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MAJOR ARTICLE

Mycobacterium bovis Infections Following Intravesical Bacillus Calmette-Guérin Instillation for Bladder Cancer in Western Australia: A 22-Year Retrospective Review

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Mycobacterium bovis bacillus Calmette-Guérin (BCG) infection following intravesical BCG instillation is a rare complication of therapy that is associated with significant morbidity and mortality. We conducted a multicenter retrospective review of microbiologically confirmed *M.bovis* BCG infections in Western Australia over 22 years. Thirty-three patients were included in our study. All patients were male with a median age of 72 years. Localized infections accounted for 22/33 cases while disseminated infections accounted for 11/33 cases. The majority (n = 21) of positive isolates were cultured from urine specimens, followed by tissue and blood. The median time between first BCG instillation and infection was 7.5 months (95% CI, 3.5–11.5). The median duration of antimycobacterial therapy for localized infections was 6 months (95% CI, 4.1–7.9) as compared with 9 months (95% CI, 7.9–10.1) for disseminated infections ($P = .039$). The attributed mortality was 14.3%. *M.bovis* BCG infections have diverse clinical presentations and clinicians must have a high index of suspicion when assessing patients with a history of intravesical BCG instillation.

Keywords. bacillus Calmette-Guérin, BCG; bladder cancer; infections; intravesical; *Mycobacterium bovis*.

Intravesical administration of bacillus Calmette-Guérin (BCG) remains the mainstay of managing noninvasive bladder cancer worldwide, with associated risk reduction of tumor progression and recurrence [1–4]. Infection with *Mycobacterium bovis* (*M.bovis*) BCG following intravesical BCG instillation is a recognized complication of therapy [1, 4–6]. While the incidence of localized and disseminated BCG infections is rare with a cumulative incidence <5%, it is associated with significant morbidity and mortality, and it affects subsequent bladder cancer management [1, 6–9]. Furthermore, there is a paucity of research to inform and guide clinicians in the assessment and treatment of these patients.

To increase our understanding of this underrecognized health care–associated infection and improve outcomes for future patients, we conducted a 22-year retrospective review of microbiologically confirmed *M.bovis* BCG infections following intravesical BCG instillation in Western Australia.

AIMS

The aims of the study were as follows:

- To conduct the first multicenter retrospective review of microbiologically confirmed *M.bovis* BCG infections following intravesical BCG in Western Australia
- To describe and compare the characteristics and management of localized and disseminated *M.bovis* BCG infections following intravesical BCG
- To assess the outcomes, including attributable mortality, associated with *M.bovis* BCG infections following intravesical BCG

METHODS

We conducted a multicenter retrospective review of microbiologically confirmed *M.bovis* BCG infections following intravesical BCG instillation across Western Australia over a 22-year period. We identified all *M.bovis* BCG–positive specimens processed at the Mycobacterium Reference Laboratory at Path

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West Queen Elizabeth II Medical Centre in Perth, Western Australia, from 1 January 2000 to 31 December 2021. The reference laboratory receives all positive *Mycobacterium* isolates in Western Australia, servicing a population of 2.9 million and a land area of 2.6 million km [2]. *Mycobacterium* culture–positive isolates undergo a multiplex real-time polymerase chain reaction assay to identify common mycobacteria species. Those isolates identified as *Mycobacterium tuberculosis* complex undergo a second real-time BCG-specific polymerase chain reaction assay based on the detection of sequence polymorphisms at the RD1 (region of deletion 1) genomic region [10].

Inclusion Criteria

Inclusion criteria were as follows:

- Patients aged ≥18 years
- A history of intravesical BCG instillation for the management of noninvasive bladder cancer
- A specimen with microbiologically confirmed *M.bovis* BCG strain

Exclusion Criteria

Exclusion criteria were as follows:

- Patients had isolated *M.bovis* BCG from a single urine specimen with no clinical signs or symptoms consistent with infection; further urine specimens did not culture *M.bovis* BCG strain; and the treating physician felt that initiation of mycobacterial treatment was not indicated.
- There was no documentation acknowledging the result nor documentation regarding decision making and management of the result.
- Patients had a clear alternative explanation for culturing *M.bovis* BCG—for example, wound infection in upper arm or buttocks after receiving BCG vaccine for prevention of tuberculosis.

