

**Pons gliomlu çocuk hastada ifosfamide bağlı gelişen hemorajik sistitin tedavisi***Management of ifosfamide induced hemorrhagic cystitis in a pediatric patient with pontine glioma***Ahmet Akça<sup>1</sup>, Oktay Akça<sup>2</sup>, Nagihan İnan<sup>1</sup>, Ahmet Kaya<sup>1</sup>, Muhammet Dönmez<sup>1</sup>, Sema Büyükkapubay<sup>3</sup>**<sup>1</sup> Kocaeli Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, Kocaeli<sup>2</sup> Kartal Eğitim Ve Araştırma Hastanesi, Üroloji Bölümü, İstanbul<sup>3</sup> Kocaeli Üniversitesi Tıp Fakültesi, Çocuk Sağlığı Ve Hastalıkları Anabilim Dalı, Kocaeli**Özet**

Bu yazıda pons gliomu nedeni ile ifosfamid kullanan ve profilaktik olarak mesna kullanmasına rağmen tedavi sonunda hemorajik sistit gelişen 5 yaşında erkek olgu sunulmuştur. Ultrason ve doppler ultrasonunda mesane sağ lateral duvarda vasküler kitle izlendi. Manyetik rezonans görüntüleme(MRG) mesane sağ lateral duvarda belirgin kalınlaşma ve kontrast tutulumu mevcut iken detrusor kas intensitesi normal izlendi. Sistoskopi ve biyopsi sonrasında biyopsi sonucu 'malign transformasyon izlenmedi' şeklinde raporlanan hasta mesna daha yüksek dozda tekrar kullanılarak tedavi edildi. Böylece pediatrik hastalarda daha zor olan sistoskopinin tekrarlanmasına ve mesane irrigasyonuna ihtiyaç duyulmadı.

**Anahtar Kelimeler:** Ifosfamid, pons gliomu, hemorajik sistit, Mesna, cerrahi.

**Abstract**

We present the case of a 5 year old boy with hemorrhagic cystitis (HS) who diagnosed after the use of Ifosfamide due to Pons glioma. Although Mesna used for prophylaxis during treatment, developed HS at the end of the chemotherapy (CT). USG and Doppler USG showed a vascularized mass at the right wall of the bladder. Magnetic resonance imaging showed righth bladder wall thickenign with significant enhancement and normal apperance of detrusor msucle. The mass evaluated by urologic endoscopic surgery and taken biopsy reported as "no any malign transformation". Mesna used once again in higher dosage and we did not need additional urologic endoscopic surgery or bladder irrigation which were very troublesome in pediatric age group.

**Keywords:** Ifosfamide, pontine glioma, hemorrhagic cystitis, Mesna, surgery

**Introduction**

The bladder masses detected after hematuria may be malignant, as well as some benign processes can also cause focal bladder wall thickening. Endometriosis, Chron disease, bacterial and viral infections, chemotherapy (CTh) or radiotherapy (RT) based hemorrhagic cystitis(HS) are examples for benign situations(1). HS is the diffuse inflammation of the mucosa of the bladder wall resulting in bleeding and may be associated with serious morbidity and mortality(2). It can be seen after bone marrow transplantation in 10-20% rates or as a complication of CTh or RT due to any oncologic cause in the pediatric population(3,4). Oxazophosphorine combination drugs, such as Cyclophosphamide and Ifosfamide are the most common causes for HS in CTh medications(2). The metabolite of these group drugs, causes HS and showing toxic effect on the bladder mucosa, is Acrolein which has no any anti-tumor effect(2,5). This toxicity is dose dependent and developing by 2-40% in patients treated with

Cyclophosphamide(2). In these patients, mostly due to the insufficiency of clinical and radiological findings, the diagnosis may be necessary to be verify by the urological endoscopic surgery and pathologic correlation(1).

In this paper, the ultrasound (USG), MRI, pathology findings and the clinical course of the bladder mass detected after macroscopic hematuria are presented in a pediatric patient who had received adjuvant Ifosfamide treatment due to Pons glioma.

**Case**

5-year old male patient admitted to pediatrics clinic with complaints of occasional headache and unbalanced walking. Pediatric neurology clinic evaluated the patient by MRI and a mass in the brain stem compatible with Pons glioma was detected. The patient underwent treatment with Dexamethasone and Mannitol because of the risk of edema and herniation and operated by

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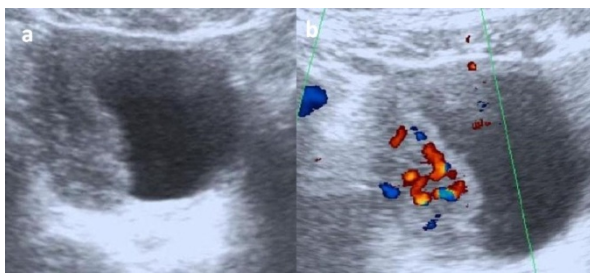
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the neurochirurgie. After two weeks, 1,8 gr/m<sup>2</sup>/day (1400mg/day) Ifosfamide treatment for 3 days with an interval of 21 days a total of 8 cures to be performed. To protect the urinary system mucosa 2000mg/m<sup>2</sup>/day i.v. Mesna infusion was given during cures. Macroscopic hematuria occurred on following second day after the eighth cure. Right lateral bladder wall thickening in the gray scale USG (Figure 1a), and significant vascularization in the Doppler USG (Figure 1b) findings were observed at this time. However, because of USG findings were insufficient to identify benign or malign mass distinction, an MRI scheduled for differential diagnosis. Right lateral bladder wall thickening observed in T1 and T2 MRI sequences again(Figure 2a,b). Despite significant contrast enhancement, the detrussor muscle viewed in normal intensity(Figure 2c). Based on these findings, cystoscopy was performed and punch biopsies were taken from the right lateral wall thickening which had has 4x3cm irregular surface. "Increased connective tissue in lamina propria and no any malign transformation" reported by pathology clinic. At this time patient diagnosed as HS then the treatment of 3000cc/day hydration and 3000mg/m<sup>2</sup> Mesna was started. Hematuria completely resolved one week after initiation of the treatment and USG control for the bladder was normal after 2 weeks. Additional urological endoscopy was not considered due to normal USG findings.



