Mycotic infrarenal aortic aneurysm due to mycobacterium after intravesical treatment for bladder cancer

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ABSTRACT

Intravesical instillation of Bacillus Calmette-Guerin, a live-attenuated strain of *Mycobacterium bovis*, is a common adjuvant therapy for bladder cancer with a low incidence of serious adverse events. The case described herein illustrates a rare complication of intravesical Bacillus Calmette-Guerin instillation that resulted from invasion of the mycobacterium into tissue outside of the bladder lining, also known as microbial dissemination, leading to infection of the aortic wall and development of a mycotic aneurysm, and highlights the therapeutic challenges presented by the aortic pathology in this clinical scenario. (J Vasc Surg Cases and Innovative Techniques 2021;7:354-6.)

Keywords: Mycotic aneurysm; Mycobacterium bovis infection

Bacillus Calmette-Guerin (BCG), a live-attenuated strain of Mycobacterium bovis, is an effective and widely used intravesical treatment for bladder cancer.^{1,2} When administered as a treatment for Ta and T1 bladder cancer, it causes an inflammatory response by host cells against tumor cells.¹ It is used as an adjunct treatment after resection of the bladder cancer tumor, where it has been shown to prevent progression and recurrence of the tumor.¹ A rare complication of this treatment is microbial dissemination and infection of the aortic wall, causing the wall to weaken and forming an aneurysm.³ This could prove dangerously fatal if not promptly addressed. The case described herein illustrates the complication of a mycotic aneurysm because of BCG therapy. The patient is deceased; however, his spouse has provided permission for use of his images for publication.

CASE

The patient is 76-year-old man with a history of chronic back pain. Three months before admission the patient

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developed progressive back pain, weight loss, loss of appetite, and underwent outpatient evaluation for this. He was in the process of being worked up for back pain, which included magnetic resonance imaging of his lumbar spine and a positron emission tomographic scan. On the positron emission tomographic scan, it was noted that there was a mass anterior to the spine on the right side. The patient was scheduled to undergo a biopsy of the mass. Before the biopsy, computed tomographic (CT) imaging was obtained by the radiologist who noted that the abnormality was related to the aorta. A subsequent CT angiogram demonstrated evidence of a 6 cm aortic aneurysm in the infrarenal aorta with characteristics suggestive of a mycotic aneurysm (Fig 1). His past medical history included biannual intravesical infusions of BCG for bladder cancer for the prior 2 years. Fig 2 demonstrates a CT urogram performed 1 year earlier, which shows mild aortic aneurysmal disease in the immediate infrarenal aorta, which became the mycotic aneurysm.

The patient was taken emergently to surgery where he first underwent an axillo-femoral-femoral-femoral bypass to accomplish extra-anatomic revascularization of his lower extremities. At the same setting, he then underwent ligation of the infrarenal aorta just below the renal arteries with excision and debridement of the aneurysm wall and ligation of the aortic bifurcation. This procedure was performed using retroperitoneal exposure through the left 11th interspace. Pathology from the excised segment of the aortic wall demonstrated necrotizing granulomatous inflammation (Fig 3). Aortic wall culture eventually revealed *Mycobacterium tuberculosis* complex by DNA probe.

The patient's postoperative course was largely uneventful and unremarkable. He was transferred to the

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Fig 1. Computed tomographic (CT) angiography demonstrating mycotic aneurysm of the infrarenal aorta (A) axial, (B) sagittal, (C) coronal planes.

inpatient rehabilitation unit on postoperative day 9 to help recover from severe deconditioning due to his long-standing back pain. Because of the pathology report of granulomatous inflammation and with the history of BCG treatment, the patient was started on rifampin, ethambutol, and isoniazid. At almost 6 weeks of incubation, the aortic tissue became positive for M. tuberculosis complex, confirmed by DNA probe. The patient was evaluated at National Jewish Health in Denver, an institution noted for expertise in treatment of Mycobacterium infections. After the evaluation, rifampin was discontinued and rifabutin was started due to the inability to achieve adequate anticoagulation effect from warfarin prescribed for atrial fibrillation. Thereafter, therapeutic anticoagulation was achieved. The patient tolerated the antimycobacterial regimen without a significant adverse effect. While on therapy, he gained weight. Five months after resection of the aneurysm, and while still on antimycobacterial therapy, the patient was diagnosed with recurrent bladder cancer. Four months later the patient died from pneumonia and sepsis while receiving chemotherapy for recurrent bladder cancer.



Fig 2. Native aorta 1 year prior on a computed tomographic (CT) urogram showing mild aneurysmal of the immediate infrarenal aorta (*arrow*) that became the mycotic aneurysm.