Data variables of the patients were collected from written and electronic medical records, pharmacy databases across public and/or private hospitals, and outpatient specialty clinics that treated the patients. Patient demographics included age, gender, Aboriginal or Torres Strait Islander status, smoking history, and presence of diabetes or immunosuppression. Immunosuppression was defined as a documented history of a primary immunodeficiency syndrome, hyposplenism, or HIV or if the patient was receiving the equivalent of prednisolone ≥0.5 mg/kg/d for ≥14 days, cytotoxic chemotherapy, monoclonal antibodies, or other biologic agents.

For those patients with available intravesical BCG instillation data, the date of first and last instillation, the number of instillations received, and the BCG vaccine strain administered were recorded. The date and site of the specimen isolating *M.bovis* BCG were recorded in all patients. The time from first and last instillation of intravesical BCG to the onset of infection, defined as the date at which the positive culture was obtained, was recorded.

Infections were categorized as localized, defined as infections with positive microbiological samples from the genitourinary tract, or disseminated, defined as infections with positive microbiological samples from outside the genitourinary tract. Furthermore, BCG cystitis was deemed present when patients had isolation of *M.bovis* BCG in urine specimens with clinical symptoms consistent with infection and/or a decision was made by the treating physician to commence directed *M.bovis* BCG treatment.

Antimicrobial susceptibilities to first-line antimycobacterial agents streptomycin, isoniazid, rifampicin, ethambutol, and pyrazinamide were performed on isolates via the Becton Dickinson BACTEC Mycobacteria Growth Indicator Tube 960 Detection System, which tests each drug at the critical concentration, with the exception of rifampicin, as determined by the World Health Organization policy [11]. Management decisions were also recorded: treatment with antimicrobials, dose and duration of therapy, and treatment outcomes including attributable mortality.

Ethics approval for the study was obtained from individual hospitals and through Governance Evidence Knowledge Outcomes application to East, North, and South Metropolitan Health Services.

Statistical Methods and Analysis

Descriptive summaries consist of number and percentage for categorical data; median, IQR, and range for continuous data; and median with 95% CI for count data (interval duration). Infection site univariate group comparisons consist of χ^2 or Fisher exact test for categorical data and Mann-Whitney *U* test for continuous data. Kaplan-Meier survival probabilities were used to examine duration data, with log rank tests for group comparisons. Kaplan-Meier survival plots were generated. Stata version 18.0 (StataCorp) was used for data analysis. Significance levels were set at $\alpha = .05$.

RESULTS

A total of 62 patients had a specimen culture for *M.bovis* from 1 January 2000 to 31 December 2021. Twenty-two patients were excluded per the study exclusion criteria: 18 specimens were isolated from pediatric patients or those who received intradermal BCG vaccination, and 4 specimens isolated *M.bovis* (non-BCG).

Forty patients were identified with a microbiologically confirmed *M.bovis* BCG isolate following intravesical BCG administration. Five patients were excluded as *M.bovis* BCG was isolated from a single urine specimen with no clinical signs

or symptoms consistent with infection, further urine specimens did not culture the *M.bovis* BCG strain, and the treating physician felt that initiation of mycobacterial treatment was not indicated. An additional 2 patients were excluded as there was no documentation acknowledging the result or specifying the decision making and management of the result. A total of 33 patients were included in our study population. Patients were treated across 13 sites, including metropolitan public and private hospitals, regional hospitals, and outpatient infectious disease and mycobacterial clinics. Demographics of the patients in the study are summarized in Table 1.

All patients in the study were male with a median age of 72 years (IQR, 65–78). Three percent of patients identified as Aboriginal or Torres Strait Islander, 10 (30.3%) had diabetes, and 2 (6.1%) were immunocompromised. Forty-eight percent of patients had a history of smoking, 14 (63.6%) of which had localized infection, as opposed to 2 (18.2%) with disseminated infection, for a statistically significant difference ($P = .026$). There were no other significant differences in patient demographics between those who developed localized and disseminated infections.

