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Hyperbaric Oxygen Therapy for Hemorrhagic Cystitis after the Allogeneic Stem Cell Transplantation-A Case Report

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Abstract Hemorrhagic cystitis (HC) is a significant clinical problem that occurs after allogeneic transplantation and is often refractory. The patient was a 40-year-old man who had HC after two months of transplantation of allogeneic stem cells. Several treatments were used to improve the patient, but no improvement. At the doctor's proposal, 5 sessions of Ozone therapy were performed for the patient. After the completion of the sessions, the clinical symptoms associated with HC disappeared completely. This study shows that HC treatment with ozone therapy is an effective and tolerable method and does not have any clinical complications.

Keywords: hyperbaric oxygen therapy, hemorrhagic cystitis, allogeneic, transplantation

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1. Introduction

Hemorrhagic cystitis (HC) is an inflammatory hemorrhagic disease and condition that can be caused due to infectious (e. g. viruses) or non-infectious cause. This disease brings about different incidents of bleeding in mucosa parts of the urine bladder [1]. In severity of HC and the results of the treatments, there are substantial obvious differences. Some patients only have microscopic bleedings and in some patients, the symptoms appear in the lower parts of the urinary tracts [2]. Due to the many different clinical observations of HC disease, different methods of treatment are used. Methods such as antiviral medicine types like vidarabine, oxygen or ozone therapy, washing the urine bladder, formalin therapy, cystoscopy and even cystectomy are utilized for treatment. Each of these methods can lead to improved patient's health and certain complications [3].

Hyperbaric (high-pressure) oxygen therapy is a non-invasive method in which pure oxygen in high pressure is used. This method is used for the treatment of the patients who have received allogeneic hematopoietic stem cell transplantation (allo-HSCT) [4]. The treatment of patients with this method shows evidence that hyperbaric oxygen therapy (HBO) is a completely effective treatment method and that this method is a tolerable method with positive

results of laboratory and clinical tests [5]. Given that HC occurs in almost certain groups at high risk, therefore our aim of this study was reporting a case of HC after allo-HSCT with acute conditions which achieved a complete recovery with using hyperbaric oxygen therapy.

2. Case Report

A 40-year-old man, having acute myeloid leukemia (AML) received bone marrow transplantation during March 2017 at Imam Reza Hospital in Kermanshah. The donor was the patient's brother. After transplantation, the patient was discharged from the hospital with a normal condition. The result of the medical test chimerism in this patient was 95% which showed the highest transplantation matching. It is necessary to mention that despite the training are given to the patient and his family about the procedure and the process of the treatment and the necessity of on-time consumption of the medicine; unfortunately, neither the patient nor his family paid attention to the on-time consumption of the medicine and the necessary dosage.

The patient returned to the hospital in June 2017 due to severe hematuria. The time to onset of HC after allo-HSCT was 52 days. Among his other clinical symptoms can be pointed out to severe weakness, lethargy, fatigue, and narcosis. In further studies, the patient

showed hematuria with grade 4 and graft-versus-host disease (GVHD) despite immunosuppressive therapy. The clinical course of HC and the relationship with GVHD is displayed in Table 1. Immediately, therapeutic measures were performed by the medical staff of the hospital were done. The first actions involved urine test, full blood count (FBC) tests, and ultrasound of the kidneys and ducts. The results of urine and blood tests showed that there was a large number of red blood cells in the urine and decreased hemoglobin and platelets. Also, the ultrasound results showed evidence of hydronephrosis. The second series of actions was a urological consultation that, according to the counselor, prescribed a cystoscopy for the patient. Therefore, pre-cystoscopy levels and stages including CT-scan of the abdomen and the pelvis, anesthesia consultation, voiding cysto-urethrogram (VCUG) and applying diagnostic ultrasound were performed again from kidneys and ducts.

At the operation room, entering the left ureter was done using the guidewire, and the checking was done until the place of the renal pelvis. There were no stones, spatial lesion or hemorrhagic (bleeding); but the left ureter had edema and erythema. In the same way, the right ureter was also analyzed and no pathologic point was observed. Due to the fact that there was no wound, formalin injection fulguration was not necessary. After the cystoscopy, the patient was transferred to the hospital unit/division but hematuria still continued. Patient's urinary bladder was washed regularly and at the same time, hemoglobin and platelets drop was compensated with the injection of packed cell products (PC) and platelets. Finally, 5 ozone therapy sessions were suggested for the patient by the physician due to due to the prolonged duration of the washing processes and not stopping bladder bleeding. After the end of each session, a urine test was performed for the patient and at the last session of the ozone therapy, the results of all tests were normal.