DISCUSSION

Mycotic aneurysms due to BCG treatment are rare and may involve large- and medium-sized blood vessels.² Seventy-nine percent of mycotic aneurysms associated with BCG treatment for bladder cancer have involved



Fig 3. Histology from the resected aneurysm wall showing granulomatous necrosis (hematoxylin and eosin, ×40).

the aorta, with the majority involving the abdominal aorta below the level of the kidneys.² Symptoms are typically nonspecific and can present as weight loss, fever, chills, malaise, and fatigue.^{2,4,5} Notably, back pain after BCG treatment should raise suspicion for possible aortic aneurysm infection.⁴ Based on previously reported cases, the average time of diagnosis of a mycotic aneurysm was 19 months after BCG treatment, suggesting that mycotic aneurysms are long-term complications.^{3,6}

It can be a challenge to diagnose the microbial cause as *M. bovis* given the tedious nature of methods required, which include strict culture parameters, polymerase chain reaction, and coloration techniques to examine the bacteria.⁷ Microbiology labs are typically only able detect that the organism is related to the to M. tuberculosis species, and thus, further biochemical to testing would be required differentiate *M. tuberculosis* from *M. bovis.*² These challenges could lead to further delay in diagnosis and difficulty in identifying the microbial culprit.

Another possible explanation for this complication is that patients who present with mycotic aneurysms after BCG treatment for bladder cancer may have an extensive history of smoking, which may predispose them to vascular disease.⁶ In our case, the patient had a 30 pack-year history of smoking but had achieved complete cessation 20 years before this event.

Once a mycotic aneurysm has been recognized, the decision on course of treatment can be based on the patient's medical history and current health status. The "gold standard" treatment is to excise the infected tissue and ensure that proper blood flow is restored to the bilateral lower extremities.⁷ Conservative management is not preferred, but rather reserved for those who are unable to undergo a surgical operation.⁷ The spectrum of treatment for a mycotic aneurysm, in general, in addition to debridement of the infected aortic tissue, includes in situ replacement with aortic homograft,^{8,9} in situ replacement with a rifampin-soaked polyester graft,¹⁰ in situ replacement with a neoaortoiliac system created with femoral veins,¹¹ and as in our patient's case, extraanatomic revascularization.¹⁰ An additional approach that avoids direct surgery on the infected aorta comprises endovascular stent graft exclusion.¹²

In conclusion, although a rare complication, mycotic aneurysm should be considered in patients who have a history of receiving BCG intravesical treatments for bladder cancer and develop symptoms that may be suggestive of symptomatic aneurysm disease such as abdominal or back pain. Suspecting a mycotic aneurysm in this setting may provide the opportunity for early diagnosis and management to prevent aneurysmal rupture with its attendant morbidity and mortality.

REFERENCES

- Shelley M, Court JB, Kynaston H, Wilt TJ, Fish R, Mason M. Intravesical Bacillus Calmette-Guérin in Ta and TI bladder cancer. Cochrane Database Syst Rev 2000;4:CD001986.
- 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.
- 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.
- 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.
- Gao CQ, Mithani R, Leya J, Dawravoo L, Bhatia A, Antoine J, et al. Granulomatous hepatitis, choroiditis and aortoduodenal fistula complicating intravesical Bacillus Calmette-Guérin therapy: case report. BMC Infect Dis 2011;11:260.
- 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.
- 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.
- Lesèche G, Castier Y, Petit M-D, Bertrand P, Kitzis M, Mussot S, et al. Long-term results of cryopreserved arterial allograft reconstruction in infected prosthetic grafts and mycotic aneurysms of the abdominal aorta. J Vasc Surg 2001;34:616-22.
- Ben Ahmed S, Louvancourt A, Daniel G, Combe P, Duprey A, Albertini JN, et al. Cryopreserved arterial allografts for in situ reconstruction of abdominal aortic native or secondary graft infection. J Vasc Surg 2018;67:468-77.
- Dubois M, Daenens K, Houthoofd S, Peetermans WE, Fourneau I. Treatment of mycotic aneurysms with involvement of the abdominal aorta: single-centre experience in 44 consecutive cases. Eur J Vasc Endovasc Surg 2010;40:450-6.
- Dirven M, van der Jagt MF, Barendregt WB, van der Vliet D. The efficacy of autologous femoropopliteal vein reconstruction for primary aortic and aortic graft infection. Ann Vasc Surg 2015;29:1188-95.
- Kan C-D, Yen H-T, Kan C-B, Yang Y-J. The feasibility of endovascular aortic repair strategy in treating infected aortic aneurysms. J Vasc Surg 2012;55:55-60.

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