Twenty-one (63.6%) positive isolates were cultured from urine specimens; 5 (15.1%) from bone and/or tissue samples from vertebrae, sternum, or phalanx; 4 (12.1%) from blood cultures; and the remainder from bladder, prostate, and sputum samples. Infections were categorized as localized to the genitourinary system or disseminated. The primary site of infection and/or organ system involved is detailed in Table 2.

Localized infections accounted for 22 of 33 (67%) cases, with most being cystitis (n = 18, 81.8%). There were 3 cases of prostate abscesses, all of which required interventional or surgical drainage. A single case of *M.bovis* BCG nephritis was noted where the patient presented with acute-on-chronic renal failure with necrotizing granulomas within the renal parenchyma. The patient required a nephroureterectomy and received 9 months of combination rifampicin, isoniazid, and pyridoxine and adjunctive glucocorticoids.

Disseminated infections accounted for 11 of 33 (33%) cases. Four patients cultured *M.bovis* BCG in peripheral blood cultures. Two patients had complicating mycotic aortic aneurysms, and 2 had evidence of pulmonary involvement with respiratory failure. There were 5 cases of osteomyelitis in our study cohort, including vertebral, phalangeal, and sternal osteomyelitis. Eight patients with disseminated infections had clinical cure on follow-up. Two patients died from their disseminated *M.bovis* BCG infection. The outcome following commencement of mycobacterial treatment for 1 patient is unknown from review of the medical records. Of note, 3 patients with *M.bovis* BCG bacteremia received 1 or more instillations with BCG vaccine strain TICE. Vaccine strain data for the fourth bacteremic case were unable to be obtained. Table 3 summarizes the data variables and management of patients with disseminated infections in detail.

Over a 10-year period, the incidence of BCG infection in 1 of the tertiary hospitals was 1.7%. During this period, 5 of the 286 patients who received BCG instillations developed localized infections. No patients developed a disseminated infection. The total number of instillations administered at this site over the 10-year period was 4078.

In relation to intravesical BCG instillation data, the median number of instillations received overall was 11.7 (IQR, 7–18). The median number in patients who developed localized infections was 10.5 instillations (IQR, 7–15) vs 14 (IQR, 6–21) in

Table 1. Patient Demographics

Variable	Total	Disseminated	Localized	*P* Value
Patients	33	11 (33.3)	22 (66.7)	
Age, y, median	72	74	70	.985
Aboriginal or Torres Strait Islander	1 (3)	0	1 (4.5)	.473
Smoking history				**.026**
Current/ex-smoker	16 (48.5)	2 (18.2)	14 (63.6)	
Never smoker	17 (51.1)	9 (81.8)	8 (36.4)	
Diabetes	10 (30.3)	2 (18.2)	8 (36.4)	.284
Immunosuppression	2 (6)	1 (9.1)	1 (4.5)	.606
Prednisolone	0	0	0	
Cytotoxic agent	1	1	0	
Primary immunodeficiency syndrome	0	0	0	
Hyposplenism	0	0	0	
HIV	0	0	0	
Other	1	0	1	
Antimycobacterial treatment received	22 (66.7)	9 (81.8)	13 (59.1)	.424

Data are presented as No. (%) unless noted otherwise. Bold indicates $P < .05$.

Table 2. *Mycobacterium bovis* BCG Infection Site

Category of Infection	No. (%)
Localized	22 (67)
Cystitis	18 (55)
Prostate abscess	3 (9)
Pyelonephritis/renal abscess	1 (3)
Disseminated	11 (33)
Bacteremia	4 (12)
With mycotic aneurysm	2 (6)
With pulmonary involvement	1 (3)
Bacteremia only	1 (3)
Pulmonary	1 (3)
Osteomyelitis	5 (15)
Sternal	2 (6)
Vertebral	2 (6)
Phalanx	1 (3)
Other	1 (3)

Abbreviation: BCG, bacillus Calmette-Guérin.

