

# Otolaryngologic Problems of Bone Marrow Transplant Patients in Hospital Isolation Period

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## Abstract

**Abstract Objectives:** Bone marrow transplantation is a preferred treatment method for some hematological diseases. During this treatment method, patients encounter many additional clinical problems independent of their illness. Some of these problems that arise are otorhinolaryngological problems. The aim of this study is to evaluate the types and frequency of otorhinolaryngological problems seen in the hospital isolation process after bone marrow transplantation and the treatments applied to them and to draw attention to the points that the transplant team should pay attention to during the hospital isolation process of these patients. **Materials And Methods:** Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed for this original observational article. Thirty of 451 patients, who were taken into isolation after bone marrow transplantation, requested consultation from the otorhinolaryngology clinic, were included in this retrospective study using hospital records. **Results:** Following bone marrow transplantation, during the hospital isolation process, the most common reasons for otorhinolaryngological consultation were hearing loss and epistaxis. **Conclusion:** Although infections are expected more in patients after transplantation, during the isolation process after bone marrow transplantation, in terms of otorhinolaryngology hearing loss and epistaxis may be more common than infections. This situation should be kept in mind by transplant teams and patients should be closely monitored. **Keywords:** Bone Marrow Transplantation, Otorhinolaryngological Consultation, Hearing Loss, Epistaxis.

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### Key Points:

- After Bone Marrow Transplantation, patients should be closely monitored for otorhinolaryngological (ORL) problems.
- The mean time between transplant and ORL review was found significantly higher in the females.
- The most common anatomical sites for ORL problems were: ear, sinonasal, and oropharyngeal.
- Hearing loss and sinonasal epistaxis are more common otorhinolaryngological problems compared to infections.
- Neurosensorial type hearing loss was more common than conductive type hearing loss.

### Introduction

Bone marrow transplantation (BMT) is the treatment of choice for many hematologic malignancies, congenital immunodeficiency disorders, and aplastic anemia [1]. Several features of human bone marrow make the transplant procedure feasible. The first is the noteworthy regenerative capacity of marrow. The second feature of marrow, which makes transplantation practical, is that after intravenous infusion, marrow cells have the capacity to home to the marrow space and their ability to survive cryopreservation with little, if any, damage. With techniques of freezing and thawing, cryopreserved autologous marrow is virtually as effective as fresh marrow in providing protection after otherwise lethal total body irradiation (TBR) [2, 3].

There are 3 types of BMT types according to the stem cell source to be used. It is the first syngeneic transplantation from the best possible donor identical twin. Second, allogeneic marrow transplantation can be performed using HLA-identical related donors, haploidentical related donors or HLA-compatible unrelated donors. The third autologous transplantation involves removing the patient's own marrow after high-dose chemotherapy or chemoradiotherapy, usually freezing and re-infusing this marrow [2]. However, the success of BMT is limited by recurrent disease and infection because of the immunodeficiency status seen after BMT [4].

As part of transplantation, the patient is exposed to a severe immunosuppressive period and hospital isolation of varying length, depending on the type and treatment of the disease before and after BMT. During this period, these patients encounter many additional clinical problems. Some of these additional clinical problems exposed are otorhinolaryngological (ORL) problems. In these patients isolated before and after BMT, some ORL problems seen more than the normal population should be managed more carefully.

The aim of this study is to show the most common ORL problems seen during the hospital isolation process after BTM of 451 patients who underwent BMT in our hospital and the treatments applied to them. In addition, to draw attention to the role of the otolaryngologist as a member of the transplantation team, especially in terms of contributing to the hospital isolation process of these patients.

### Materials and Methods

Our hospital is a tertiary university hospital that performs the isolation of BMT patients before and after their transplantation and their treatment during this isolation. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed for this original observational retrospective study designed based on data collected from our hospital records. BMT was applied to 451 patients between March 2014 and October 2018 in our hospital's adult hematology clinic. Our ORL clinic received 30 consultations from these BMT patients at that time. All these patients had BMT for different diagnosis. Depending on their diagnosis and stem cell sources, some patients had TBR prior to BMT, while others received chemotherapy for bone marrow suppression. After BMT, all patients had different lengths for immunosuppressive therapy to prevent rejection and complications. All patients were isolated in the hospital and followed closely until their immune system reached a certain level and the side effects caused by the treatment were controlled. ORL problems and their treatment processes, which are the subject of our study, include this isolation process. Patients' applications that developed after discharge and made outpatient were not included in the study. If the patient was re-hospitalized for a condition that developed in the future

and a new BMT was not performed, the consultations performed for these patients were also excluded from the study. Ethical institution name is blinded for review.

