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Description of the First Case of Mycobacterium tuberculosis Beijing Strain Isolated in Cameroon

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Authors' contributions

This work was carried out in collaboration between all authors. Authors FKK, SIE, FXE and JRFE designed the study, performed the statistical analysis, wrote the protocol, wrote the first draft of the manuscript and managed literature searches. Authors FKK, JRFE, LKA, JN, YKS, FFP managed the analyses of the study and literature searches. All authors read and approved the final manuscript.

Article Information

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Case Study

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ABSTRACT

Aims: Beijing remain the most *M. tuberculosis* lineage distributed and associated to multidrug resistance known worldwide. Its detection in a young person urge to make a large molecular epidemiology study in the concerned region since this can significantly impact tuberculosis (TB) control and vaccine strategies development.

Presentation of Case: In this study, we described the first case of *M. tuberculosis* Beijing strain isolated from a 20 years old girl in Cameroon. This strain was resistant to Isoniazid, Rifampicin, Streptomycin and Ethambutol. Spoligotyping and MIRU/VNTR genotyping analysis showed that the strain belonged to SIT1. The patient responded well to 12 months drug therapy of 4

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KmGfxPtoHCfzEZ / 8 GfxPtoCfzEZ; although she was probably contaminated by her elder sister who died from TB few months before. This case may traduce a transmission event in Cameroon. **Conclusion:** This was the first study that isolated *M. tuberculosis* Beijing lineage in Cameroon and showed the importance to purchase a large study in the concerned regions.

Keywords: M. tuberculosis; Beijing strain; Cameroon; MIRU/VNTR genotyping; multi drug resistance; spoligotyping.

1. INTRODUCTION

The Beijing genotype is a *M. tuberculosis* lineage responsible for large epidemic and is associated to multidrug-resistance worldwide [1,2]. It was first described in 1995 [3] and was defined as a strain that hybridizes to at least three of the spacers 35–43 in the genomic Direct Repeat region, and that showed absence of hybridization to spacers 1–34 in standard spoligotyping with the 43 spacers [4].

This family represents about 50% of strains in East Asia and is highly endemic in certain European geographic areas throughout Russia [5]. Their emergence might be linked to escape from BCG vaccination, and to multidrug resistance [6,7].

However, its distribution in Africa is less documented due to the lack of data [8]. Nevertheless scarce studies have identified Beijing in certain African countries including Burkina Faso [9], Gambia (03 strains) [10], Mozambique (33 strains) [8],South Africa (5, 81 to 16, 5%) [11,12,13].

In Central Africa region, in the best of our knowledge, Beijing strain has never been described. In Cameroon for example all the previous molecular epidemiology studies did not isolate Beijing strains [14,15,16]. We describe here the first case of Beijing strain causing pulmonary TB in Cameroon and that was associated to multidrug resistance.

2. CASE REPORT

We described here the first Beijing strain responsible of pulmonary TB in Cameroon. This strain was isolated from a young female patient who, after many unsuccessful treatments at Kumba district hospital in the South West Region of Cameroon, was referred in February 2011 to the Jamot hospital (National reference Hospital for respiratory disease) where she was later sent to the Mycobacteriology service (Reference Laboratory of NTP, Centre Pasteur of Cameroon) for TB diagnosis and Monitoring. Her sputum was received. Acid-fast bacilli were detected on Ziehl-Neelsen stained impression smear and culture was made in Löwenstein-Jensen and in Löwenstein-Jensen media supplemented with 0.4% of pyruvate. After sixteen days of incubation at 37°C, colonies appeared on a Löwenstein-Jensen slant. These colonies were then Ziehl-Neelsen stained for confirmation of M. tuberculosis infection concomitantly, drug susceptibility was performed using a standard proportional method and the result showed that, the isolate was resistant to Isoniazid, Rifampicin, Streptomycin and Ethambutol. The Resistance result to Isoniazid and Rifampicin was confirmed using Genotype MTBDR plus assay (Hain Lifescience, Nehren, Germany). Identification of M. tuberculosis complex (MTC) was done using the standard 43 spoligotyping method [17] and a modified standard 15 MIRU/VNTR set typing [18] (MIRU 4, MIRU10, MIRU 16, MIRU 24, MIRU 26, MIRU 27, MIRU 31, MIRU 40, ETRA, QUB-26, QUB-11b, VNTR 43, VNTR 47, VNTR 48, VNTR 49) was used to further characterize this strain. These analyses identified a M. tuberculosis family known as Beijing characterized by the absence of hybridization to spacers 1-34 and hybridization to spacers 35-43. The modified standard 15 loci MIRU/VNTR analysis gave the profile 424125356544235, as presented in Table 1.

A detailed epidemiological investigation was conducted. It was found that, the patient was a 20 years old female coming from Kumba in the South West Region of Cameroon. After many unsuccessful treatments at Kumba district hospital, she was referred to the Jamot hospital where his sputums were sent to the NRL for diagnosis. Her human immunodeficiency virus serology was negative. The patient did not report contact with any person coming from South Africa, Asia or other regions where Beijing family is prevalent. Nevertheless, she was apparently infected by her elder sister who died from active pulmonary tuberculosis few months ago. We

Table 1. Phenotypic and molecular characteristic of the first Beijing strain isolated in
Cameroon

First line drug susceptibility profile	Spoligotype description			MIRU/VNTR Profile
	Binary format	SIT	Lineage	
HRSE		1	Beijing Lineage	424125356544235

could not obtain either sample nor trace back information from her. The girl recovered after 12 months treatment of 4 KmGfxPtoHCfzEZ / 8 GfxPtoCfzEZ (Pto: Prothionamide; Gfx: Gatifloxacine; Cfz: Clofazimine; Km: kanamycine; H: Isoniazide; E: Ethambutol; Z: Pyrazinamide).

3. DISCUSSION

Pulmonary TB remain a serious public health problem in Cameroon and data on multi drug resistance are scarce since Mycobacterium tuberculosis complex strains culture is not routinely done on every case. This situation can lead in the point of view of molecular epidemiology, to the missing of a lot of data concerning *M. tuberculosis* complex species circulation and endemic clone prevalence. But since this last decade scarce molecular epidemiology studies using culture and the drug susceptibility of MTC strain have evidence a shift in the population structure of this complex in Cameroon with the decline of *M. africanum* and the emergence of a *M. tuberculosis* family called Cameroon family and some other family like Ubigitus T, Haarlem, U families associated to multidrug resistance [14,15,16]. But none of these studies did isolated M. tuberculosis Beijing lineage. The reason of this situation remained unknown while this lineage is known to be associated - to the increased febrile response in patients during treatment [19]- or to Human Immunodeficiency Virus (HIV) infection [20]- or to enhance virulence [21] and have ability to escape to Bacillus Calmette Guerin (BCG) protective immunity [3]. The identification of this strain in a young patient could imply a transmission event in the South West Region of Cameroon.

4. CONCLUSION

This study was the first that isolated *M. tuberculosis* Beijing lineage in Cameroon. It showed the urge to purchase a detailed molecular epidemiology investigation in Kumba Subdivision as the establishment of this strain may significantly impact TB control strategies.

ETHICAL CONSIDERATIONS

Patient permission to conduct more experiment in his case was obtained through consent.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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