Table 3. Baseline Characteristics, Clinical Features, Installation Data, Treatment, and Outcome of Patients With Disseminated *Mycobacterium bovis* BCG Infection

			Installation			Site					
No.	Age, y	DM + Smoking History	First to Infection, d	No.	Vaccine Strain	Infection	Specimen	AST Results	Clinical Summary	Treatment	Outcome
1	72	Y + N	NA	6	NA	Pulmonary	Sputum	R = S H = S St = S E = S Z = Rs	Disseminated infection with widespread pulmonary infiltrates and psoas abscess. Admission complicated by renal failure and ischemic cardiac event.	9 mo: initially H/R, then changed to R/MFX due to LFT results	Clinical cure
2	75	N + N	3123	34	Connaught Russian TICE	Bacteremia	Blood	R = S H = S St = S E = S Z = Rs	Disseminated BCG	9 mo: H/R/E	Clinical cure
3	74	N + Y	631	18	TICE	Bacteremia–mycotic aneurysm	Blood	NA	Presented systemically unwell with infrarenal aortic aneurysm and pulmonary nodules. Mycobacterial infection initially thought to be unlikely—directed therapy not commenced. Blood cultures noted growth of *M bovis* BCG after the patient died.	No treatment	Death / attributable mortality
4	64	N + N	19	2	Connaught	Other	Urine	NA	Disseminated BCG	H/R	NA
5	75	N + N	225	11	TICE	Bacteremia–mycotic aneurysm	Blood	NA	Initially presented with fevers and pneumonitis thought to be secondary to a hypersensitivity reaction—treated with oral prednisolone only. Re-presented 11 mo later with a mycotic aneurysm requiring EVAR.	9 mo: H/R/E/LVFX	Clinical cure
6	59	N + Y	NA	17	NA	Bacteremia-pulmonary	Blood	NA	Presented within 24 h after BCG installation with fevers, tachycardia, hypotension, and respiratory failure with widespread pulmonary infiltrates	6 mo: H/R/E for 2 mo, H/R for further 4 mo	Clinical cure
7	68	Y + N	NA	NA	NA	Osteomyelitis-sternal	Tissue	R = S H = S St = S E = S Z = Rs	Presented with chest wall swelling. CT noted ulceration, abscess formation, and osteomyelitis of the eighth rib sternum.	9 mo: H/R/E/Z (unknown duration) then H/R to complete total 9 mo	Clinical cure
8	65	N + N	NA	NA	NA	Osteomyelitis-sternal	Tissue	R = S H = S St = S E = S Z = Rs	Unknown	6 mo: H/R	Clinical cure
9	81	N + N	NA	NA	NA	Osteomyelitis-phalanx	Tissue	R = S H = S St = S	Sustained traumatic hand injury requiring multiple surgical debridements. *M bovis* BCG subsequently cultured from	9 mo: H/R/E for 2 mo, H/R for further 7 mo	Clinical cure

Table 3. Continued

No.	Age, y	DM + Smoking History	Installation			Site			AST Results	Clinical Summary	Treatment	Outcome
			First to Infection, d	No.	Vaccine Strain	Infection	Specimen					
									E = S Z = Rs	intraoperative specimens after implant extraction.		
10	74	N + N	470	6	Russian	Osteomyelitis-vertebral	Tissue		R = S H = S St = S E = S Z = Rs	Presented with acute-on-chronic back pain with T11/12 vertebral osteomyelitis/discitis with epidural abscess—required surgical management.	12 mo: empirical H/R/E/Z + prednisolone; Z ceased after 1 mo after AST results; E ceased after 6 mo, then H/R for further 6 mo	Clinical cure
11	82	N + N	672	24	Russian TICE	Osteomyelitis-vertebral	Tissue		R = S H = S St = S E = S Z = Rs	Presented with recurrent fevers with imaging noting L5 lesion. Bone biopsy confirmed *M bovis* BCG. After bone biopsy, patient requested transition to palliative care.	No treatment	Death / attributable mortality

All patients were male; none were Aboriginal or Torres Strait Islander. Only patient 10 had immunosuppression.

