Cooperation between the Gulf Centre for Cancer Control and the Gulf Federation for Cancer Control
GCC Annual Cancer Awareness Week (Feb 1-7)
Table of Contents

Case Reports /Review Articles

An Unusual Breast Malignancy .................................................................07

Nuchal Fibroma: A rare entity of neck masses ........................................10
N. Alsaleh, H. Amanguno

Epinephrine–secreting large incidental pheochromocytoma in a normotensive male with stormy intraoperative hemodynamics........13
O. Nazir, T. Sharma, M. Maqsood, A. Khatuja, R. Misra

Everolimus induced Pneumonitis............................................................18
Q. Badar, N. Masood, A. N. Abbasi

Primary Mantle Cell Lymphoma of Appendix .........................................25
VL Gaopande, SD Deshmukh, VC Shinde

A Rare Variant of Multiple Myeloma: Non–Secretory Myeloma with diffuse Osteolytic Lesions..........................................................28
S. Sultan, S.M. Irfan

Pain and Cancer: A systematic review ..................................................32

Original Articles

Tumor Thickness: A predictor of nodal disease in early squamous cell carcinomas of buccal mucosa ..........................................................38
G. Deshpande, S. Das

Hypofractionated Simultaneous Integrated Boost (SiB) versus Conventional Fractionation in Localized Prostate Cancer: A Randomized Pilot Study ............................................................44
K. Al– Ghamrawi, M. El–Haddad, S. Hanna, A. Ali, M. Kamal

Quantitative evaluation of the dosimetric effects of balloon deformation and source position in high–dose rate mammosite breast brachytherapy.................................................................54
I. Ali, S. Negusse, S. Ahmad, O. Algan

Spectrum of Ovarian Tumors: Histopathological study of 218 cases..........................................................64
N.A. Mansoor, H.S. Jezan

Rare Chromosome Structural Aberration Characterizing Oncology Malignancy .................................................................71
A. Movafagh, A. Sayad, M. Hashemi, H. Darvish, D. Zare–Abdollahi, B. Emamalizadeh, F. Shahvaisizadeh,
N. Mansouri, S. A. Mortazavi–Tabatabaei

Infectious complications after allogeneic bone marrow transplantation: Sheikhha Badryia Center, Kuwait ........................................79
S. AlShemmari, S. Refaat, A. A. Abdullah, M.A. Abul

Cancer News and Scientific Events in the Arab Region

- News Notes .........................................................................................87
- Advertisements ..................................................................................90
- Scientific events in the GCC and the Arab World for 2015 ......................91
Abstract

Objective

To present our experience of post-transplant infections in allogeneic stem cell transplants at Sheikha Badryia Stem Cell Transplant Centre, Kuwait.

Methods

Retrospective analysis of 21 consecutive patients with malignant and non-malignant hematological disorders who received a transplant of an unmanipulated bone marrow graft from an HLA-identical sibling donor from November 2011 to December 2013. Pre-transplant infection surveillance was carried out, and strict prophylaxis against infection was observed. Bone marrow stem cells were used as the stem cell source. Cyclosporin and methotrexate with or without mycophenolate mofetil/methylprednisolone were used as graft-versus-host disease (GVHD) prophylaxis. The engraftment was monitored with molecular analysis. Survival was calculated from the date of transplant to death or last follow-up.

Results

Twenty-one patients received allogeneic stem cell transplants from HLA-matched siblings for various hematological disorders. Twelve patients were female. The median age of the patient cohort was 34 years (range 3–41 years). All patients and donors were cytomegalovirus (CMV) IgG-positive. Seventeen patients (80.95%) developed febrile episodes in different phases of post-transplant recovery. Post-transplant infections were confirmed in 20 patients (90.2%) on the basis of clinical assessment and microbiological, virological, and histopathological examination. Mortality related to infections and chronic graft versus host disease was one patient (4.8%).

Conclusion

90% of our patients developed febrile episodes with relatively low culture yield. The majority of infections were treated effectively.

Keywords

Allogeneic stem cell transplants, Infections, Kuwait
Infections post allogeneic stem cell transplant, S. AlShemmari, et. al.

