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You Are Better Than Them

Abstract

Peripheral T-cell lymphoma is an aggressive form of lymphoma that has traditionally been treated with high dose chemotherapy. This course of treatment has had a reasonable success rate in partial remission and some complete remission. The long-term survival rate however has not been very successful with this course of treatment. The addition of autologous stem cell transplant has shown results that prove an increase in long-term survival rate, decreased hospitalization, economic efficiency, and improved psychologically well-being following the procedure, indicating that is a better course of treatment compared to an allogenic transplant which requires hospitalization and immunosuppressive therapy.

Peripheral T cell lymphoma is an aggressive and destructive form of Non-Hodgkin's lymphoma causing many deaths each year. Peripheral T cell lymphoma has previously been treated with combination high dose chemotherapy to achieve complete remission in patients with advanced disease; however, the use of high dose chemotherapy alone as treatment has often been unsuccessful due to the high percentage of recurrence associated with peripheral T- cell lymphoma, meaning the disease is likely to return in later years following treatment with chemotherapy. The aggressive nature and rapidly multiplying cells of peripheral T – cell lymphoma makes the cancer difficult to treat with chemotherapy and increasingly more difficult to destroy completely to prevent recurrence. Chemotherapy destroys the cancerous cells; however, it does not help the affected organ heal or replenish, meaning the organ continues to be vulnerable to a recurrence of the cancer because it is weak following the chemotherapy

treatment. According to Texas Oncology, the majority of patients that experience a relapse in a subset cancer of Non-Hodgkin's lymphoma such as peripheral T-cell lymphoma will typically be diagnosed with the relapse within two years of the initial treatment ("Relapsed Aggressive NHL").

In recent years, studies have shown success in achieving complete remission of patients with advanced peripheral T cell lymphoma using a technique known as autologous hematopoietic stem cell transplant – a procedure designed to harvest stem cells from the patient's body, treat specifically the cells that have been removed from the body for the cancer with high dose chemotherapy, and replace them back into the patient's body without a surgical intervention required. Following the procedure, the patient is permitted to leave the hospital without a need for admission to the intensive care unit or isolation precautions creating a more psychologically positive environment for the patient to recover in as well as an environment with decreased risk of postoperative infection secondary to other sick patients in the hospital or intensive care unit. Due to the structure and administration of the autologous hematopoietic stem cell transplant compared to the allogenic stem cell transplant, the procedure is a physically safer, psychologically beneficial, and economically responsible treatment for patients diagnosed with advanced peripheral T cell lymphoma.

Per the National Cancer Institute, in the year 2016, 1,685,210 new cases of the various forms of cancers have and will be diagnosed, claiming the lives of 595,690 individuals in solely the United States ("Cancer Statistics"). On a global scale, cancer is considered one of the leading causes of death with 8.2 million deaths secondary to cancer after 14 million new cases of cancer were diagnosed in 2012 per the World Health Organization ("Cancer"). Cancer statistics, similarly to those listed above, are broadcast across television, radio, and social media regularly

causing a normalization of a disease that can often be deadly. Cancer is a disease that is still not understood by an average citizen causing assumptions to be made in the general population regarding treatment and prognosis, specifically that if a patient is not treated with a constant course of chemotherapy and then have the affected organ removed, they will not recover and will perish; this is considered the "normal" treatment for cancer.

Cancer, while sounding like a singular disease, is a collection of approximately 100 diseases that in simplest terms are characterized by abnormal growths of cells that can occur in all organs of the body and migrate to other sites in the body, away from the original location (Longe). Cancer is a disease that can affect the major organs of the body – including breasts, lungs, cervix, brain, stomach – to name several. Because the basic definition of cancer is an abnormal growth of cells, cancer can grow in any location of the body where cells are present – meaning cancer can grow anywhere and everywhere in the body. There are several varieties of cancer that are less well known to the public because they do not grow in a specific organ but affect cells that travel throughout the body.

