Failed endovascular abdominal aortic aneurysm repair due to *Mycobacterium bovis* infection following intravesical bacillus Calmette-Guérin therapy

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ABSTRACT

A mycotic aneurysm after intravesical instillation of bacillus Calmette-Guérin (BCG) for early-stage bladder cancer is a rare, but life-threatening, complication. In the present report, we have described the case of a patient who had undergone endovascular aneurysm repair for a rapidly growing saccular abdominal aortic aneurysm after BCG therapy. Three months after endovascular aneurysm repair, the patient had developed an abscess that required open surgery. Cultures from a blood sample and the abscess revealed *Mycobacterium bovis* BCG. A mycotic aneurysm due to BCG therapy should be suspected in patients with a history of BCG treatment. Such patients should immediately start antitubercular therapy. (J Vasc Surg Cases Innov Tech 2022;8:807-12.)

Key words: bacillus Calmette-Guérin; endovascular aneurysm repair; infectious aortic aneurysm

Intravesical instillation of bacillus Calmette-Guérin (BCG) is widely used to treat superficial bladder tumors.[1] Although the procedure is generally considered safe, serious complications have been reported.[2-5]

In the present study, we have described a case of an abdominal aortic aneurysm (AAA) secondary to *Mycobacterium bovis* infection after intravesical BCG therapy. The infection was exacerbated by endovascular aneurysm repair (EVAR) and required open surgery. The patient provided written informed consent for the report of his case details and imaging studies.

CASE REPORT

A 72-year-old man had been admitted to our hospital with a chief complaint of fever lasting for >1 month. The patient also complained of fatigue, a poor appetite, and a weight loss of 2 kg. Contrast-enhanced computed tomography (CT) revealed perivascular inflammation of the abdominal aorta (Fig 1, *A*). Because bacterial cultures of his blood samples were negative, antimicrobial therapy was not administered.

Three years before the current admission, the patient had been diagnosed with superficial transitional cell carcinoma of the bladder and idiopathic thrombocytopenic purpura, for which he had received oral steroid therapy (5 mg of prednisolone once daily for 6 months) and undergone two transurethral resections. The patient had subsequently received two courses of intravesical instillation of BCG (Immunobladder; Nippon Kayaku Co, Tokyo, Japan). The first course (six times, once a week) had been completed 3 years before admission, and the second course (six times, every 3 months) had been completed 2 months before admission.

Two months later, a follow-up CT scan revealed a saccular AAA with a diameter of 4.2 cm (Figs 1, *B*, and 2). The patient had a 40 pack-year smoking history, body mass index of 21 kg/m^2, pulse rate of 64 bpm, and blood pressure of 124/82 mm Hg and was afebrile. The laboratory tests showed a leukocyte count of 5.7/mL, hemoglobin level of 135 g/L, and C-reactive protein level of 50.8 mg/L, indicating a significant inflammatory response. Because of its rapid formation, the aneurysm was suspected to be mycotic, and the CT findings suggested an impending rupture. EVAR (AFX; Endologix, Irvine, CA) was selected because of the patient's favorable aortic anatomy (Fig 3). An angiographic catheter was used intraoperatively to collect a blood sample from the area directly adjacent to the aneurysm for bacterial culture. Tazobactam/piperacillin (9.0 g/d for 15 days) was administered intravenously. The patient was discharged on postoperative day 14, and oral antibiotics (750 mg of amoxicillin daily for 24 days) were prescribed. Because *M. bovis* BCG infection was not suspected at the time, antitubercular therapy was not initiated.

A bacterial culture in Ogawa medium showed BCG-induced *M. bovis* 6 weeks after EVAR. A polymerase chain reaction test was positive for the *Mycobacterium tuberculosis* complex. Oral antitubercular therapy with isoniazid (100 mg once daily), ethambutol (10 mg once daily), and rifampicin (150 mg once daily) was initiated.