### Statistical analyses

Differences were evaluated using ANOVA and chi-square tests as appropriate. A chi-square test was used to test the similarity of gender distribution. The differences between the age of the patients, the duration of the ORL consultation between transplant and ORL examination were evaluated using the One-way ANOVA F test, considering gender characteristics. Data were analyzed using SPSS Statistics version 22.0 (IBM, New York, USA) and Microsoft Excel® 2010 software. Statistical significance was accepted as  $p < 0.05$ .

## Results

Between March 2014 and October 2018, 451 patients had BMT in our adult hematology clinic. 30 patients had an ORL consultation visit in our ORL clinic. Among these 30 patients, 14 (46,7%) of them were female, and 16 (53,3%) were male (female to male ratio of 0,87). The youngest patient was 24 years old, and the oldest patient was 72 years old. The mean age of transplantation was 46,55 years. Considering gender, the average age was 46,85 years in women and 49,5 years in men. There was not any statistically significant difference in age between female and male groups ( $p > 0.05$ ). The ORL consultation period between the transplant and the ORL examination was from the 8th day at the earliest to the 333rd day at the latest. The average time between transplant and ORL review is 72.73. was the day. Considering the gender, the average ORL consultation time between transplantation and ORL examination was 101.42 days in women and 47.62 days in men. The mean time between transplant and ORL review was significantly higher in the female group ( $p = 0.001$ ). When we looked at patients according to anatomical sites, 17 (56,7%) patients had ear problems; 8 (26,7%) patients had sinonasal problems and 5 (16,6%) patients had oropharyngeal problems. All these distributions are shown in table 1.

Table 1: Patient Distribution by ORL Consultation Time, Gender and Anatomical Regions

Three (10%) of these 30 patients had TBR prior to BMT, and the remaining 27 (90%) received chemotherapy for bone marrow suppression.

Hearing loss was the most common ear manifestation in BMT after transplantation. It was seen in 13 (76,48%) patients. Among these patients 10 had only hearing loss, one of these had hearing loss with tinnitus, one of these had hearing loss with vertigo and one of these hearing losses with external ear canal edema. In these hearing losses, 8 (61,54%) of them were neurosensorial type hearing loss and 5 (38,46%) of them were conductive type hearing loss. 6 (46,15%) patients of them were treated with medical ways (Ear drops or oral medication), 7 (53,85 %) of them referred for hearing aid devices. Among all ear manifested patients 2 (11,76%) of them had ear discharge and treated by ear drops; and last 2 (11,76%) of them had obstruction of outer ear canal by ear wax and they treated by cleaning of ear wax. This distribution is shown in table 2.

Table 2: Ear Findings of Patients with BMT After Transplant

Sinonasal problems were the second most common ORL consultation reason for BMT patients. Eight (26,7%) patients were sent to ORL clinic for consultation because of sinonasal problems. Among these 7 (87,5%) of them applied for epistaxis which was not controlled by transplantation team. Three (42,8%) of them had bleeding come from right nasal cavity, 2 (28,6%) of them had bleeding from left nasal cavity and 2 (28,6%) of them had bleeding from both nasal cavities. 5 (71,4%) of these patients were treated by silver nitrate cauterization. Two (28,6%) of them were treated by other nonsurgical treatment methods such as topical decongestants and nose moisturizer agents. None of these patients needed surgical epistaxis treatment methods. One (12,5%) patient consulted for cough problem which diagnosed as sinusitis and treated with antibiotics and nasal saline wash. This distribution is shown in table 3.

Table 3: Sinonasal Findings of Patients with BMT After Transplant

In 30 ORL consulted patients, 5 (16,6%) of them consulted for oropharyngeal problems. Among them 3 (60%) patients had widespread severe mucosal lesions and submucosal bleedings. They were diagnosed as severe

mucositis and treated by medical measures. One (20%) patient had acute pharyngitis and treated with antibiotics. One (20%) patient had abscess formation within mouth and treated by surgical drainage. This distribution is shown in table 4.