Lymphoma is one such cancer that does not affect the cells of a specific organ and is less understood than other varieties of cancers. Lymphoma is a unique form of cancer because rather than affecting an organ, lymphoma is an abnormal growth of cells in the lymphatic system which is comprised of lymph tissues or lymph nodes and the lymph fluid. Lymph fluid is defined by the The Gale Encyclopedia of Nursing and Allied Health as a "milky fluid that contains the lymphocytes or white blood cells" (Narins). The lymphocytes are the infection fighting cells in the body that are stored in the lymph nodes throughout the body until an infection is sensed, causing them to be released into the body to fight the infection. Lymph nodes are dispersed

throughout the body including in the neck, groin, underarm, chest, and abdominal regions (Narins).

Lymphocytes are categorized into two different subtypes based on what function they perform during the infection fighting process and where they are produced in the body. T lymphocytes are produced in the thymus gland located in the central chest area. T lymphocytes are the first cells that respond to a new infection in the body (Lerner). The other category of lymphocytes, B lymphocytes, is produced in the bone marrow. B lymphocytes, also called memory cells, are the cells that create antibodies against an infection once the body has identified the infection. These antibodies "remember" the infection and are able to react more quickly when the body is infected by the same infection a second time (Lerner).

Because of the traveling of the lymphocytes throughout the body, lymphoma can metastasize, or spread, to all organs of the body. The primary infection fighting cells are the cells affected by lymphoma, so patients who are diagnosed are at a significantly higher risk of developing infections because the cells designed to fight the infection are the cells that are "sick." Because lymphoma is such a large category of cancer, it is divided further – into Hodgkin's and Non-Hodgkin's lymphoma - based on the type of lymphocyte that is affected by the disease.

Non-Hodgkin's lymphoma is the more aggressive and more fatal subset of lymphoma. According to Columbia University, Non-Hodgkin's lymphoma is defined as a lymphoma in which the Reed-Sternberg cells are not present on the light microscopy examinations of lymph node biopsies (Lagasse). Non-Hodgkin's lymphoma is a much faster growing cancer, causing it to spread to other lymph nodes and organs more quickly than it can be detected and treated. The symptoms of lymphoma – including swelling of the lymph nodes, fever, chills, night sweats,

itching, and weight loss (Lagasse) – are also common symptoms associated with many different infections and can easily cause a physician to misdiagnose a patient until the disease is much further progressed – making it difficult to treat. Non-Hodgkin's lymphoma can affect both B lymphocytes and T lymphocytes. For this reason, there are several further classifications of Non-Hodgkin's lymphoma. The main case study that will be followed during this argument, Patient BGK, was diagnosed with subset Peripheral T Cell Lymphoma, Not Otherwise Specified in August 2015.

According to the American Society of Hematology, peripheral T cell lymphoma is a group of "clinically aggressive diseases associated with poor outcome" (Foss). Peripheral T cell lymphoma is a rare subset of lymphoma, affecting less than one patient per 100, 000 people living in the United States, per the United States Surveillance, Epidemiology, and End Results registry (Foss). As mentioned previously, peripheral T cell lymphoma is a subset of Non-Hodgkin's lymphoma; however, it is also a variety of lymphoma that is classified as a cutaneous T cell lymphoma – cutaneous meaning that it is a disease that affects primarily the skin. Peripheral T cell lymphoma not otherwise specified (PTCL-NOS) is included in the nodal lymphoma classification and is responsible for 25.9% of all peripheral T cell lymphoma cases – making it the most common subgroup of the disease (Foss).

As stated above peripheral T cell lymphoma is classified as such because the main organ involved with the disease is the skin. The most common clinical presentation of the disease is a diffuse rash across the entire body that resembles small blisters. There is also commonly itching associated with the rash due to the irritation of the endothelial cells in the skin. After developing the rash, many individuals seek medical treatment, just as patient BGK did. Upon physical exam, physicians typically observe a diffuse, full body rash, minimally swollen lymph nodes

throughout the body, and possible splenomegaly – enlargement of the spleen (Leukemia and Lymphoma Society). In addition to these physical exam findings, a patient may report to the physician that he/she has had fevers, chills, or night sweats at home (Leukemia and Lymphoma Society). Based on these findings, many physicians would expect an infectious process to be causing the patient's symptoms and would order laboratory testing on blood specimens. The main laboratory testing for a suspected infectious process is a complete blood count (CBC).

