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Tuberculosis in adult patients with sickle cell disease☆

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Summary *Objective:* Although infection, in particular pulmonary infection, is a common complication of sickle cell disease (SCD) and although SCD is frequent in populations where the prevalence of tuberculosis is high, the relationship between the two diseases has never been studied. We conducted a study to assess the epidemiological and clinical pattern of tuberculosis in adult patients with SCD.
Methods: We retrospectively reviewed the cases of tuberculosis reported within our cohort of 457 SCD patients from January 1998 to April 2006 in the adult sickle cell center of Hôpital Tenon, Paris, France.
Results: We identified 12 cases of tuberculosis, 8 men and 4 women. There were 7 lymph node lesions, 3 pulmonary lesions and 2 vertebral lesions. The incidence of pulmonary and extrapulmonary tuberculosis was respectively of 82 and 246 cases per 100,000, to compare with an expected incidence of 184 cases, and 65 cases per 100,000. Three of the patients with lymph node tuberculosis were asymptomatic. No case of multi-organ involvement was seen. No other cause of immunodepression than the functional asplenia was found. All the patients showed clinical improvement under treatment.

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Conclusions: In SCD patients, lymph node tuberculosis appears to have a higher incidence than that in an epidemiologically comparable population, and has a rather indolent presentation and a favourable outcome. Pulmonary tuberculosis seems to be less frequent than expected.

Introduction

Tuberculosis (TB) remains an enormous global health problem worldwide. One-third of the world's population is estimated to be latently infected with *Mycobacterium tuberculosis* (*M. tuberculosis*).[1] In Sub-Saharan Africa, the prevalence of TB and sickle cell disease (SCD) are both particularly high. In SCD, impaired perfusion of blood vessels by sickled red cells leads to ischemia of the tissue supplied, and to the protean complications of the disease. Damage to the splenic vasculature leads to asplenia early in the first months of life, and therefore infection is a major complication of SCD,[2] and a common cause of death. Bone is the site of frequent local infarctions (that favour the occurrence of osteomyelitis). Chest involvement is frequent, consisting mainly in acute chest syndrome, infectious pneumonia, pulmonary hypertension, and lung fibrosis.[3] In West Europe, the greatest part of patients with SCD come from French West Indies, and above all from West Africa, where the prevalence of TB is high.

So, there are epidemiological, local (sequels of organ damage by vasoocclusion leading to alteration of local host defense)[4] and general (perturbations in immune system, malnutrition) conditions that could favor the development of TB in patients with SCD. Surprisingly, very little is known about TB in this population. The aim of this study was to supply data on incidence, patient's profiles, disease's specificity of TB within our population of patients with SCD. We reviewed our single institution experience between 1998 and April 2006 at the adult sickle cell center in Hôpital Tenon, Paris, France.

Methods

We reviewed the records of the 457 adult (age $\geq$ 18 years) patients with SCD evaluated in our institution between January 1998 and April 2006, to identify patients diagnosed with TB. No routine screening for TB was made during this time, and the patients were evaluated only after they became symptomatic. We used the database of positive *M. tuberculosis* cultures from the Microbiology Laboratory to assess the exhaustiveness of our research. The charts of these patients were retrospectively reviewed for the following data: sex, age, geographic origin, previous manifestations of SCD, BCG vaccine, clinical presentation, risk factors for TB infection, HIV status, management, and outcome. The diagnosis of TB was made on the basis of bacteriologic, or pathologic findings. A patient was considered to have TB if one of the following criteria was present: acid-fast bacilli on direct microscopy; *M. tuberculosis* detected in a culture of any clinical specimen; biopsy specimen showing caseating granuloma or non-caseating granuloma with a clinical response to antituberculous therapy specifically directed against *M. tuberculosis*. Patients in whom the sites of disease were exclusively extrathoracic were considered to have extrapulmonary TB. The date of TB diagnosis was defined as the date that antituberculosis therapy was initiated. The measure of the follow-up began at this date. The patients diagnosed with *M. tuberculosis* primary infection with no subsequent organ involvement were not included in the study.

Results

During the period under review, 457 patients with SCD were evaluated, and 12 cases of TB were found. The procedure that leads to the diagnosis of TB was bacteriologic in 8 cases, pathologic in 2 cases, bacteriologic and pathologic in 2 cases. In fact, there were 13 cases, but one was excluded by following reasons. He was said to have been treated for TB in another country in 1998, without precision about the history, the diagnostic procedures and the localisation. All the patients had been screened for HIV infection.

Patient' characteristics

These patients included eight males and four females, with a mean age of 22.6 $\pm$ 6.61 years (range, 17—39 years). Ten patients had homozygous sickle-cell disease, and two had sickle-cell/β-thalassemia (one had S/β^0 and one had S/β^+). No patient had sickle-cell/haemoglobin C. All the patients were of African or French West Indies ethnicity. Six of them were born in France (4 in the metropolitan France, 1 in Guadeloupe and 1 in Martinique). Their family origins were French West Indies for two, Mali for two, and Senegal for two others. The six other patients emigrated from Mali (two), Haiti (two), Cameroon (one) and Democratic Republic of the Congo (one). The mean number of years of residence in France for the foreign-born patients was 12 years (median, 15 years; range, 5—16 years). They all were living in the Paris area. No patient made a trip to his country of origin for a duration exceeding 1 month, in the 2 years preceding the diagnosis of tuberculosis. The mean age at diagnosis for the patients having a pulmonary and a extrapulmonary disease was respectively of 22.7 and 22.6 years, and the mean time from entry in France to the diagnosis of TB was 16 and 10 years. The number of cases of TB diagnosed each year was stable during the study.

Tuberculosis presentation

Three patients had pulmonary TB, seven patients had lymphatic TB, and two patients had vertebral TB. Characteristics of the cases of lymphatic TB are summarized in Table 1, and the cases of pulmonary and vertebral localisations in Table 2.

The clinical findings at the time of diagnosis were fever in seven patients (which was present in all three patients