Abbreviations: AST, antimicrobial susceptibility testing; BCG, bacillus Calmette-Guérin; CT, computed tomography; DM, diabetes; E, ethambutol; EVAR, endovascular aneurysm repair; H, isoniazid; LFT, liver function test; LVFX, levofloxacin; MFX, moxifloxacin; N, no; NA, not available; R, rifampicin; Rs, resistant; S, susceptible; St, streptomycin; Y, yes; Z, pyrazinamide.

patients who developed disseminated infections ($P = .973$). The overall median time between first BCG instillation and infection was 7.5 months (95% CI, 3.5–11.5). The interval from first BCG installation to infection is illustrated in Figure 1. The median time between first BCG instillation and localized infection was 7.2 months (95% CI, .8–13.7), as opposed to 15.6 months (95% CI, 0–31.6) in patients with disseminated infections ($P = .119$). The overall median time between last BCG instillation and infection was 0.2 months (95% CI, 0–.2). The median time between last BCG instillation and localized infection was 0.1 months (95% CI, 0–.2), as compared with 3.7 months (95% CI, 0–13.1) in patients with disseminated infections ($P = .376$).

Of the isolates that underwent antimicrobial susceptibility testing (AST), all tested susceptible to rifampicin, streptomycin, and ethambutol. Twenty-two percent of tested isolates were resistant to isoniazid. All tested isolates were resistant to pyrazinamide.

Among the 22 patients who received treatment, regimens varied significantly with respect to the number of antimycobacterial agents, the duration of therapy, and whether adjunctive glucocorticoids were used. Figure 2 illustrates the duration of therapy in localized and disseminated infections. Isolates from 2 patients tested resistant to isoniazid. The first patient was treated for a prostate abscess and was initially prescribed isoniazid, rifampicin, and pyrazinamide following surgical drainage. Following the resistance testing results, the patient continued taking rifampicin and isoniazid despite detected isoniazid resistance for a total of 6 months. The second patient was initially treated for cystitis with isoniazid monotherapy but reported persistent symptoms to his treating physician. Several months later, following the availability of susceptibility results, isoniazid was ceased, and the patient was prescribed rifampicin and ethambutol for a total of 9 months. Both patients achieved clinical cure.

Only 2 patients were treated with isoniazid monotherapy, both of whom had localized infections. All other patients who received treatment received ≥2 antimycobacterial agents. The duration of antimycobacterial therapy ranged from 1 to 12 months. The median duration of antimycobacterial therapy for localized infections was 6 months (95% CI, 4.1–7.9) while that for disseminated infections was 9 months (95% CI, 7.9–10.1). This was statistically significant with a P value of .039.

The overall median time from onset of infection to death was 31.4 months (95% CI, 0–72.5). The attributed mortality in patients with disseminated infections was 2 of 6 (33.3%). There were no attributable deaths in patients with localized infections. The overall attributed mortality in our patient cohort was 2 of 14 (14.3%), with all attributed deaths in males >70 years of age with disseminated infections. Figure 3

illustrates the Kaplan-Meier curve of months from infection to death.

DISCUSSION

The benefit and favorable outcomes associated with intravesical administration of BCG in the management of noninvasive bladder cancer are well established [1, 12, 13]. While infection with *M.bovis* BCG following intravesical BCG instillation is a recognized complication of therapy, much uncertainty remains regarding the pathophysiology, associated risk factors, diagnostic criteria, and treatment of these patients [1, 14].

Current knowledge of this health care–associated infection has predominately been obtained from case reports and small case series [1, 4, 9]. A lack of consensus regarding the diagnostic criteria and classification of *M.bovis* BCG infections remains and so results in heterogeneity across the limited published literature [1, 4]. To our knowledge, this statewide multicenter review of microbiologically confirmed *M.bovis* BCG infections stands as the largest and longest retrospective study conducted internationally.

The underlying pathophysiology for the development of infection following intravesical BCG is yet to be established, with many supporting the opinion that it is a hypersensitivity reaction to BCG antigens that leads to clinical manifestations and cases should be managed with systemic glucocorticoids [1, 14]. In our study, the evidence of acid-fast bacilli and culture of *M.bovis* BCG in various specimens, including blood cultures, sputum, bone, and tissue, challenges this opinion and supports the hypothesis that complications arise from the direct invasion and hematogenous spread of BCG [1, 14].

