BK Virüse bağlı hemorajik sistitte süperselektif mesane arter embolizasyonu

Superselective embolization of vesical arteries for management of hemorrhagic cystitis caused by BK polyomavirus

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Geliş tarihi (Submitted): *02.01.2018*
Kabul tarihi (Accepted): *10.05.2018*

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Özet

Otuz altı yaşında erkek hasta, non Hodgkin lenfoma tanısıyla allojenik kök hücre nakli sonrası 19. günde makroskopik hematüri ile başvurdu. Hematürinin BK virüse bağlı geliştiği saptandı. Konservatif yaklaşım ile hematüri kontrol altına alınamadı. Hiperbarik oksijen tedavisi ve Sidofovir intravezikal tedavisi denendi ancak başarılı olmadı. Takiben hastaya bilateral perkütan nefrostomi takılıp 1 hafta sonra kanayan mesane arterleri selektif olarak embolize edildi. İşlemden 2 hafta sonra nefrostomi klempe edildi, hastanın rahatlıkla idrar yaptığı ve hematürisinin olmadığı görüldü. Basamaklı hızlı multidisipliner yaklaşım ile hemorajik sistit yönetimi kök hücre nakli başarısı açısından da önem arz etmektedir.

Anahtar Kelimeler: anjiyoembolizasyon, hematüri, kök hücre nakli, lenfoma, sistit.

Abstract

A 36 year- old male patient who had received an allogeneic stem cell transplantation from a non- familial identical donor for the treatment of non- Hodgkin lymphoma 19 days ago admitted to the emergency department with macroscopic hematuria. A BK virus induced hematuria was diagnosed and conservative measures failed to get his heamaturia under control.Hyperbaric oxygen therapy and Cidofovir treatment had also failed. Then bilateral percutaneous nephrostomies were inserted followed by selective angioembolization of vesical arteries one week later. Two weeks after angioembolization both nephrostomies were clamped sequentially and the patient was able to pass urine comfortably without any haematuria. Management of heamorrhagic cystitis by a stepwise, rapid multi-disciplinary approach can be a critical factor in the success of stem cell transplantation.

Keywords: angioembolization, cystitis, hematuria, lymphoma, stem cell transplantation.

INTRODUCTION

Hemorrhagic cystitis is a significant complication, commonly seen after bone marrow transplantation (BMT) which is characterized by diffuse inflammation and bleeding from the bladder mucosa. Its management requires a stepwise approach to control the bleeding which is associated with prolonged hospitalization and urinary tract obstruction and can lead to death (1). Early onset hemorrhagic cystitis, particularly occurring within 72 hours, is mostly related to chemotherapy however these are now less frequently seen due to widespread use of mesna and hydration. Late onset hemorrhagic cystitis, defined as those seen after 72 hours of chemotherapy, has become a more commonly seen form of hemorrhagic cystitis. BK virus is commonly identified in patient's urine after BMT. Nearly 80% of BMT recipients are reported to have BK virus in the urine tests, however only 10-25% of recipients have significant hemorrhagic cystitis which needs treatment. Hyperbaric oxygen treatment was reported to have successful effects on hemorrhagic cystitis in experimental and case studies. Intravesical administration of cidofovir for viral hemorrhagic cystitis was also used as an alternative method in previous reports (2, 3). Superselective embolization of bladder vessels with microcatheters and embolization particles were reported recently in some studies with comparable success rates as a minimal invasive method when compared to radical surgery (4, 5).

CASE PRESENTATION

A 36 year old man with non-hodgkin lymphoma was admitted to the hospital because of hematuria occurring 19 days after receiving non-familial-identical allogenic stem cell transplantation (SCT). Macroscopic haematuria was detected because of hemorrhagic cystitis (grade 2) and the patient had difficulty in voiding. Initially he was treated with hydration, platelet transfusion and bladder irrigations. Two weeks later grade 3 haematuria was observed again *(with Urine BK virus 241356687 copies/ml)* and could not be treated with conservative measures. Hyperbaric oxygen therapy was performed for ten days however it was subsequently discontinued due to no improvement in heamaturia. During the follow up urethra catheterization was avoided until the patient had painful urinary retention. Usually the patient was able to void most of the clots in his bladder spontaneously, but when he was catheterized he had blockages of his Foley catheter