A follow-up CT scan performed 3 months after EVAR showed significant abscess formation in the retroperitoneal space (Fig 4). Emergency surgery was performed with the patient

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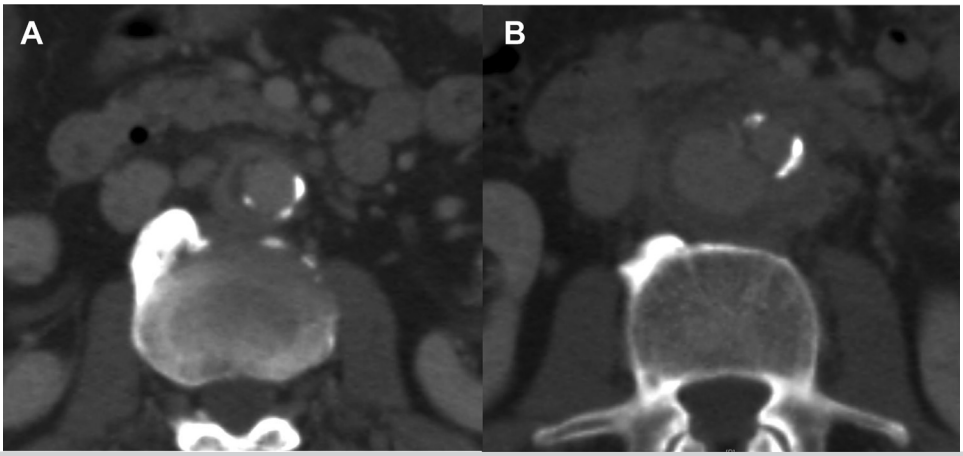

Fig 1. Contrast-enhanced computed tomography (CT) images of abdominal aorta of a patient with *Mycobacterium bovis* infection. **A,** Aortitis was visible 2 months before endovascular aneurysm repair (EVAR). **B,** Preoperative image of the patient's saccular aneurysm just before EVAR.

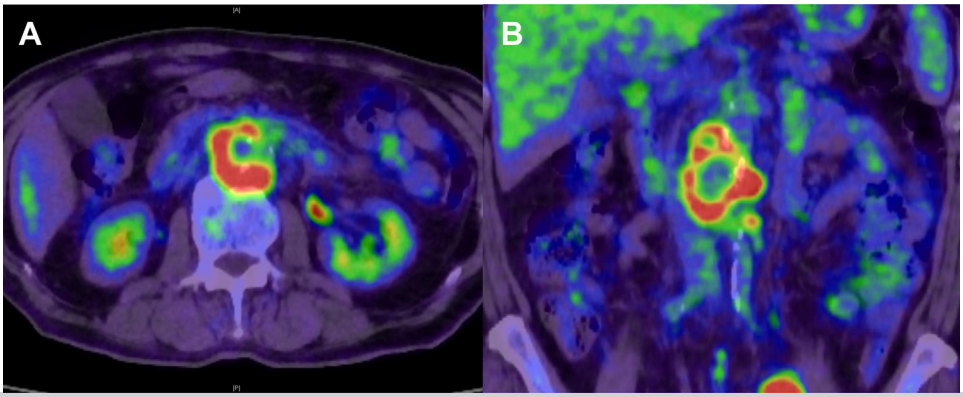

Fig 2. Preoperative fused positron emission tomography/computed tomography (CT) image of a patient with *Mycobacterium bovis* infection before endovascular aneurysm repair (EVAR). Intense fluorodeoxyglucose uptake was apparent around the infrarenal aorta, with a maximum standardized uptake value of 26.8. **A,** Axial image. **B,** Coronal image.

under general anesthesia. We began with right axillobifemoral bypass (Intergard AXL-BIF, 8 × 8 mm; Getinge, Gothenburg, Sweden), followed by laparotomy. The abscess around the aorta extended up to the origin of the superior mesenteric artery. However, we were unable to dissect the aorta up to that point because of significant adhesions and inflammation. Therefore, the supraceliac aorta was dissected and clamped. The celiac artery, superior mesenteric artery, and bilateral renal arteries (clamp time, 20 minutes for left side and 111 minutes for right side) were reconstructed with artificial grafts (Hemashield Gold, 14 × 7 mm^2; Getinge; and Propaten, 6 mm; W.L. Gore & Associates, Flagstaff, AZ), which were covered with an omental pedicle flap. The stent graft was removed, and the infected aneurysm wall and abscess were debrided extensively. After surgery, the patient had developed abdominal compartment syndrome, which caused acute renal failure and necrosis of the left hemicolon. Two days after onset, emergency left hemicolectomy was performed. The patient subsequently underwent open abdominal management and hemodialysis. Because of his prolonged ventilator dependence and extended hospital stay, the patient had required a tracheostomy. Administration of enteric antitubercular preparations was continued via a jejunostomy tube. After a 6-month stay in our hospital, the patient was discharged to a hospital in his community for further convalescence. No infection had recurred during the 11-month follow-up period.