(IBMTR), causes of death after transplants done in 2010 – 2011 were: infections contributed to 12% of deaths in HLA-identical sibling allogeneic SCT, 17% in unrelated allogeneic SCT and 8% in autologous SCT. (2) The epidemiology of these infections depends on the degree, type, and duration of immune suppression, the use of prophylactic antibiotics, surveillance for organisms associated with nosocomial infections, the emergence of drug-resistant organisms, and the use of isolation precautions. (3) Because of different pathogenetic and epidemiological backgrounds of post–transplant infections, three consecutive time periods post–transplant are separately described: the early post–transplant period (pre-engraftment, comprising 3 weeks), the intermediate post–transplant period (3 weeks to 3 months), and the late post–transplant period (later than day + 100). The relative frequencies of opportunistic pathogens vary at different periods post–SCT. (4) Factors that influence the risk of infections include mucosal damage, presence of a right atrial catheter, and prolonged neutropenia prior to SCT. The role of graft versus–host disease (GVHD) and its treatment in the pathogenesis of these infections have been well documented. (5) Blood stream infections and systemic fungal infections in patients with profound neutropenia are serious complications as they carry higher morbidity and mortality. Antifungal prophylaxis with fluconazole during the early post–transplant period has been shown to significantly reduce the incidence of candidemia and improve short–term survival. (6,7) For decades, various approaches have been undertaken in an attempt to reduce the risk of translocated oral and bowel flora, which, along with central venous catheters are the source of serious infections in SCT patients through the years. Numerous regimens have been tried, including neomycin and polymyxin, trimethoprim—sulfamethoxazole (TMP—SMX), and most recently, the oral quinolones, particularly ciprofloxacin. Although the practice of oral prophylaxis is routine in many SCT centers, the current problems with drug resistance may force a careful reconsideration of this still unproven approach. (6,8) Cytomegalovirus (CMV) infection remains one of the most important complications of allogeneic SCT, although the impact on morbidity and mortality has been reduced during the last decade by improvements in management. (10,11) BK polyoma virus infection has been connected with development of hemorrhagic cystitis after allogeneic stem cell transplant, but most studies detected the virus at the time of bleeding, therefore not allowing the risk imposed by asymptomatic infection to be estimated. (12)

The Sheikha Badryia Stem Cell Transplant Centre has provided stem cell transplant facilities in Kuwait. The allogeneic bone marrow transplant program is in the evolutionary stages in this country. With this background we analyze herein our initial experiences of post–transplant infectious complications.

Patients, materials, and methods

Patient, donor, and transplantation characteristics

To study the incidence of infections after bone marrow transplantation, we retrospectively analyzed 21 consecutive patients with malignant and non–malignant hematological disorders who received a transplant of an unmanipulated bone marrow graft from an HLA–identical sibling donor. The age limit of patients with β-thalassemia major was 20 years. For aplastic anemia, the age limit of patients was 40 years, and for myelodysplastic syndrome (MDS), acute leukemias, chronic myeloid leukemia (CML), and lymphomas, the age limit of patients was 55 years. Patients with β–thalassemia major were categorized into risk classes I, II, and III on the basis of presence or absence of hepatomegaly, degree of fibrosis on liver biopsy, and adequacy of iron chelation according to Lucarelli’s Pesaro group risk classification. Table 1 summarizes the patient, disease, donor, and transplantation characteristics of the 21 analyzed patients.

Pre–transplant infection surveillance

As per our transplant protocol, after HLA–typing all patients and sibling donors underwent pre–transplant infection surveillance. Prospective surveillance was carried out to detect the spectrum of microbial pathogens in our patients and to treat them with appropriate antibiotics. Surveillance cultures were taken from the nose, throat, stool, and urine. All stool samples were also examined microscopically for intestinal parasites.