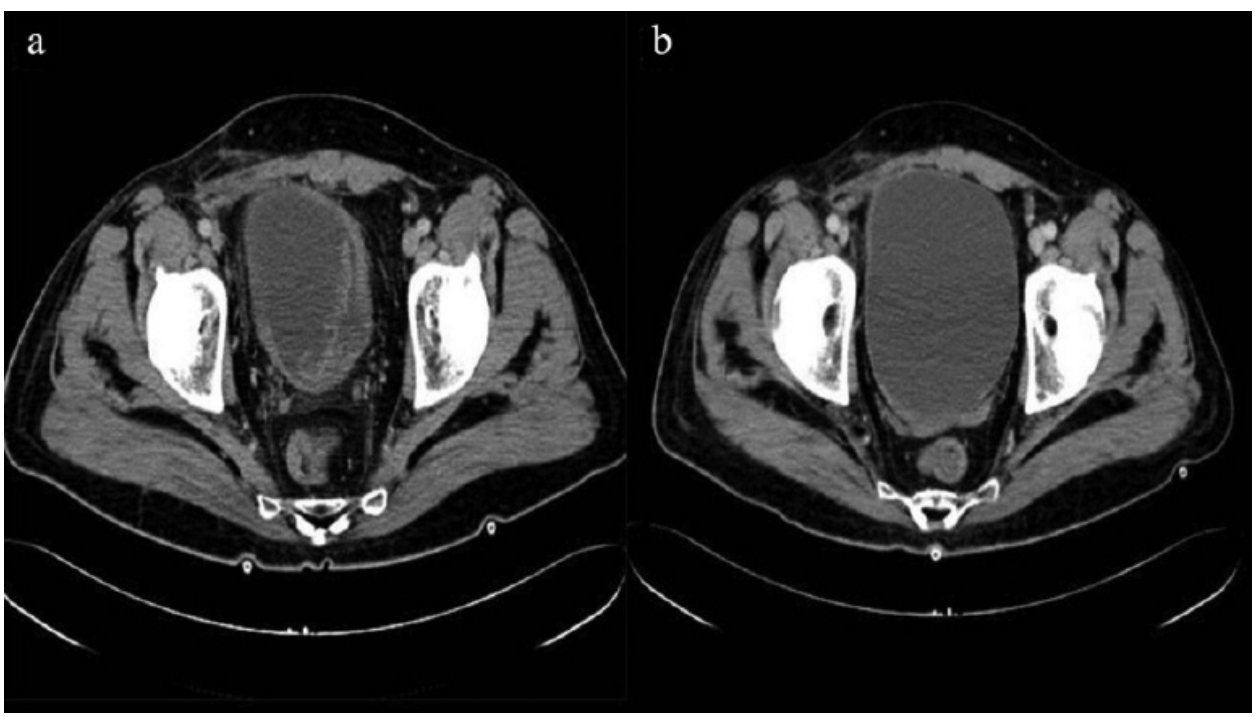

Figure 1: a. Bleeding in the bladder before the angioembolization procedure**.** b. Normal bladder structure after angioembolization procedure.