A culture of a pus sample from the abscess in Ogawa medium yielded *M. bovis*-related BCG. Pathologic examination of permanent sections showed abscess formation and granulation tissue with histiocyte aggregation, plasmacyte infiltration, and lymph follicle formation. Non-necrotizing epithelioid granulomatous formations were also observed. Ziehl-Nielsen staining, periodic acid-Schiff staining, Gram staining, and Grocott staining were performed but did not reveal bacilli.

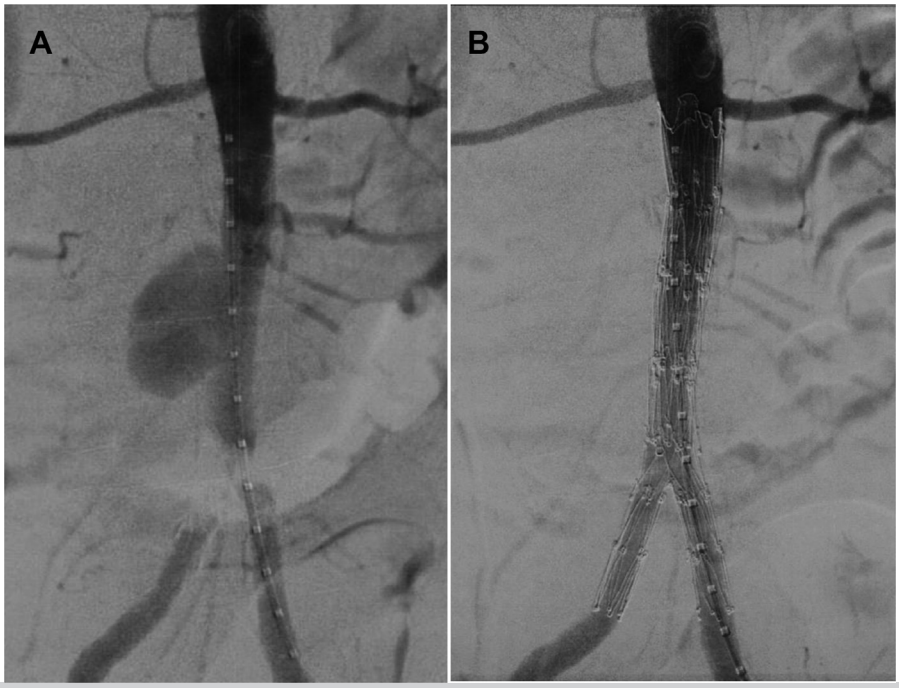

Fig 3. Intraoperative angiogram of a patient with *Mycobacterium bovis* infection taken during endovascular aneurysm repair (EVAR). **A,** Initial angiogram of abdominal aortic aneurysm (AAA). **B,** Angiogram taken after EVAR.