Peripheral blood films were screened for malarial parasites by conventional microscopy after preparing...
Characteristics | Median | (range) | N | %
--- | --- | --- | --- | ---
Age, y | 34 | (3 – 41) | 12 | 57.14
Female | 21 | 100 | 13 | 61.9
Positive CMV IgG | 5 | 23.8 | 1 | 4.67
Underlying diagnosis | 2 | 9.52
Non–malignancies§ | 4 | 19
Acute leukemia† | 1 | 4.67
Chronic myeloid leukemia* | 2 | 9.52
Other malignancies‡ | 1 | 4.67
Disease stage (for malignancies) | 1 | 4.67
Advanced|| | 4 | 19
Donor Age, y | 6 | (3 – 39)
Sex match | 2 | 9.5
Donor F recipient M | 2 | 9.5
Donor M recipient M | 7 | 33.3
Donor M recipient F | 6 | 28.5
Donor F recipient F | 6 | 28.5
ABO Compatibility | 5 | 28.5
Major & bidirectional | 2 | 9.5
Minor | 5 | 28.5
Positive CMV IgG | 21 | 100
Transplantation | 10 | 47.6
GVHD prophylaxis
Cyclosporin + methotrexate + MMF
Cyclosporin + methotrexate
Cyclosporin + methotrexate + MP
Conditioning | 1 | 4.67
Bu + Cy | 10 | 47.6
Bu + Cy + Thiotepa | 8 | 38.1
Bu + Cy + ATG | 2 | 9.5
Cy + Fludarabin + ATG | 1 | 4.67
Cell dose | 3.52 | (0.651 – 7.56)
NC, 10⁹/kg
CD34, 10⁹/kg | 4.45 | (1.47 – 11.9)
Neutrophil engraftment | D+13 | (D+13 – D+27)
Platelet engraftment | D+12 | (D+12 – D+45)
Acute GVHD | 13 | 61.9
Grade I – II
Grade III – IV
Chronic GVHD | 2 | 9.5
7 | 33.3

CMV indicates cytomegalovirus; GVHD, graft–versus–host disease; Bu, busulphan; Cy, cyclophosphamide; ATG, antithymocyte globulin; MP, methylprednisolone; NC, nucleated cells; MMF, mycophenolate mofetil.

§10 Thalassemia major: 7 in class II, and 3 in class III, 1 Severe aplastic anemia, 1 aplastic anemia / paroxysmal nocturnal hemoglobinuria, and 1 congenital dyserythropoietic anemia.

*1 chronic myeloid leukemia (CML) in first chronic phase (CP).

†2 acute lymphoblastic leukemia (ALL): 1 ALL Ph+ in first complete remission (CR1), 1 in CR2, and 3 acute myeloblastic leukemia (AML): 1 in CR1, 1 in CR2, and 1 secondary on top of MDS in refractory disease.

‡1 Non–Hodgkin lymphoma (NHL), 1 myelodysplastic syndrome (MDS).

||Advanced stage: AML/ALL in relapse or refractory disease, NHL in resistant or untreated relapse.

thick and thin Giemsa–stained peripheral blood smears. All patients and donors were screened for tuberculosis by Mantoux test and chest X–ray, while sputum for acid–fast bacilli (AFB) examination and PCR for Mycobacterium tuberculosis were done in suspicious cases to give anti–tuberculosis prophylaxis (isoniazid) for 6 months to patients after transplantation and to donors before bone marrow donation.

Virological screening for hepatitis B, hepatitis C, HIV, CMV, and Epstein—Barr virus (EBV) was carried out by enzyme immunoassay (ELISA) and molecular analysis (PCR) where indicated. One patient with congenital dyserythropoietic anemia Anti–HCV–positive antibodies with normal ALT and negative PCR was considered for transplant, while HCV PCR–positive patients were considered unfit for transplant. Pre–transplant screening for Varicella zoster virus (VZV) was carried out by IgM enzyme immunoassay. Varicella zoster virus (VZV) positive patients were given acyclovir prophylaxis in high doses for longer duration (9 months). CMV, EBV, Adenovirus, and BK–polyoma virus in blood and urine were prospectively monitored by molecular analysis (PCR) weekly starting on hospital admission for conditioning and transplantation, followed by CMV molecular analysis (PCR) weekly for the first 100 days and thereafter monthly for one year.

