear while 10 patients were lost to follow-up. Cervical lymphadenopathy persisted in 2 patients at the lymph node locations of tuberculosis. A laryngeal sequelae of the persistent dysphonia type was observed in a patient with laryngeal localization of tuberculosis. Figure 3 represents the general evolution of the main physical signs during the 6 months of anti-tuberculosis treatment.

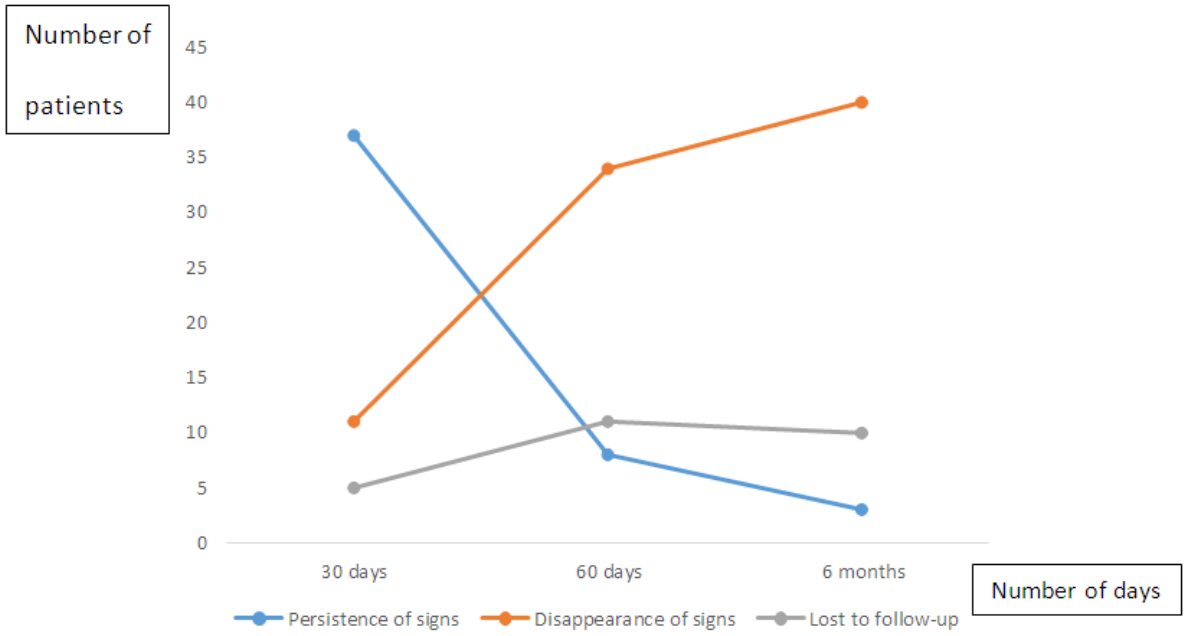

Figure 3: Evolution of functional signs during anti-tuberculosis treatment.

DISCUSSION

When it is not lymph node, tuberculosis of the ENT sphere remains rare. Its prevalence is around 5.6% of all tuberculosis worldwide, and 6.7% in sub-Saharan Africa.[5] This study found 13.9% of tuberculosis of the ENT sphere including the lymph node locations. Following the efficacy of anti-tuberculosis chemotherapy, there has been a significant decrease in the global incidence of tuberculosis.[1,4,6] On the other hand, the resurgence of extra pulmonary forms whose ENT localization of tuberculosis has been reported[4] following the increase in immunosuppression by HIV infection and precarious living conditions, especially in developing countries,[7,8] and the emergence of multi-resistant strains of tuberculosis bacilli.[9,10] Only 2 patients had an HIV infection in our series despite systematic screening in tuberculosis patients. The high frequency of promiscuity was one of the characteristics of the patients in this study, in relation to precariousness. ENT tuberculosis occurs in young people in developing countries like ours. The average age is 33 years in Morocco, Burkina Faso and Tunisia[9,11,12] while the peak frequency is between 25 and 65 years in the United States.[7] Exposure to the Tuberculosis bacillus is earlier and higher in developing countries due to poor social conditions such as work requiring significant physical effort in precarious living conditions.[13]

The notion of contact with treated or evolving tuberculosis is considered to be a factor furthering the occurrence of tuberculosis with an ENT localization.[14] All patients in this

study have had at least one contact with a tuberculosis patient or have concomitant pulmonary tuberculosis. Laryngeal and atrial localizations are most often associated with pulmonary tuberculosis,[4] which was the case in this study. The effectiveness of BCG vaccination is discussed in protecting against tuberculosis in adults. It rather protects against severe forms of infants and children, but in adults, its effectiveness varies from 0 to 80%.[15] While BCG vaccination is compulsory in Madagascar, this study presents 83.01% of childhood vaccinated patients who nevertheless have ENT tuberculosis.

In a meta-analysis of 57 studies of ENT tuberculosis, the cervical lymph nodes are the most affected by tuberculosis in 87.9% followed by the larynx in 8.7%. Tuberculosis of other ENT organs are rares.[16] In an Indian study, the most common site in their 211 patients was the cervical lymph nodes in 95.3% of the cases, followed by the middle ear at 2.8%, the larynx at 1.4% and the nasal cavity at 0.5%.[17] In this series, lymph node localization was the most frequent with 69.8% of cases, followed by laryngeal localization in 13.2% of cases and nasopharyngeal localization in 5.6%. Most studies therefore report that lymph node localization remains the most common.