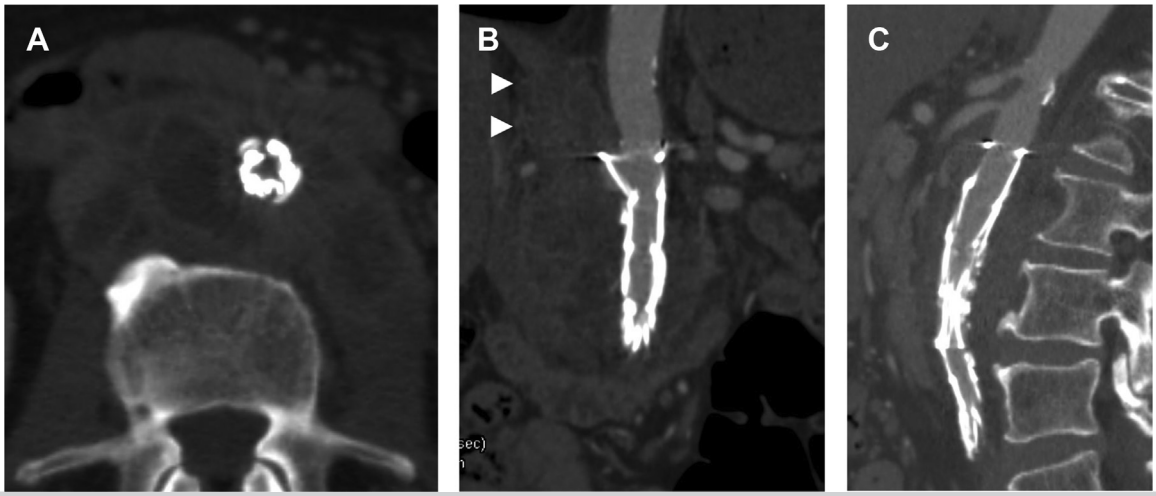

Fig 4. Contrast-enhanced computed tomography (CT) images of abdominal aorta of a patient with *Mycobacterium bovis* infection. **A,** Significant abscess formation was visible 3 months after endovascular aneurysm repair (EVAR). **B,** Coronal CT reconstruction image at 3 months after EVAR. The stent graft was deployed just below the renal arteries. The abscess around the aorta extended to the level of the origin of the superior mesenteric artery (*arrowhead*). **C,** Sagittal CT reconstruction image at 3 months after EVAR.

LITERATURE REVIEW

To the best of our knowledge, to date, 20 patients (including our patient) with a mycotic aortoiliac aneurysm who had undergone EVAR after BCG therapy have been reported (Table).[5-23] All 20 patients were men, and their mean age at diagnosis was 71 years (range, 57-82 years). The aneurysms had been diagnosed at a mean interval of 19 months (range, 0-69 months) after BCG therapy. The most common aneurysm location was the abdominal aorta (n = 13; 65%), followed by the descending aorta (n = 5; 25%). Of the 20 patients, 6 (30%) had undergone emergency surgery for aneurysm

Table. Characteristics of reported cases of endovascular aneurysm repair (EVAR) for mycotic aortoiliac aneurysms due to *Mycobacterium bovis* infection after intravesical bacillus Calmette-Guérin (BCT) therapy

Investigators	Age, years	Sex	Interval from BGC therapy, months	Aneurysm location	Size, mm	Rupture	Aortoenteric fistula	Psoas abscess	Spondylodiscitis
Rozenblit et al[6]	76	M	69	AA	NS	No	No	No	No
LaBerge et al[7]	75	M	8	AA	60	No	No	Yes	Yes
Santbergen et al[8]	58	M	22	AA	NS	No	No	Yes	Yes
Mizoguchi et al[9]	81	M	24	AA	70 × 45	No	No	Yes	No
Leo et al[5]	81	M	36	AA	NS	Yes	No	Yes	No
Floros et al[10]	57	M	14	AA	86	Yes	No	No	No
Smith[11]	69	M	NS	AA	20	No	No	No	No
Witjens et al[12]	60	M	0	AA	NS	No	No	Yes	No
Duvnjak et al[13]	63	M	7	CIA	NS	No	No	No	No
Leeman et al[14]	71	M	10	CIA	92	Yes	No	Yes	No
Wadhwani et al[15]	73	M	6	DA	63 × 56	No	No	No	No
Higashi et al[16]	65	M	12	DA	25 × 19	Yes	No	No	No
Viviani et al[17]	69	M	12	CIA	115	No	No	No	No
Ribeiro et al[18]	79	M	30	DA	48 × 32	No	No	No	No
Berchiolli et al[19]	70	M	3	AA	45	Yes	Yes	No	No
Koterazawa et al[20]	80	M	20	DA	NS	No	No	No	No
Liechty et al[21]	82	M	61	AA	14	Yes	No	Yes	Yes
Akabane et al[22]	76	M	12	DA, AA	39 × 35; 52 × 47	No	No	No	No
Flynn et al[23]	72	M	7	AA	31	No	No	No	No
Present case	72	M	2	AA	42	No	No	Yes	No