The complete blood count will be tested for the patient's hemoglobin levels, indicating how much oxygen they are able to carry throughout the body, hematocrit, red blood cell count, platelet count – indicating how many cells the patient has available to form blood clots, and a white blood cell count including differentiation of the cells, indicating whether the body is currently fighting an abnormal condition. The white blood cell count is the most common laboratory result indicating whether an infection is present in the body. In the case of peripheral T cell lymphoma, the white blood cell count will be elevated (leukocytosis) with an increased number of eosinophils (eosinophilia), which are typically considered cells that are responsible for responding to parasitic infections or allergens. Based on the laboratory results, many physicians suspect either an allergy or a parasitic infection based on the patient travel history and will begin to treat the patient for such conditions. As the condition worsens, the laboratory results will continue to deteriorate because the treatment is not treating the actual condition, as did patient BGK's results.

As the disease progresses, the white blood cell count will continue to rise as the eosinophil count elevates. Many patients will also begin to become anemic – meaning that their hemoglobin and hematocrit levels are decreasing. These laboratory results will cause the patient to have additional weakness and fatigue because the blood is not getting enough oxygen which is

carried by hemoglobin. As the physician notes that the patient is not improving samples of the skin rash and biopsies, or small tissue samples, may be taken from the lymph nodes that were enlarged on physical exam. These samples will then be sent to the clinical laboratory to be evaluated by a hematologist and pathologist under light microscopy. As stated previously, because peripheral T cell lymphoma is a Non-Hodgkin's lymphoma, no Reed – Sternberg cells will be seen in the tissues. After the light microscopy, the sample may be sent to a flow cytometry laboratory for marker testing. There is no definite tumor marker identified for peripheral T cell lymphoma; however, according to a study performed by the Institute of Hematology and Clinical Oncology, there is a strong correlation with the loss of expression of CD5 and CD7 cell markers that is associated with the diagnosis of peripheral T cell lymphoma (Went). Many cases of peripheral T cell lymphoma are diagnosed based on the clinical presentation of the rash and the associated complete blood count results – as was patient BGK.

As previously mentioned, the prognosis of patients diagnosed with peripheral T cell lymphoma is poor because the disease presents similarly to an infectious process and is a fast progressing, aggressive disease; however, there is treatment available for the disease. As is the approach to many cancers, the first option is typically chemotherapy treatment; however, because the disease is highly aggressive, studies have shown that it is more beneficial to give patients a combination of several different medication therapies in order to be successful in reducing the number of cancerous cells present in the body effectively. According to a study performed in Amsterdam, patients that received a combination therapy (in this case CHOP, abbreviated for the drugs used in the combination therapy (cyclophosphamide, doxorubicin (hydroxydaunomycin), vincristine (Oncovin), prednisolone (a steroid) ("CHOP Chemotherapy")), had a complete remission rate that improved the prognosis and survival rate to

one year greater than other treated with single medications (Jia). Based on this information, as well as other studies, it has been shown that chemotherapy can be used to treat peripheral T cell lymphoma; however, complete remission (meaning the disease has not returned after the treatment) has been shown to be increasingly more possible with autologous stem cell transplant. Once the cancer has been reduced with high dose chemotherapy, administration of an autologous stem cell transplant will reintroduce healthy stem cells into the bone marrow – causing a proliferation of healthy cells where the diseased cells had existed. This course of treatment has also been shown to reduce the rate of relapse commonly associated with Non-Hodgkin's Lymphoma, particularly peripheral T – cell lymphoma – causing the long-term survival rate associated with the disease to increase.