Table 4: Oropharyngeal Findings of Patients with BMT After Transplant

## Discussion

Organ transplantation is one of the most advanced and sophisticated treatment methods used by modern medicine. Developments in this field have made it necessary to plan and carry out pre-transplant and post-transplant care services to increase the treatment course. BMT, a type of organ transplantation, has also become the gold standard in the treatment of a certain group of hematological diseases [1]. Immunosuppressive treatments to prevent rejection applied after organ transplantation can lead to morbidity and treatment failures in many organ systems.

The ORL system is one of the systems where such problems are most common. Although there are studies on ORL complications that develop following various organ transplantations, we have not seen a study on ORI complications that develop during hospital isolation after BMT and their ENT consultations in the literature.

It has been reported that otological problems are seen after various organ transplantations. Ganzel et al reported 9% otological complications after cardiac transplantation patients, including infection origin, hearing loss and vertigo [5]. After kidney and liver transplantation otological problems reported as 17.7% including hearing loss, otalgia, tinnitus, vertigo, and ear bleeding [6]. Otological problems are not the most common type of ORL problems in those studies. In our study, otologic problems stand out as the most common ORL problem with 56% in the hospital isolation process after BMT. It was found to be the most common hearing loss among these otological problems. Because most of these losses were of neurosensorial type, patients were referred to hearing aids. It was thought that such high incidence of hearing loss was due to the deterioration of the hematological parameters of the drugs used for preparation for BTM and to provide immunosuppression after BTM, or the drugs themselves were ototoxic. In otological problems other than hearing loss, it was also attributed to the increase in infection risk and deterioration in blood values caused by the preparation for BTM and immunosuppressive therapy to prevent rejection after BTM.

Sinonasal problems are the most common and studied problems in organ transplant patients. Sinonasal problems in Cardiac transplant patients were found to be the most common ORL problem with 37%. Sinusitis is the most common type of sinonasal problem in these patients [5]. In addition, sinonasal problems in Liver and Renal transplantation patients were found to be the most common ORL problem with a rate of 41.5%. These patients have rhino sinusitis in the first place among the sinonasal problems, followed by epistaxis [6]. Various aspects of sinonasal problems in BMT patients have been addressed in studies. Sinusitis and its diagnostic and treatment strategies are among the most well-known and studied topics [4, 7-10]. In our study, sinonasal problems were found to be the second most common ORL problem with 26%. Although infection was the most common sinonasal problem in other studies [4, 7-10], we mostly dealt with epistaxis (87.5%). This difference seen in other studies can be explained by the fact that our period of seeing the patients in our study and including them in the study is limited to the hospitalization period in which the patients were isolated for BTM. Epistaxis seen in the early period of BMT treatment can be attributed to the deterioration in bleeding processes and damage to the nasal mucosa due to the radiotherapy and drug therapies used to suppress the bone marrow in preparation for BMT and to prevent rejection after BTM.

The oropharyngeal area is another anatomic ORL region affected after organ transplantation. ORL problems in the oropharyngeal area have been reported at a rate of 5% after cardiac transplantations [5]. Herpes and cytomegalovirus infections were often seen as oropharyngeal problems in these cardiac transplant patients [5, 11-13]. Oropharyngeal problems were reported in 36.3% of liver and renal transplant patients, with sore throat being the most common complaint [6]. Oropharyngeal problems in BMT patients have been reported with a high frequency of 80% in some review studies [14]. The majority of these are simple mucositis, which can be easily controlled and treated by the transplant team. The transplant team treated mild and

uncomplicated mucositis so they were not consulted with us. Severe oropharyngeal problems consulted in our study were observed with a rate of 16%. All of these were infectious processes that the transplantation team could not cope with, and 20% of them were treated with surgical drainage.

Considering all ORL areas, almost all the ORL problems were found to be associated with morbidity, while not causing mortality in patients.

The value of this study is that patients' ORL problems are identified and consulted during their hospitalization. For this reason, the probability of more reliable consequences is that the problems are less likely to cause misleading consequences, such as passing at home or going to other centers. Since the results are not the results of outpatients, but include problems before the patient is discharged in the acute period, it may provide a better idea to transplantation teams about what to consider in terms of ORL before BMT and what to expect after transplantation

## Conclusion

When these results are evaluated, although infections and the problems caused by them are expected more in patients after transplantation; As seen in this study, during isolation after BMT, otologically, hearing loss and sinonasally epistaxis are more common ORL problems compared to infections. This situation should be kept in mind by transplant teams and patients should be closely monitored in this regard.

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