Patients were nursed in protective isolation rooms, equipped with a HEPA filter positive–pressure laminar airflow ventilation system. All patients were provided with a bacteria–reduced diet. Leuko–depleted and irradiated blood products were used during the post–transplant period.
Graft–versus–host disease prophylaxis, conditioning regimen, and supportive therapy

Prophylaxis for graft–versus–host disease (GVHD) consisted of the combination of cyclosporine, methotrexate, and mycophenolate mofetil in 10 (47.6%) patients, mycophenolate mofetil was used for the first 28 days post–transplant, cyclosporine, and methotrexate in 10 (47.6%) patients, and cyclosporine, methotrexate, and methylprednisolone in one patient (4.67%). All patients received a chemotherapy–based conditioning according to diagnosis. Ten patients (47.6%) with acute leukemia, chronic myeloid leukemia, Non–Hodgkin’s lymphoma (NHL), one thalassemia major class II, and one patient with congenital dyserythropoietic anemia received busulphan and cyclophosphamide. Eight patients (38.1%) with thalassemia major, 5 class II and 3 class III, received busulphan, cyclophosphamide, and thiopeta. Two patients (9.5%) with myelodysplasia, and aplastic anemia/paroxysmal nocturnal hemoglobinuria, received busulphan, cyclophosphamide, and antithymocyte globulin. One patient (4.67%) with severe aplastic anemia received cyclophosphamide, fludarabine, and antithymocyte globulin.

Selective gut decontamination with oral antibiotics and bacterial/viral/fungal prophylaxis were performed according to local policy. A preemptive treatment with ganciclovir for cytomegalovirus (CMV) infection based on CMV positivity by PCR screening was used. A diagnostic driven management of aspergillosis with weekly monitoring of serum galactomannan was used.

Statistical methods

Survival was calculated from the date of transplant to death or last follow–up, descriptive multivariate analysis was performed with IBM SPSS statistics 20 software and MS excel software.

Results

From November 2011 to December 2013, a total of 21 patients received allogeneic SCT from HLA–matched sibling donors at the Sheikha Badryia Stem Cell Transplant Centre, Kuwait, for various hematological disorders. Diseases included were β–thalassemia (10), acute leukemia (5), CML–chronic phase (1), aplastic anemia (1), aplastic anemia/paroxysmal nocturnal hemoglobinuria (1), NHL (1), myelodysplasia (1), and congenital dyserythropoietic anemia (1).

Twelve patients were female (57%). The median age of the patients was 34 years (range 3–41 years). Thirteen donors were males (61.9%). Eight patients (38.1%) were transplanted across gender. Eight patients (38.1%) had ABO mismatch transplants. All our patients and donors were CMV–IgG positive.

Out of 21 patients who underwent SCT, 17 patients (80.9%) had febrile episodes either alone or in association with other signs and symptoms during different post–transplant recovery phases. Relevant cultures and samples were taken in all febrile patients. Post–transplant infection was confirmed in 13 out of 17 patients (76.5%) on the basis of clinical assessment and microbiological, virological, and fungal antigen assay by enzyme immunoassay.

Bacterial infections were seen in 13/21 (61.9%) patients. The majority of bacterial pathogens were Gram–negative organisms (84.6%) compared with Gram–positive organisms (15.4%). Infective organisms isolated in our patients in order of frequency were Escherichia coli in 12 patients (92.3%) in 20 episodes of infections, Stenotrophomonas maltophilia in 7 patients (53.8%), Klebsiella spp in 6 patients (46.2%), Pseudomonas spp in 5 patients (38.5%), coagulase–negative Staphylococcus (CoNS) in 4 patients (30.8%), followed by Enterobacter spp in one patient (7.7%), and Enterococcus faecalis in one patient (7.7%). The majority of bacterial pathogens were isolated from either sputum (25%), urine (22.7%), followed by blood stream (9%), central line (6.8%), throat (4.5%), and maxillary paranasal sinus (2.3%). Pneumocystis jiroveci was diagnosed clinically in 2 patients (15.4%).