Antitubercular therapy duration before EVAR, months	Intervention	Device	Interval from EVAR to OS, months	Follow-up duration, months	Outcome
8	EVAR	Barone	NA	15	Died of myocardial infarction
0	OS after EVAR	NS	NS	NS	NS
0	OS after EVAR	NS	6	18	Alive
0	OS after EVAR	Zenith	30	NS	NS
0	EVAR	NS	NA	12	Died of cerebral hemorrhage
0	EVAR	Zenith	NA	3	Alive
0	EVAR	NS	NA	9	Alive
0	EVAR	NS	NA	6	Alive
9	EVAR	AFX	NA	NS	Alive
3	OS after EVAR	Endurant	3	9	Alive
0	TEVAR	NS	NA	6	Alive
0	TEVAR	NS	NA	11	Alive
5	EVAR	Endurant	NA	17	Alive
12	TEVAR	Zenith	NA	6	Alive
0	OS after EVAR	AFX	10 days	25 days	Died of infection
10	TEVAR	NS	NA	24	Alive
0	EVAR	Excluder	NA	14	Alive
0	TEVAR + OS	C-TAG	NA	12	Alive
0	EVAR	NS	NA	8	Alive
0	OS after EVAR	AFX	3	7	Alive

AA, abdominal aorta; *CIA*, common iliac artery; *DA*, descending aorta; *M*, male; *NA*, not available; *NS*, not specified; *OS*, open surgery; *TEVAR*, thoracic endovascular aneurysm repair.

rupture. Another six patients (30%) had undergone endograft removal and open aneurysm repair 10 days to 30 months after the initial endovascular surgery, and five of the six patients had not received antitubercular therapy before endovascular surgery. In contrast, 5 of the 14 patients who had not undergone endograft explant surgery had received antitubercular therapy for 5 to 12 months before endovascular surgery and had survived for 6 to 24 months.

DISCUSSION

Since 1988, 51 cases of a mycotic AAA attributable to BCG therapy have been reported.[4,5,8,10-12,19,21-38] In our patient, infectious aortitis had progressed rapidly, and a saccular AAA or pseudoaneurysm had developed within 2 months after BCG therapy. In hindsight, a follow-up CT scan should have been performed sooner to monitor for any aneurysmal changes.

Furthermore, the introduction of the stent graft into the infected area without wide debridement of the infected tissue had exacerbated the infection and led to abscess formation. Failure to administer antitubercular preparations further worsened the situation. In the case of our patient, a follow-up CT scan should have been performed earlier than 3 months after EVAR, especially after positive blood culture results had been obtained. In addition, an aortic cuff above the aortic bifurcation might have been a better choice than the bifurcated stent graft used for greater ease of explantation.

Given the presenting symptoms of our patient, our choice of EVAR as the initial surgery was a clinical judgment error, and we have learned from that error. If such aneurysms have been sterilized with antitubercular therapy before EVAR, this treatment might have long-term benefits.

CONCLUSIONS

A mycotic aneurysm due to BCG therapy should be suspected in patients with a history of BCG treatment and indicative clinical characteristics. EVAR is not appropriate for patients stable enough to undergo open repair. EVAR should be considered only for cases of rupture in which the patient's life is threatened and should be used as a temporizing measure to the long-term solution. The device of choice for EVAR should be a device without suprarenal fixation to allow for relatively easy explantation.