According to Dr. Fritz Lower, a former pathologist and immunology expert, an autologous hematopoietic stem cell transplant is achieved by harvesting stem cells – or cells that have not yet been differentiated into specific cells – from the bone marrow via aspiration or more commonly through peripheral blood cytapheresis (Lower). During this procedure, the patient is attached to an apparatus similar to that used in dialysis treatments that removes the blood circulating throughout the body via a line similar to an intravenous line that is inserted during hospitalization. The line removes the blood from the body and into an apparatus that spins the blood causing the stem cells to be separated from the other blood components. The remaining components are filtered back to the patient's bloodstream as the procedure continues. The stem cells are then stored in a tank within the apparatus until the procedure is complete. After the collection process is complete, the stem cells are individually treated for cancer using a high dose chemotherapy directed at the individual cells to ensure the cells are healthy and free from cancer. The healthy stem cells are then frozen to a temperature causing them to cease their maturation

process until the patient is healthy enough for transplant. The maturation process must be stopped so that the cells do not continuing growing and maturing into specialized cells but rather remain undifferentiated. Once the patient has completed high dose chemotherapy and/or other types of treatment to reduce the number of cancerous cells in the body, the stem cells are thawed so that the healthy cells may be transfused back into the patient, similarly to a peripheral blood transfusion (Lower). Because the stem cells are healthy and free of cancer, they are able to mature into healthy cells than can replace the dead or dying diseased cells affected by the chemotherapy and cancer. In a sense, these cells provide a "blank canvas" effect that allows the patient's body to begin producing new and healthy cells as opposed to the cancerous cells that were being produced previously.

According to a study published in Oncology by Matthew Lunning, the treatment of peripheral T cell lymphoma with a combination of high dose chemotherapy followed by an autologous hematopoietic stem cell transplant has been shown to provide the most positive outcomes for those patients diagnosed with common nodal lymphoma (Lunning). An additional study performed in the Czech Republic reported similar outcomes. Based on the study performed in 2009, eighty-four patients diagnosed with aggressive forms of Non-Hodgkin's lymphoma were treated with high dose chemotherapy followed by an autologous stem cell transplant between the years of 2000 and 2007. Following the procedure, 61% of the treated patients were diagnosed with complete remission from the cancer – indicating that there were no longer any cancerous cells present in the patient's body. In addition to those who achieved complete remission, 17% of patients achieved partial remission indicating that there were still several cancerous cells present in the body; however, the number was greatly reduced from initial diagnosis. This study concluded that this particular course of treatment – high dose

chemotherapy followed by autologous stem cell transplant – was a valid and successful treatment that could present patients with an increased survival rate from the lymphoma as well as an increased long term survival rate not previously possible with high dose chemotherapy treatment alone (Prochazka).

One of the advantages presented by Dr. Fritz Lower regarding the autologous hematopoietic stem cell transplant, is the reduced risk of a complication known as graft – versus – host disease (Lower). Graft – versus – host disease is a complication that occurs after bone marrow (stem cell) transplants that causes the donor cells (new cells that have been transplanted) to attack the patient's cells – causing them to die (Medline). During a study performed in 2005, twenty out of twenty-six patients developed graft -versus – host disease following a transplant; of theses twenty patients, half expired secondary to complications caused by the disease (Zheng).

Because autologous stem cell transplant patients are receiving their own cells back into their body, the body does not see them as foreign cells and therefore does not attack them in an effort to destroy them. This process means there is no need for additional immunosuppressive therapy following the procedure because there is no foreign material being introduced into the patient's body. Immunosuppressive therapy inhibits the function of the patient's immune system to allow the newly introduced cells to grow and thrive in the body without being attacked by the patient's white blood cells. However, these immunosuppressive medications, by inhibiting the patient's immune system, also prevents the patient from being able to fight common bacteria encountered in a common space. Patients who have undergone transplant typically are required to be in isolation for many days following their surgery and are allowed limited contact with others in order to lower the risk of infection. After leaving the hospital, these patients are still required to wear a mask in public in order to protect themselves from potential infection and are

required to take immunosuppressive drugs for the rest of their lives in order to decreased the risk of possible infection from the air. The immunosuppressive therapy will continue over the patient's lifetime to prevent the immune system from fighting common infections. This lack of an immune system compromises the general health of the patient, typically causing he/she to be hospitalized for extensive periods of time following a traditional donor (allogenic) stem cell transplant.

Even though a hospital is considered a safe place, hospitals are places of increasing infection rates. As mentioned above, patients who receive allogenic stem cells transplants are instructed to begin taking immunosuppressive therapy medications that suppress their natural immune system and prevent the patient's body from fighting common infections – including common viruses such as Rhinovirus that causes the common cold as well as increasing fungal infections particularly caused by the Candida species that can commonly by found on the skin or in the human body. Due to the immunosuppressive therapy, patients are required to stay in the hospital for several days – many of which is spent in the intensive care unit – following the stem cell transplant procedure.