Fungal infections were seen in 9 patients (42.9%). Candida non–albicans were isolated from the sputum in 5 patients (66.7%), and from central venous catheter in one patient, and candida albicans was isolated from the sputum in 2 patients (22.2%). Probable pulmonary Aspergillosis was diagnosed in pediatric patient with myelodysplasia based on positive galactomannan test by ELISA in the sputum and radiological evidence of pulmonary Aspergillosis in computed tomography of the chest.
Candida infection was common among non-Hodgkin’s lymphoma, and acute lymphoblastic leukemia patients.

Microbiological culture yield of 136 specimens taken from different sites was 81 positive culture specimens (59.6%) for bacterial and fungal infections.

CMV infection in the first 100 days post-transplant was detected by molecular analysis by PCR in blood in 10 patients (47.6%) and beyond 100 days in 10 patients (47.6%). CMV disease was observed in 2 patients (9.5%). The frequencies of infections seen in our patients are shown in Table 2. CMV disease was seen in thalassemia class III and acute lymphoblastic leukemia patients. Early and late CMV reactivation was observed in patients had mainly GVHD, hematologic malignancies, myelodysplasia, thalassemia class III and aplastic anemia/paroxysmal nocturnal hemoglobinuria. The number of positive CMV samples was 37 out of 295 samples examined (12.5%) throughout the study period. Unquantifiable BK polyoma-viruria was observed in 14 patients (66.7%). Six patients out of the 14 patients (42.9%) had BK-polyoma virus associated hemorrhagic cystitis, 3 of them had acute leukemia, 2 patients had thalassemia class III, and one patient had myelodysplasia. The number of positive samples of BK-polyoma virus in urine was 61 out of 186 samples examined (36.3%) throughout the study period.

Infection-related morality was observed in one patient Thalassemia class III (4.8%) due to interstitial pneumonia and chronic extensive GVHD liver, lung, and skin. The only isolate in this patient was Enterococcus faecalis from endotracheal secretion study. The patient was diagnosed Pneumocystis jiroveci clinically and with computed tomography of the chest. The frequency of infections in the early, mid, and late recovery phases is shown in Table 3.

In our study, the overall survival and disease-free survival were 95.2% and 90.5%, respectively, with a median follow-up of 15 months (range 2 – 26 months).

Multivariate analysis showed that patients with underlying advanced malignancy and donor–patient sex mismatch, and infused nucleated cell dose were significantly correlated with BK-polyoma viruria and hemorrhagic cystitis, (p value 0.035, 0.027, and 0.005 respectively). However the multivariate analysis did not reveal any significant correlation between the developments of febrile neutropenia, early, mid, and late cytomegalovirus infection and disease with the studied parameters.

**Discussion**

Opportunistic infections of varying severity with bacterial, viral, and fungal organisms occur in >90% of patients after allogeneic SCT and contribute significantly to morbidity and mortality after engraftment. (3) Fatal opportunistic infections have been reported in 4—15% of related transplant recipients and 12—28% of unrelated transplant recipients. (13) Common organisms encountered were CMV, P. jiroveci, Streptococcus pneumoniae, Pseudomonas spp, and Aspergillus spp with mortalities of 84%, 67%, 33%, 85%, and 87%, respectively. (14)

Bacterial infections are frequently seen during the post-transplant neutropenia phase. The most common pathogens are Gram—positive bacteria, especially CoNS. Besides these, Gram—negative organisms including Escherichia coli, Klebsiella spp, and P. aeruginosa are the most common bacterial pathogens during the early post-transplant neutropenic phase. (15)

Over the past two decades the percentage of infections caused by Gram—negative organisms has

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**Table 2 : Frequency of infections, number of febrile episodes, and microbiological yield**

<table>
<thead>
<tr>
<th>Infections</th>
<th>Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial infections</td>
<td>13/21 (61.9%)</td>
</tr>
<tr>
<td>Fungal infections</td>
<td>9/21 (42.9%)</td>
</tr>
<tr>
<td>Pneumocystis Jiroveci</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Cytomegalovirus disease</td>
<td>2/21 (9.5%)</td>
</tr>
<tr>
<td>Cytomegalovirus reactivation</td>
<td>20/21 (95.2%)</td>
</tr>
<tr>
<td>Unquantifiable BK-polyoma viruria</td>
<td>14/21 (66.7%)</td>
</tr>
<tr>
<td>BK-polyoma virus hemorrhagic cystitis</td>
<td>6/14 (42.9%)</td>
</tr>
</tbody>
</table>