REFERENCES

1. Schellhammer PF, Ladaga LE, Fillion MB. Bacillus Calmette-Guérin for superficial transitional cell carcinoma of the bladder. J Urol 1986;135:261-4.
2. Alexandroff AB, Jackson AM, O'Donnell MA, James K. BCG immunotherapy of bladder cancer: 20 years on. Lancet 1999;353:1689-94.
3. Harding GEJ, Lawlor DK. Ruptured mycotic abdominal aortic aneurysm secondary to Mycobacterium bovis after intravesical treatment with bacillus Calmette-Guérin. J Vasc Surg 2007;46:131-4.
4. Coscas R, Arlet JB, Belhomme D, Fabiani JN, Pouchot J. Multiple mycotic aneurysms due to Mycobacterium bovis after intravesical bacillus Calmette-Guérin therapy. J Vasc Surg 2009;50:1185-90.
5. Leo E, Molinari AL, Rossi G, Ferrari SA, Terzi A, Lorenzi G. Mycotic abdominal aortic aneurysm after adjuvant therapy with bacillus Calmette-Guérin in patients with urothelial bladder cancer: a rare but misinterpreted complication. Ann Vasc Surg 2015;29:1318.e1-6.
6. Rozenblit A, Wasserman E, Marin ML, Veith FJ, Cynamon J, Rozenblit G. Infected aortic aneurysm and vertebral osteomyelitis after intravesical bacillus Calmette-Guérin therapy. AJR Am J Roentgenol 1996;167:711-3.
7. LaBerge JM, Kerlan RK Jr, Reilly LM, Chuter TA. Diagnosis please. Case 9: mycotic pseudoaneurysm of the abdominal aorta in association with mycobacterial psoas abscess—a complication of BCG therapy. Radiology 1999;211:81-5.
8. Santbergen B, Vriens PH, de Lange WC, Van Kasteren ME. Combined infection of vertebroplasty and aortic graft after intravesical BCG treatment. BMJ Case Rep 2013;2013:bcr2012008161.
9. Mizoguchi H, Iida O, Dohi T, Tomoda K, Kimura H, Inoue K, et al. Abdominal aortic aneurysmal and endovascular device infection with iliopsoas abscess caused by Mycobacterium bovis as a complication of intravesical bacillus Calmette-Guérin therapy. Ann Vasc Surg 2013;27:1186.e1-5.
10. Floros N, Meletiadis K, Kusenack U, Zirngibl H, Kamper L, Haage P, et al. Ruptured mycotic aortic aneurysm after bacille Calmette-Guerin therapy. Ann Vasc Surg 2015;29:1450.e1-4.
11. Smith DM. BCG-osis following intravesical BCG treatment leading to miliary pulmonary nodules, penile granulomas and a mycotic aortic aneurysm. BMJ Case Rep 2016;2016:bcr2016215635.
12. Witjens AC, Witjes JA. Clinical case discussion: mycotic aortic aneurysm and psoas abscess as a complication of bacillus Calmette-Guérin instillations. Eur Urol Focus 2016;2:353-4.
13. Duvnjak P, Laguna M. Left anterior descending coronary artery and multiple peripheral mycotic aneurysms due to Mycobacterium bovis following intravesical bacillus Calmette-Guerin therapy: a case report. J Radiol Case Rep 2016;10:12-27.
14. Leeman M, Burgers P, Brehm V, van Brussel JP. Psoas abscess after bacille Calmette-Guérin instillations causing iliac artery contained rupture. J Vasc Surg 2017;66:1236-8.
15. Wadhwani A, Moore RD, Bakshi D, Mirakhur A. Mycotic aortic aneurysms post-intravesical BCG treatment for early-stage bladder carcinoma. CVIR Endovasc 2018;1:28.
16. Higashi Y, Nakamura S, Kidani K, Matumoto K, Kawago K, Isobe J, et al. Mycobacterium bovis-induced aneurysm after intravesical bacillus Calmette-Guérin therapy: a case study and literature review. Intern Med 2018;57:429-35.
17. Viviani E, De Gregorio C, De Capua A, Giribono AM, Bracale U, Del Guercio L, et al. Ruptured iliac pseudoaneurysm after intravesical bacillus Calmette-Guérin: urgent endovascular treatment. Case report and literature review. Ann Vasc Surg 2018;53:269.e1-9.
18. Ribeiro L, Rajendran S, Stenson K, Loftus I. Rare case of a proximal descending thoracic aorta mycotic aneurysm following intravesical BCG injections for the treatment of bladder cancer. BMJ Case Rep 2019;12:e231595.
19. Berchiolli R, Mocellin DM, Marconi M, Tomei F, Bargellini I, Zanca R, et al. Ruptured mycotic aneurysm after intravesical instillation for bladder tumor. Ann Vasc Surg 2019;59:310.e7-11.
20. Koterazawa S, Watanabe J, Uemura Y, Uegaki M, Shirahase T, Taki Y. A case of infectious thoracic aortic aneurysm after intravesical bacillus Calmette-Guérin instillation therapy for a superficial bladder cancer. Urol Case Rep 2021;36:101574.
21. Liechty AE, Pacifico A, Brant-Zawadzki P. Successful endovascular treatment of abdominal aortic rupture secondary to bacillus Calmette-Guérin vaccine. J Vasc Surg Cases Innov Tech 2022;8:19-22.
22. Akabane K, Uchida T, Matsuo S, Hirooka S, Kim C, Uchino H, et al. Hybrid operation for infectious thoracic and abdominal aortic aneurysms complicated with bacillus Calmette-Guérin therapy for bladder cancer: a case report. Medicine 2021;100:e24796.
23. Flynn D, Ogi A, Subedi S, Langton J, Choong K, O'Donnell J. Mycotic aortic aneurysm formation following intravesical BCG treatment for transitional cell carcinoma of the bladder. BMJ Case Rep 2021;14:e246389.
24. Holmes BJ, LaRue RW, Black JH III, Dionne K, Parrish NM, Melia MT. Mycotic aortic aneurysm due to intravesical BCG immunotherapy: clinical manifestations and diagnostic challenges. Int J Mycobacteriol 2014;3:60-5.