According to a study performed by the National Nosocomial Infection Surveillance System, between the years of 1986 and 1990, over 2,000 hospitals were monitored for nosocomial infections, or infections that were acquired while the patient was hospitalized. During these years, it was calculated that there was a rate of infection of 9.2 infections per 100 patients; however, when the patient population was reduced to that of the intensive care unit, the infection rate rose to 23.7 infections per 100 patients. It was also determined through this study that there was a positive correlation between the increasing number of days a patient was admitted to the intensive care unit and the increasing rate of infection (Jarvis). It should be noted

that this study was performed on all patients admitted to the intensive care units of the hospitals being monitored and does not have specifications regarding if the patients were immunosuppressed or otherwise had an intact immune system to protect the body against infection. According to a study published in the Journal of Critical Care, an increased duration of hospitalization in the intensive care unit, usually greater than seven days, was associated with an increased risk of development of a blood infection and increased risk of in hospital death by 3-fold (Brunelli). This study was performed on non-immunosuppressed patients that had a long period of hospitalization.

Based on this information, it can be inferred that a patient being given immunosuppressive medications would have an increased risk of infection and subsequent expiration compared to a patient with a natural immune system. While patients that are admitted to the intensive care unit are already at a high risk of developing infection, immunosuppressed patients would have an increased risk of infection from the already high risk of infection. An additional study published in the World Journal of Clinical Oncology earlier this year indicates that the mortality rate for allogenic stem cell transplant patients (who are required to take immunosuppressive therapy) that are admitted to the intensive care unit is greater than 50% (Bayraktar).

In contrast to the allogenic stem cell transplant, an autologous stem cell transplant that does not require immunosuppression therapy, surgical intervention, or hospitalization – all factors increasing the risk of infection and in hospital death. Patients have the procedure performed in an exam room and are discharged from the hospital following the procedure and are not required to take immunosuppression therapy after discharge from the hospital. This decreased exposure to hospital patients and environment as well as a partially intact immune

system significantly decreases the possibility of post procedure infection in the autologous stem cell transplant patients – providing a safer treatment option compared to that of an allogenic stem cell transplant. These patients are permitted to go home and spend time with their family and support system while beginning their recovery process.

As stated previously, autologous stem cell transplant recipients are released from the hospital on the same day as their procedure. While this is beneficial to the patient's physical health and well-being, there is also evidence that this structure of treatment is also beneficial to the patient's mental state of mind regarding their disease and treatment, which could affect their prognosis. For the majority of the population, hospitals are mentally associated with illness and death. There is no positive correlation for many individuals regarding hospitalization and the prognosis of their illness or that of a loved one. Patients who have received an allogenic stem cell transplant, as mentioned above, are admitted to the intensive care unit following surgery in an effort to protect the them from possible infection. In an effort to protect the patient from other patients in the intensive care unit, transplant patients are typically placed in isolation, meaning they are segregated from other patients. Those individuals entering the isolations rooms must be limited in number and must wear many forms of protective apparel including masks and gloves in order to protect the patient from natural bacteria present on their skin and in their secretions.

Studies have shown that both admission to the hospital as well as isolation precautions can cause detrimental effects to the patient's psychological well-being, which could delay the healing process. According to a study performed in 1998, the process of hospitalization solely caused many negative feelings within the observed patients that greatly affected their emotional and mental well-being. The hospitalization also affected how the patients were able to cope with their diagnosis and treatment while in the hospital. Furthermore, the study also validated that

there were increasingly negative psychological effects on patients that were isolated following illness compared to those that were simply hospitalized on general medical floors with limited visitor restrictions. The study goes on to state that patients that were hospitalized and then placed into isolation due to either surgical procedure or medical diagnosis were shown to have increasing feelings of anxiety and depression. These patients were also found to have a lower self-esteem and sense of control over their illness, treatment, and prognosis compared to those patients admitted to a general medical floor. These increasing feelings of anxiety and depression as well as the worsening self-esteem continued to have an even worsening effect on the patient's ability to cope with their diagnosis and treatment.