**Febrile episodes**

| Febrile episodes | 17/21 (80.9%) |

**Microbiological yield**

<table>
<thead>
<tr>
<th>Microbiological yield</th>
<th>81/136 (59.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial and fungal culture yield</td>
<td>37/295 (12.5%)</td>
</tr>
<tr>
<td>BK-polyoma virus – PCR</td>
<td>61/186 (36.3%)</td>
</tr>
</tbody>
</table>

---

(11.1%). Infection-related mortality was observed in one patient Thalassemia class III (4.8%) due to interstitial pneumonia and chronic extensive GVHD liver, lung, and skin. The only isolate in this patient was Enterococcus faecalis from endotracheal secretion study. The patient was diagnosed Pneumocystis jiroveci clinically and with computed tomography of the chest. The frequency of infections in the early, mid, and late recovery phases is shown in Table 3.

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**Discussion**

Opportunistic infections of varying severity with bacterial, viral, and fungal organisms occur in >90% of patients after allogeneic SCT and contribute significantly to morbidity and mortality after engraftment. (3) Fatal opportunistic infections have been reported in 4—15% of related transplant recipients and 12—28% of unrelated transplant recipients. (13) Common organisms encountered were CMV, P. jiroveci, Streptococcus pneumoniae, Pseudomonas spp, and Aspergillus spp with mortalities of 84%, 67%, 33%, 85%, and 87%, respectively. (14)

Bacterial infections are frequently seen during the post-transplant neutropenia phase. The most common pathogens are Gram—positive bacteria, especially CoNS. Besides these, Gram—negative organisms including Escherichia coli, Klebsiella spp, and P. aeruginosa are the most common bacterial pathogens during the early post-transplant neutropenic phase. (15)

Over the past two decades the percentage of infections caused by Gram—negative organisms has
In our series, bacterial infections were observed in 61.9% of patients during the post-transplant period, Gram-negative infections 84.6% and Gram-positive infections 15.4%. Escherichia coli and coagulase-negative Staphylococcus were major bacterial pathogens.

PCP accounted for fewer than 10% of the cases of interstitial pneumonia in patients with allogeneic SCT.

Two of our patients were diagnosed clinically and

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Early recovery phase (pre-engraftment) (&lt;30 days)</th>
<th>Mid recovery phase (post-engraftment) (30—100 days)</th>
<th>Late recovery phase Total (&gt;100 days)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoNS</td>
<td>1</td>
<td>¾</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>MRSA</td>
<td>1</td>
<td>¾</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1</td>
<td>¾</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>¾</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Staphylococcus hemolyticus</td>
<td>¾</td>
<td>¾</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Streptococcus group C</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>ESBL—producing Klebsiella</td>
<td>¾</td>
<td>1</td>
<td>¾</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>8</td>
<td>5</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
<td>1</td>
<td>¾</td>
<td>¾</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>¾</td>
<td>¾</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>¾</td>
<td>2</td>
<td>¾</td>
<td>2</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>2</td>
<td>5</td>
<td>¾</td>
<td>7</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>¾</td>
<td>¾</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pneumocystis jiroveci</td>
<td>¾</td>
<td>¾</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>1</td>
<td>1</td>
<td>¾</td>
<td>2</td>
</tr>
<tr>
<td>Candida non—albicans</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Aspergillus spp</td>
<td>1</td>
<td>¾</td>
<td>¾</td>
<td>1</td>
</tr>
<tr>
<td>Cytomegalovirus infection and disease</td>
<td>¾</td>
<td>10</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>BK—polyoma virus</td>
<td>11</td>
<td>6</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>Total number of infections</td>
<td>32</td>
<td>38</td>
<td>40</td>
<td>110</td>
</tr>
</tbody>
</table>