A clear strength of our study is the inclusion of patients with exclusively microbiologically confirmed *M.bovis* BCG, enabling a more robust interpretation of results and conclusions to be drawn. This is compared with most other case reports and studies that have included patients with a presumptive diagnosis of infection based on clinical presentation, epidemiologic risk factors, or the presence of granulomas on specimens [1, 4].

The patient demographics in our cohort are similar to previous studies, with an older male predominance [1, 4, 9], which reflects the higher incidence of bladder cancer in males. The baseline characteristics between patients who developed localized and disseminated infections were similar in our study, with the notable exception of smoking status. Fourteen (63.6%) patients with localized infections were current or ex-smokers, as opposed to 2 (18.2%) patients with disseminated infections, which was statistically significant ($P = .026$). Safety concerns have been raised regarding the risk of disseminated *M.bovis* BCG infection following intravesical BCG in the context of preexisting immunosuppression [1, 15, 16]. Only 2 (6%) patients in our study were immunocompromised, which is similar to findings in other studies [1, 4]. This highlights the imperative for additional research within this patient cohort, considering its potential exclusion from intravesical BCG treatment. This is especially significant given the well-established benefits and improved outcomes associated with intravesical BCG in the management of noninvasive bladder cancer [1, 14]. A limitation of our study is the absence of a comparator group that did not develop infection following intravesical BCG installation. Consequently we are unable to compare baseline characteristics between patients who developed infection and those who did not. However, it is noteworthy that other published studies have not reported statistically significant differences in patient demographics [1, 4]. The overall incidence of *M.bovis* BCG infection could not be calculated due to missing data, which is a further limitation of our study. A limited incidence from 1 of the tertiary hospitals was calculated to be 1.7%, which is aligned with incidence rates <5% reported in published literature.

The heterogeneity across studies with the inclusion of patients with presumed and definite infections and the different categorization of infection sites pose challenges in comparing results [1, 4]. Our results noted an increased proportion of localized infections as compared with disseminated infections. In contrast to our findings, a Spanish study reported localized infections in only 23.4% of patients [1]. It is important to note that these results were obtained from a pooled analysis of 271 patients from published case reports and studies [1], which raises concerns of potential publication bias and an underrepresentation of the incidence of localized infections [4]. A nationwide retrospective review conducted in Denmark categorized infections as either pulmonary or extrapulmonary and found that 78.4% of patients with extrapulmonary infections had infections localized to the genitourinary tract [4].

It has been historically described that disseminated infections present early, typically within 3 months of BCG instillation, whereas localized infections tend to occur beyond 3 months [1, 4, 17]. Our results did not reflect this, with the median time from first instillation of BCG to onset of localized infection being 7.2 months (95% CI, .8–13.7), whereas the median time from first instillation of BCG to onset of disseminated infection was 15.6 months (95% CI, 0–31.6). Of note, some patients receive induction and maintenance BCG therapy. The median time from last instillation of BCG to onset of localized infection was 0.1 months (95% CI, 0–.2), whereas the median time from last instillation of BCG to onset of disseminated infection was 3.7 months (95% CI, 0–13.1). On review of the medical records, several patients reported fevers and persistent lower urinary tract symptoms following instillation. Treating clinicians, however, perceived these symptoms as expected side effects rather than complications of therapy. Consequently, patients continued to receive intravesical BCG. Only after isolation of *M.bovis* BCG from a nonurinary specimen did clinicians decide to cease further BCG instillations and initiate directed antimycobacterial therapy. Of note, our