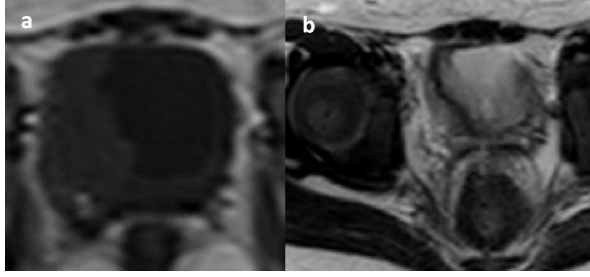
**Figure 1a, b:** Right lateral bladder wall thickening in gray-scale ultrasound (a) and significant vascularization of the mass in Doppler USG (b) observed.

## Discussion

Frequent causes of hematuria such as stone, cyst, and tumor must be excluded in patients suspected with HS(6). In 21 years experience of

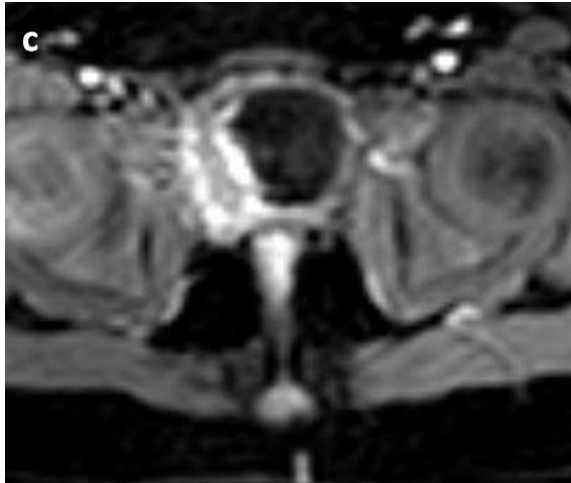
Huppman et al.; although mass in the bladder is occasional in pediatric population, the most common one is rhabdomyosarcoma and masses of children in the bladder has a very wide variation(7). Although underlying the use of chemotherapy, bladder mass detected after macroscopic hematuria complicates the differential diagnosis in this case of children. For example, clinical and MRI findings of rhabdomyosarcoma are similar to HS(8). Specificity of the radiological features of bladder masses secondary to nonneoplastic diseases is less but still valuable in the evaluation. Focal or diffuse irregular bladder wall thickening is seen in imaging. MRI is helpful in showing inflammation and edema on T2 sequences. In addition, MRI is able to distinguish between hematoma and bladder wall(1). In our case, where there is a massive wall thickening was being distinguished from the normal bladder wall muscle structure. HS is a life-threatening complication in pediatric oncology patients and options such as embolization, endoscopic laser coagulation, hydrostatic pressure, use of hyperbaric oxygen, instillation of formalin, prostaglandins, and oral sodium pentosan polysulfate is used in the treatment(4). In fact, cutaneous vesicostomy can be opened for resistant clot retention until the end of treatment(9). Difficulty of these treatments for the patient cannot be denied in pediatric population. All these show that perhaps the best treatment option for HS is prophylaxis. Indeed, in this case the regression of the mass in radiologic images and the hematuria due to use of prophylactic mesna again in higher dosage in a week-long period supports this idea. Although limited in the literature, pediatric HS cases are often encountered after bone marrow transplantation or oncologic disease induced chemotherapy(3,4). Although primary diagnoses of HS patients have not urinary tract origin, perhaps to continue treatment with in urology clinic may be more appropriate in terms of patient comfort after the development of macroscopic hematuria. Stillwell et al. reported that; the necessity of cystectomy and development of bladder cancer is 9% and 5% respectively in 100 adult patients diagnosed with ifosfamide induced HS(10). Kijima et al. reported the development of bladder cancer after the use

of Cyclophosphamide is just 17 cases for all of Japan(11).



**Figure 2a, b:** Right bladder wall thickening on T1 and T2 MRI sequences.

Although to follow up pediatric HS patients in urology clinic in the light of pediatric and radiology clinics evaluations is more appropriate in terms of patient comfort, urological endoscopic intervention would be more appropriate in cases that cannot be responded to treatment with mesna, that have clot retention or that cannot be distinguished from malignancy. In this case, to use appropriate dose of mesna in prophylaxis and in treatment facilitated differential diagnosis and perhaps rescued patient from clot retentions which needs even more troublesome treatment in pediatric age group due to anesthesia necessity in all retentions.



**Figure 2c:** Right bladder wall thickening and enhancement whereas the detrusor signal intensity is normal.

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