25. Samadian S, Phillips FM, Deeab D. Mycobacterium bovis vertebral osteomyelitis and discitis with adjacent mycotic abdominal aortic aneurysm caused by intravesical BCG therapy: a case report in an elderly gentleman. Age Ageing 2013;42:129-31.
26. Akita H, Okamura T, Nakane A, Kobayashi T, Yamada K, Tanaka Y. Infectious aortic aneurysms occurring 1 year after bacillus Calmette-Guérin bladder instillation therapy. Int J Urol 2015;22:234-5.
27. Nam EY, Na SH, Kim SY, Yoon D, Kim CJ, Park KU, et al. Infected aortic aneurysm caused by Mycobacterium bovis after intravesical bacillus Calmette-Guérin treatment for bladder cancer. Infect Chemother 2015;47:256-60.
28. Davis FM, Miller DJ, Newton D, Arya S, Escobar GA. Successful treatment of a mycotic multifocal thoracoabdominal aortic aneurysm as a late sequelae of intravesical bacillus Calmette-Guerin therapy: case report and literature review. Ann Vasc Surg 2015;29:840.e9-13.
29. Coddington ND, Sandberg JK, Yang C, Sehn JK, Kim EH, Strope SA. Mycotic aneurysm after bacillus Calmette-Guérin treatment: case report and review of the literature. Case Rep Urol 2017;2017:4508583.
30. Simar J, Belkhir L, Tombal B, André E. Ruptured aortic aneurysm due to Mycobacterium bovis BCG with a delayed bacteriological diagnosis due to false negative result of the MPB 64 immunochromatographic assay. BMC Res Notes 2017;10:64.
31. Okon E, Stearns J, Durgam AK. Tuberculous psoas abscess and worsening vascular aneurysm: all from bacillus Calmette-Guerin (BCG) therapy? Am J Case Rep 2017;18:810-2.
32. Rohailla S, Kitchlu A, Wheatcroft M, Razak F. Mycotic aneurysm formation after bacillus Calmette-Guérin instillation for recurrent bladder cancer. CMAJ 2018;190:E467-71.
33. Roeke T, Hovsibian S, Schlejen PM, Dinant S, Koster T, Waasdorp EJ. A mycotic aneurysm of the abdominal aorta caused by Mycobacterium bovis after intravesical instillation with bacillus Calmette-Guérin. J Vasc Surg Cases Innov Tech 2018;4:122-5.
34. Kusakabe T, Endo K, Nakamura I, Suzuki H, Nishimura H, Fukushima S, et al. Bacille Calmette-Guérin (BCG) spondylitis with adjacent mycotic aortic aneurysm after intravesical BCG therapy: a case report and literature review. BMC Infect Dis 2018;18:290.
35. Lareyre F, Reverso-Meinietti J, Carboni J, Gaudart A, Hassen-Khodja R, Raffort J. Mycotic aortic aneurysm and infected aortic graft after intravesical bacillus Calmette-Guérin treatment for bladder cancer. Vasc Endovascular Surg 2019;53:86-91.
36. Vudatha V, Ranson M, Blair L, Ahmed AA. Rapid detection of bacille Calmette-Guérin-associated mycotic aortic aneurysm using novel cell-free DNA assay. J Vasc Surg Cases Innov Tech 2019;5:143-8.
37. Buerger M, Kapahnke S, Omran S, Schomaker M, Rief M, Greiner A, et al. Aortic aneurysm and aortic graft infection related to Mycobacterium bovis after intravesical bacille Calmette-Guérin therapy—a case series. BMC Surg 2021;21:138.
38. Zaza SI, Ghasemzadeh A, Bennett KM. Mycobacterium bovis causing mycotic aneurysm secondary to intravesical treatment with bacillus Calmette-Guérin: a case report. Ann Vasc Surg 2022;79:437.e1-6.

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