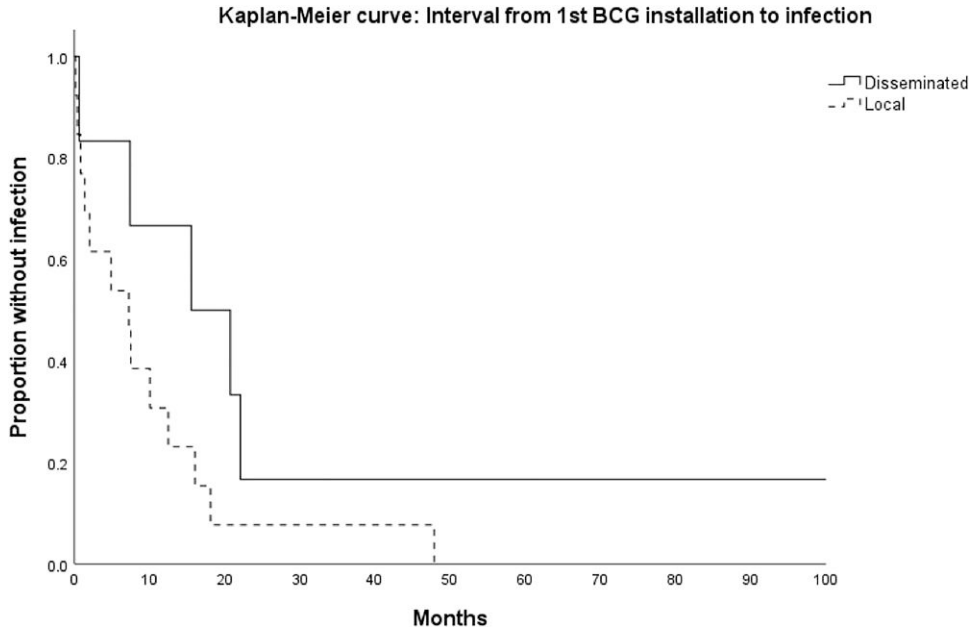

Figure 1. Kaplan-Meier curve of the interval from the first bacillus Calmette-Guérin installation to infection.

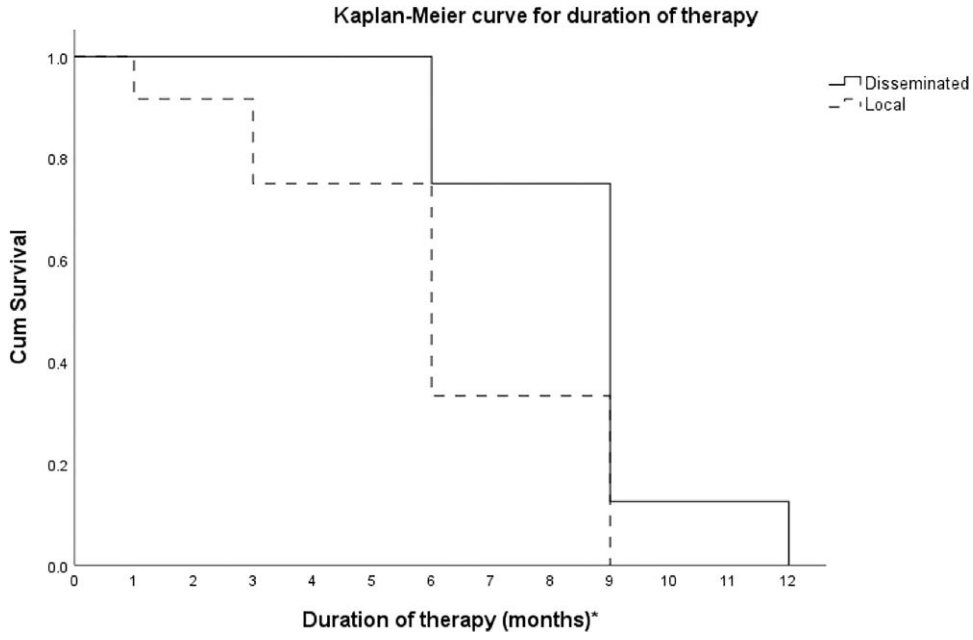

Figure 2. Kaplan-Meier curve for duration of therapy in localized and disseminated infections.

results did not demonstrate a statistically significant difference in the number of instillations received among those who developed localized or disseminated infections, aligning with the current literature [1].