The signs of deterioration of the general condition, present in ENT tuberculosis, are part of the classic bacillary impregnation signs of tuberculosis.[17] They constitute signs of referrals towards the presence of a tuberculous infection. Deterioration of the general condition was found in 67.6% of patients with lymph node tuberculosis and in 6 out of 7 patients with laryngeal tuberculosis, the latter was related to anorexia caused by dysphagia due to inflammation of the larynx. In addition, the clinical diagnosis of ENT tuberculosis remains difficult because this pathology can borrow the symptoms of other non-infectious malignant or benign diseases, or infectious diseases with an ENT localization.

Tuberculous adenitis develops after reactivation of quiescent bacilli of the lymph nodes most often or more rarely, after direct exposure to the infection.[16] The clinical presentation in the form of abscessed or fistulised adenitis reflects the delay in the treatment of tuberculous adenitis[18] and constitutes a diagnostic orientation criterion for tuberculous adenitis. These forms were found in 27% of primary tuberculous adenitis in this study. The prevalence of multiple unilateral cervical lymphadenopathy in this study has also been reported by some authors.[12,19] Other hand, cervical lymphadenopathy can translate other generalized pathologies, the research of which accelerates the diagnosis. In fact, the fear of malignant

pathologies responsible for superficial lymphadenopathy justifies a complete ENT examination associated with a histological examination of the primary lesion.[6]

Laryngeal tuberculosis appears to be fostered by smoking intoxication in 60% of cases.[9] This frequency was 57.1% in our series. Laryngeal localization most often occurs in the context of pulmonary tuberculosis because the larynx constitutes a gateway to the upper airways. Dysphonia is the main sign of this localization, calling for an endoscopic examination of the larynx, which will show clinical aspects in several confusing forms with larynx cancer. It is the anatomopathological examination with sputum test which allows the diagnosis of laryngeal tuberculosis and to eliminate the neoplastic pathology.[9,20] However, laryngeal or pulmonary tuberculosis can be associated with cancer of the larynx.[21,22]

The clinical signs of nasopharyngeal tuberculosis are similar to those of benign or malignant tumor pathologies of the nasopharynx, with nasal obstruction, epistaxis, rhinorrhea, unilateral cervical lymphadenopathy or signs of serous mucosal otitis. The radiological and endoscopic signs are in favor of a malignant process of the nasopharynx.[23] A histological examination is thus essential, allowing an often fortuitous diagnosis. Oropharyngeal tuberculosis remains dominated by tonsillitis and readily takes on a pseudotumoral appearance, most often of histopathological discovery.[21] The symptomatology is dominated by odynophagia and upper dysphagia. Clinicaly, the presence of an ulceration of the oropharyngeal mucosa or an asymmetric enlargement of a tonsil is generally noted.[24]

The clinical aspects of auricular tuberculosis are very misleading because these chronic signs lack specificity, often responsible for a delay in diagnosis. It presents in the form of suppurative otitis media, resistant to treatment with otoscopy an aspect of multiple tympanic perforations or a naked aspect of the promontory of which only the histological examination of a fragment of the mucosa of the ear average allows diagnosis.[25] The ear infections reported in this study were associated with pulmonary tuberculosis confirmed by radiography and sputum examination. Ahead the persistence of the otorrhea, a biopsy of the mucosa of the middle ear confirmed the diagnosis.

Thyroid localization of tuberculosis is a very rare form of extra pulmonary tuberculosis because of the defense mechanism of the thyroid gland.[26] There are many clinical presentations ranging from a simple nodular goiter,[27] through a goiter that increases rapidly in volume to the fistulated nodule[28] as in this study. It can be primary or secondary, in this

case associated with pulmonary tuberculosis. According to these clinical forms, thyroid tuberculosis poses a real diagnostic problem especially with other infectious thyroiditis and cancer and often remains of incidental diagnosis. Only histological examination confirms the diagnosis as in all ENT tuberculosis by showing an inflammatory granuloma with caseous necrosis. The other glandular localizations of tuberculosis were absent from this series.

The treatment of ENT tuberculosis is most often strictly medical, based on anti-tuberculosis drugs for at least 6 months, allowing favorable results.[9,19] ENT tuberculosis surgery has only a limited place in pseudo-tumor forms for the purpose of anatomopathological confirmation. In this study, the functional signs disappeared after two months of treatment. As a result of this relief, the rate of lost to follow-up treatment increases from this date, while stopping treatment favors the emergence of anti-tuberculosis resistant strains, thus furthering relapses and therapeutic failures. Reinforced education of patients on anti-tuberculosis treatment which is free in our country would limit these interruptions of treatment.

CONCLUSION

ENT-localized tuberculosis is not uncommon in our clinical practice. The clinical manifestations are atypical and varied and can appear as malignant or non-infectious pathologies of the ENT sphere. However, we must always think about it in the presence of the factors that cause tuberculosis and in our context of endemic area. Although conventional anti-tuberculosis treatment is effective against ENT tuberculosis, early diagnosis and education of patients over the long course of treatment is necessary to avoid treatment failures.

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