Table 3: Post-transplant opportunistic bacterial, fungal, and viral infections by recovery phase

CoNS – coagulase—negative Staphylococcus; MRSA – methicillin—resistant Staphylococcus aureus; ESBL— extended spectrum beta—lactamase.

steadily decreased from 70% to 30%, and Gram—positive bacteria now account for 70% of bacterial infections compared with 30% 25 years ago. (16)
with computed tomography of the chest interstitial pneumonia during the late recovery phase (>100 days) post-transplant. One of them was thalassemia class III was associated with severe chronic GVHD liver, lung, and skin, and it was fatal. The second case was NHL patient made a complete recovery. Our data goes in concordance with the data from developing countries, though limited, that show 40—50% of patients develop bacterial infections; Gram-negative bacteria are still the major organisms, although incidence of Gram-positive organisms seems to be on the increase, consistent with Western data. (17)

Studies from Asian countries like Israel and India have observed an increasing incidence of fungal infections in BMT units. (19) In our series, fungal infections were observed in 42.9% of patients. Candida non-albicans spp was the major fungal pathogen (66.7%) as compared to Aspergillus spp (11.1%). The overall incidence of fungal infections in our patients is similar to that found in other Asian countries like India; however, candidiasis was the more common infection in our patients. Eight patients (38.1%) developed Candida spp infection during the post-transplant period, and only one of our patients developed probable pulmonary aspergillosis in the early recovery phase responded to voriconazole and made a complete cure. Though these data should be taken with caution due to the small number of patients.

CMV infection is the most common fatal infection following a SCT, accounting for 15—20% mortality. (20,21) In our series, CMV infection was documented in 20/21 (95.2%) patients and CMV disease was seen in 2 patients (10%), one patient thalassemia class III developed CMV disease during the mid-recovery phase and one patient NHL developed CMV disease during the late recovery phase. CMV infection in early recovery phase was seen mainly in patients with hematologic malignancies, aplastic anemia/paroxysmal nocturnal hemoglobinuria, and thalassemia class III patients, all these patients had acute GVHD grade I—II mainly skin, except one patient thalassemia class III had severe acute GVHD grade III—IV skin, liver and gastrointestinal tract. Late CMV infection occurred mainly in 7 patients with chronic GVHD (33.3%) and on heavy immunosuppression.

BK polyoma virus-associated hemorrhagic cystitis (BK–PyVHC) affects 5–15% of allogeneic hematopoietic stem cell transplantation (HSCT) patients. (22) BK–PyVHC appears to result from significant cytopathic damage and mucosal denudation caused by high—level BKV replication in the urothelial cell layer damaged by conditioning regimen, extensive inflammation potentiated during engraftment and viral leakage into the blood detectable as BKV viremia. (23) In our series BK polyoma viruria occurred in 14/21 patients (66.7%), 6 out of the 14 patients (42.9%) had BK–PyVHC, three of these 6 patients were acute leukemia and 3 were thalassemia patients, 2 of them Thalassemia class III. Although discovered over thirty years ago, many aspects of the epidemiology of BK virus and John Cunningham virus (JCV) in the general population, such as the source of infectious virus and the mode of transmission, are still unknown. BK polyoma virus–associated hemorrhagic cystitis (BK–PyVHC) is a significant complication after allogeneic HSCT and critical issues of incidence, risk factors and treatment are far from resolved. (24)

In summary, bacterial infections were documented in 61.9% of our patients, fungal infections were documented in 42.9%, Cytomegalovirus infection was documented in 95.2%, and BK–polyoma viruria and BK–polyoma virus associated hemorrhagic cystitis in 85.7%. Infection–related morality was observed in one patient Thalassemia class III (4.8%).

The high rate of CMV and BK–polyoma virus in our series was probably due to the immunosuppression in patients with hematologic malignancies/bone marrow failure or in patients with GVHD in 42.9%. None of our patients developed protozoal or helminthic infections.

These are the results of the first two years of hematopoietic stem cell transplant in a single center. Larger case series will be reported in the future.
References