Our results revealed a statistically significant difference ($P = .039$) in the duration of directed antimycobacterial therapy between patients treated for localized infections and those treated for disseminated infections. Due to the scarcity of data on treatment of *M.bovis* BCG infections following intravesical BCG, our results suggest a treatment >6 months in those with disseminated infections [1, 9]. Additionally, all isolates that underwent AST were resistant to pyrazinamide,

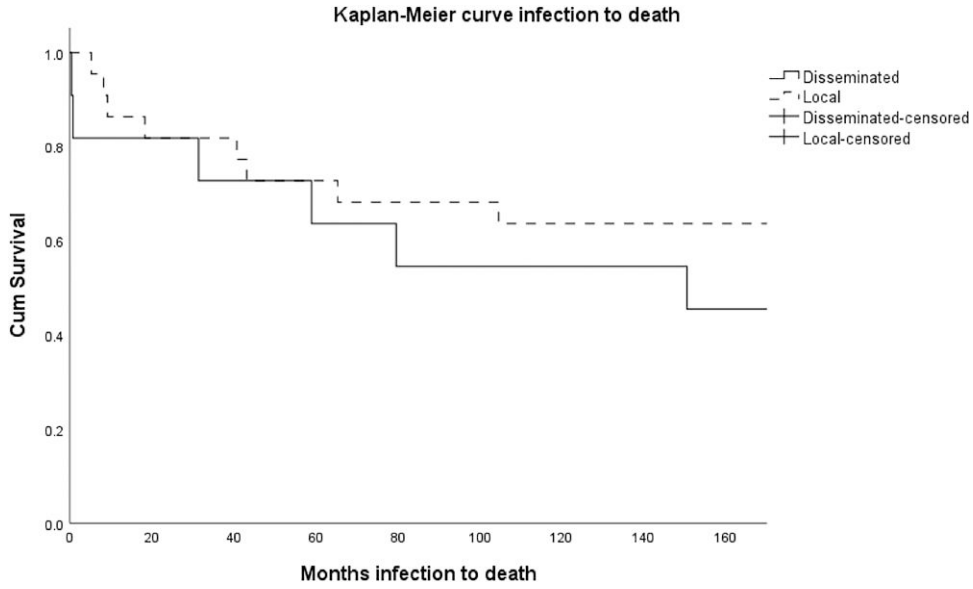

Figure 3. Kaplan-Meier curve of infection to death.

supporting evidence that *M.bovis* BCG is intrinsically resistant to pyrazinamide [1, 9]. We recommend conducting formal AST on all isolates. Our study revealed that >20% of isolates were resistant to isoniazid. Additionally, most clinicians opted to treat patients empirically with standard *M.tuberculosis* agents and follow the treatment paradigm of an intensive phase with ≥3 agents, followed by maintenance therapy with rifampicin and isoniazid. The evidence supporting this treatment approach for *M.bovis* BCG infection is unclear and warrants further research.

The attributed mortality in our cohort was 2 of 14 (14.3%), exceeding rates reported in other studies [1, 7]. Notably, all attributed deaths occurred in males >70 years of age with disseminated infections, factors consistently observed in multiple other case series and pooled analyses [1].

The risk of infection associated with specific BCG strains following instillation has not been well described in the recent literature. A review published by Lamm et al in 1992, encompassing 2602 patients treated with various BCG strains, such as Armand Frappier, Tice, Connaught, Pasteur, or RIVM, did not identify a significant difference in complication rates [7]. In contrast, our observational study noted that 3 patients with bacteremia and an additional patient with vertebral osteomyelitis received the TICE BCG strain, which has been recognized for its higher virulence as compared with other BCG strains in mouse modeling [18]. Additionally, a Spanish epidemiologic study of health care–associated *M.bovis* BCG infections in patients with cancer and infected central venous catheters in the absence of prior BCG instillation reported the presence of the *M bovis* BCG TICE strain in 7 of 8 patients [19]. While higher virulence may confer increased efficacy and the desired antitumor effects [4, 18], these observations warrant further research into the specific risk profiles associated with BCG strains in the development of localized and disseminated infections.

CONCLUSION

M.bovis BCG infections following intravesical BCG are infrequently described but are associated with significant mortality [1]. Our study describes the diverse clinical presentations, sites of infection, timing of presentation, and treatment courses, which present considerable challenges in diagnosis, management, and prevention [1, 4]. Currently the treatment of these patients would support the use of a prolonged course of multiple antimycobacterials. Antimicrobial susceptibilities should be attained to assist in the treatment of patients given the potential for isoniazid resistance. Clinicians should maintain awareness of this complication and exercise a high index of suspicion when assessing patients with a recent or distant history of intravesical BCG instillation [1].

Notes

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