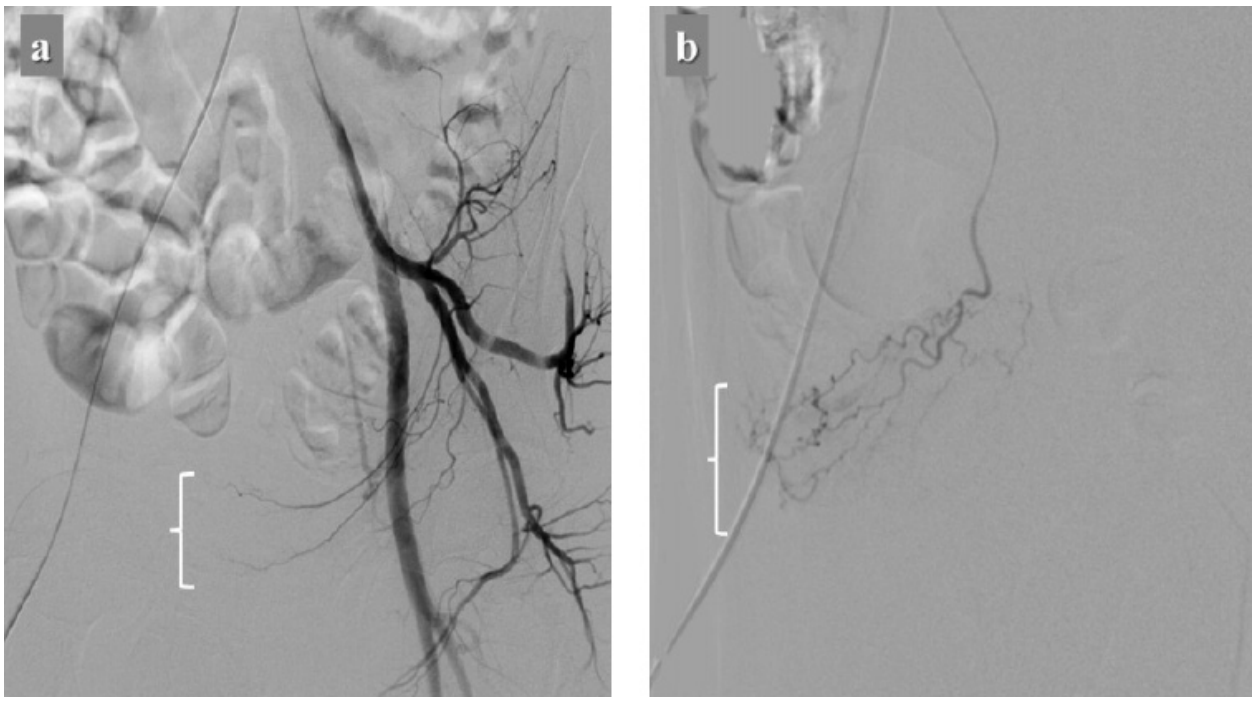

Figure 2: a. Branches of left superior vesical artery. b. Right superior vesical artery and bleeding location in the bladder.

with big clots in two separate instances. After removal of the blocked catheters the patient was able to void the clots. Subsequently we planned to order intravesical instillation of cidofovir because the patient's creatinine started to increase up to 1,8 mg/dl and amount of BK virus in urine was increased to serious levels. BK virus reported in urine 37734914 copy/ml. A dose of 5 mg/kg cidofovir that was diluted with 100 ml saline was slowly instilled in the bladder via 10 Fr catheter which was taken off immediately due to pain. The patient was warned not to void for 1 hour. This procedure was applied 4 times in two weeks as if platelet levels was greater than $50x10^3$/uL. Unfortunately blood clots did not decrease during this period and the need for blood transfusion continued. After cidofovir treatment, the amount of BK virus in urine (669925524 copy/ml) increased rapidly. Then bilateral percutaneous nephrostomies were inserted into both kidneys to reduce the quantity of urine in bladder. One week later the need for blood transfusion was still continuing. Therefore a selective angioembolization of vesical arteries was eventually performed (Figures 1 and 2).

Analgesics were necessary only for a few days after the procedure. Two weeks after the angioembolization both nephrostomies were clamped sequentially; patient was able to void urine and there was no haematuria. This situation continued for two months, then haematuria suddenly started again. The patient died of *graft versus host disease* (pulmonary infection, sepsis and multiorgan dysfunction).

DISCUSSION

We avoided performing cystoscopy and urethral catheterization unless it was essential, because it could also cause or increase haematuria. We decided to give treatment with intravesical cidofovir. Systemic use of cidofovir among BMT recipients has been hampered by the nephrotoxicity of this drug. As we mentioned before, our patient's BK virus load was high in urine while lesser in blood. Fanourgiakis et al. first reported the intravesical instillation of cidofovir in the treatment of hemorrhagic cystitis caused by adenovirus type 11 in a BMT recipient; hemorrhagic cystitis was improved and blood clotting was stopped after two cycles of treatment (2). Sakurada et al. also reported successful results of intravesical instillation of cidofovir in their four cases with hemorrhagic cystitis caused by adenovirus and BKV (3).

There was no improvement of haemorrhagic cystitis after intravesical cidofovir was administered, so we

planned to perform bilateral nephrostomies and then selective embolization of vesical arteries. Angioembolization of vesical arteries was performed by our interventional radiology team with particle embolization agents (350 micron Embozene® Microspheres). The analgesic requirement was less than we expected based on reports of previous studies (4, 5). After a few days of the procedure the blood transfusion requirement significantly decreased. After two weeks the nephrostomies were clamped and the patient voided easily with no haematuria being observed. No sensorial or voiding problem was observed which could be a serious problem. And also there was no sign of necrosis of bladder mucosa (Figure 2).

During the follow-up period of two months after embolization, the patient had a sepsis due to pulmonary infection and graft versus host disease. Previously, in another patient we were not able to treat the hemorrhagic cystitis, bladder perforation was reported and patient died because of sepsis. We observed that severe hemorrhagic cystitis (>grade 3) after BMT or SCT is a poor prognostic factor for graft and overall survival (3). So it is crucial to make a quick multidisciplinary management of severe hemorrhagic cystitis after BMT or SCT.

CONCLUSION

Superselective angioembolization of vesical arteries seems to be an excellent /a more efficient/more successful option to take effective control of hemorrhagic cystitis with very low complication rates.

Conflict of interest

None.

Source of funding

None

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