According to a study published in the International Journal of Geriatric Psychology, patients with increasing signs and symptoms of depression were less likely or able to actively participate in their recovery and rehabilitation as needed following hip replacement surgeries. These patients required longer periods of hospitalization and based on the age group that was evaluated were more likely to be discharged to a nursing home or long term care facility because they were not able to cope with their diagnosis. These patient as did not recover as well physically as would have been expected. Patients with worsening signs of depression in this study were compared to patients with baseline cognitive impairment due to their impaired ability to cope with the treatments and participate in rehabilitation following their surgeries (Lenze). Based on the provided evidence, it is apparent that psychological well-being of a patient is affected by hospitalization, particularly isolation hospitalization.

Patients who undergo allogenic stem cell transplants are therefore subjected to worsening anxiety and depression because they are admitted to the intensive care unit following their procedure. This could also affect their recovery time following their procedure, causing a longer

hospitalization, exposing the patient to increased risks of infection, and worsening depression. Contrastingly, patients who undergo the autologous stem cell transplant are permitted to leave the hospital hours after their procedure, requiring no hospitalization. It can then be inferred that patients who undergo autologous stem cell transplants will have increasingly more positive psychological outcomes following their procedure compared to those patients that have undergone an allogenic stem cell transplant. These autologous stem cell recipients will also have a decreased recovery time allowing them to return to their families and support systems more quickly following the procedure, decreasing the risk of worsening anxiety and depression – presenting the patient with an overall improved psychological state of mind during their recovery.

For similar reasons as stated previously, an autologous stem cell transplant is also more economically responsible compared to an allogenic stem cell transplant. When a patient has an allogenic stem cell transplant, hospitalization fees are required regarding the patient as well as the donor providing the stem cells. Costs are also incurred to compensate a surgical staff as well as to reserve space in an operating room to perform the procedure. Costs are also incurred for the postoperative immunosuppressive medications required after surgery to prevent graft – versus – host disease. Postoperative infections often associated with hospitalization in the intensive care unit also create a financial burden on the patients and their family. According to the study performed by Brunelli, admission to the intensive care unit and hospital associated infection caused a significant increase in the cost of care for the patient. Per Brunelli, an additional $129,000 was required to cover the costs of the intensive care hospitalization. In contrast, a patient receiving an autologous stem cell transplant that is released from the hospital following the procedure is not subjected to these additional costs of the allogenic procedure or

postoperative hospitalization fees, making the autologous stem cell transplant more economically efficient for the patient.

In conclusion, patients suffering from peripheral T cell lymphoma are more likely to have a more positive outcome resulting in a better opportunity for complete remission if treated with high dose chemotherapy followed by an autologous stem cell transplant contrasted to an allogenic stem cell transplant. The use of an autologous stem cell transplant prevents the patient from exposure to immunosuppressive therapy which would make he/she more susceptible to infection as well as prevents extensive hospitalization in the intensive care unit. This lack of a hospitalization period is critical in preventing likely blood infections, possible in hospital death, and increased costs of care. The lack of hospitalization also increases the patient's psychological well-being following the procedure due to the decreased risk of worsening anxiety and depression that accompany hospitalization and isolation precautions required after an allogenic stem cell transplant. Based on the presented studies and information and compared to the allogenic stem cell transplant, the autologous stem cell transplant is a safer, psychologically beneficial, and economically efficient treatment option for those patients diagnosed with peripheral T cell lymphoma.

Patient BGK had an autologous hematopoietic stem cell transplant performed on 11 February 2016. BGK was released from the hospital after three hours of observation following the procedure and has had no infectious processes since the transplant. Patient BGK's state of mind has also improved since the procedure. After being able to watch college students perform a polar plunge event following her procedure, patient BGK no longer has a negative opinion of her illness but rather sees it as an eye-opening experience. BGK has had no recurrence of the cancerous cells since the stem cell transplant and has ceased to have any symptoms, including

the rash which has completely resolved from the skin. Patient BGK is today considered cancer free status post peripheral T-cell lymphoma treated with high dose CHOP chemotherapy and autologous stem cell transplant.

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