Ozone therapy inside the urinary bladder for curing hematuria was done for the first time in Iran. This method, by blocking capillaries and very small vessels of the urinary bladder, stopped the bleeding. All of the primary and routine treatment was done for the patient, but the responses were not very significant. Despite all these, using ozone therapy, valuable results were achieved and the patient became stable.

3. Discussion

Hemorrhagic cystitis and host's reaction to the transplantation are the complications of allogeneic transplantation of hematopoietic stem cells [6]. Hemorrhagic cystitis is a common cause of mortality after allogeneic transplant [4]. The procedure of allogeneic hematopoietic stem cell transplant and the treatment of the increase in immunity system's reaction for GVHD may be so long and time-consuming due to the defect, and malfunction in the humoral and cellular immunity system. GVHD can be either acute or chronic [7].

In acute GVHD, it gets obvious within less than the first 100 days after the transplantation (often 30-40 days after the transplantation) and affects the skin, the liver, and the digestion system. The chronic form of it occurs

100 days after the transplantation and is less severe than the acute form; though it affects joints, the mouth, and the tear glands [7]. As a cure and a control method for GVHD, medicine types such as methotrexate, cyclosporine and high dosages and quantities of corticosteroids are used. The use of these drugs can be likened to a double-sword, if these are taken more than the certain dosage, it leads to various types of infections because these drugs greatly reduce the immune system's performance. But, if these are taken less than the determined necessary dosage, this leads to GVHD. In this patient, due to the lack of attention to the on-time consumption of the medicine, GVHD caused disorders in the urinary system [8].

Also, for curing GVHD, Bone marrow mesenchymal stem cells (BM-MSCs) of a third party are used which can cause suppression of the immunity system and stops the GVHD progression [12]. Hemorrhagic cystitis is the inflammation and erythema of the urinary bladder due to infectious or non-infectious, which leads to bleeding in the urine bladder. The clinical symptoms of this complication including intermittent hematuria, irritable abdominal pains, urinary tract obstruction, bladder tamponade [5].

There are several different methods for curing HC, such as the injection of hyaluronic acid and aluminum salt, chemotherapy, radiotherapy, ozone therapy, cystectomy, etc [11]. As mentioned above, HC is one of the complications of allogeneic transplantation, that based on the amount of hematuria and the patient's pain is graded into three levels as mild, moderate and severe. For mild HC, supportive therapies would respond, but it is possible that the patient needs other therapeutic methods such as antiviral medicine like vidarabine, oxygen or ozone therapy, washing the urine bladder, formalin therapy, cystoscopy and even cystectomy [3,8].

Cystectomy is the invasive treatment for HC which has less than 5% mortality. Among its complications are sexual disorder and urine deflection, although the patient's quality of life is reported to be good [10,11]. Ozone therapy method was known 18 years ago for HC [12]. A retrospective study by Elzimaity showed that HC in matched unrelated donor (MUD) and unrelated cord blood (UCB) transplant occurs more than other cases of allogeneic transplantation. The occurrence of this condition in people younger than 26 years of age who receive this transplantation is much greater than those of other ages and a large number of symptoms of this disorder is detected 30 days after transplantation [13]. Dellis et al reported that HBO has a significant effect on the repair of radiation-induced damage in patients. Moreover, they reported years ago, the positive effect of HBO in HC after pelvic radiotherapy [14]. R F M Bevers and colleagues reported that 16 patients who had HC after allo had HSCT, HBO therapy reduced hematuria and also significantly reduced viral infection (BK virus) after it [12,15].

In the present study, we also found that HBO treatment for this patient with HC with severe clinical symptoms of hematuria and abdominal pain was successful. In the first stage of the treatment, several bladder washes were performed several times, Hyperbaric oxygen therapy (HBOT) was chosen for the last action, which resulted in valuable results, the patient's bleeding was completely discontinued and the patient's condition returned to normal.

4. Conclusion

Regarding surveying all the possible causes of hemorrhagic cystitis, especially the viral and infectious causes, we found that the complication of GVHD was supplemented treatments that managed to control hematuria by using the ozone therapy method. Given the patient's sensitive conditions and the lack of attention to taking medications, it was possible that GVHD would occur in this patient as HC. Following the referral of the patient to the hospital, various treatment methods were used. But only after ozone therapy, the patient's bleeding was completely stopped and he returned to normal conditions. We used ozone therapy for HC for the first time in Iran and fortunately had valuable results.

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