SBTMO

17TH EDITION

JOURNAL OF BONE MARROW TRANSPLANTATION AND CELLULAR THERAPY

JBMTCT

VOL. 5, SUPPLEMENT 1, JULY 2024

XXVIII CONGRESSO SBTMO

FORTALEZA 2024

31 DE JULHO A 3 DE AGOSTO • CENTRO DE EVENTOS DO CEARÁ

TMO: EM CONSTANTE EVOLUÇÃO

ISSN 2675-374X
10.46765/2675-374X.2024v5nSuppl1

TRANSCRIPTOMIC META-DATASET DISPLAYED DISTINCT ONCOGENIC SIGNATURE AND POTENTIAL MEMBRANE TARGETS FOR CAR-T CELL THERAPY IN CHRONIC LYMPHOCYTIC LEUKEMIA

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INTRODUCTION

Chronic lymphocytic leukemia (CLL) is a lymphoproliferative disorder characterized by the proliferation of neoplastic B cells with a mature appearance. CLL treatment ranges from observation to chemo-immunotherapy and targeted therapies. Recently, several studies have shown CAR-T (anti-CD19) therapy as a promising strategy. So far, over 100 CLL patients have been treated with anti-CD19 CAR-T cells. However, the overall response rate is still insufficient for some refractory/relapsed patients (mean of ORR = 58.6%) and adverse events are commonly present. In this sense, it is important to identify novel molecular targets for CAR-T therapy development to overcome the difficulties encountered.

AIMS

The present study aims to produce transcriptomic meta-data and evaluate potential differences in genetic expression profiles in CLL patients to seek novel target biomarkers.

METHODS

The transcriptomic meta-dataset was constructed with 37 healthy and 254 CLL samples from three independent studies (GSE26725, GSE79196, and GSE50006). First, datasets were downloaded from the Gene Expression Omnibus, and expression values were normalized and subsequently merged. Batch effects were identified and removed using empirical Bayes estimation (ComBat). Finally, differentially expressed genes (DEGs) and functional analysis were performed using Limma, gene set enrichment analysis (GSEA), and Gene Ontology (GO). Then, a subcellular location filter was applied for genes that express in cell membrane proteins (ECO:0000269). Human Protein Atlas was used to verify the protein expression (pTPM). Furthermore, modeled FCRL1 protein was obtained in Alfaphold (Uniprot: Q96LA6), and potential epitopes were predicted using the IEDB database (www.immuneepitope.org).

RESULTS

There were 544 upregulated (36.11%) and 491 downregulated (63.89%) genes in CLL compared to normal cells (Figure 1A). The top 10 up- and down-regulated genes are presented in Figure 1B. It was possible to verify that 41 genes were commonly observed in Limma and GSEA analysis (Figure 1C, D). Thereafter, only DEGs with subcellular locations for cell membranes were analyzed to determine the top 20 genes overexpressed in CLL samples (Figure 2A). The GO analysis revealed that these genes are closely related to immune response signaling, (Figure 2B). FCRL1 (CD307a) gene was the most relevant biomarker identified, confirmed in the TCGA database (Figure 2C), and is predominantly expressed in B-cell lineage (Figures 2D and 3). Using machine learning, 18 epitopes were predicted (Figure 4).

CONCLUSION

The global transcriptome for CLL patients displayed a significant oncogenic profile. Furthermore, when filtered by cell membrane sublocation, the FCRL1 gene was the most enriched in CLL. Therefore, this study proposes the FCRL1 as a relevant biomarker for CLL and other B-cell malignant and a potential target for CAR-T cell therapy.

KEYWORDS

Transcriptome, CAR-T, Biomarkers, Chronic lymphoid leukemia.

Figure 1 – Global transcriptome analysis in CLL merged samples.

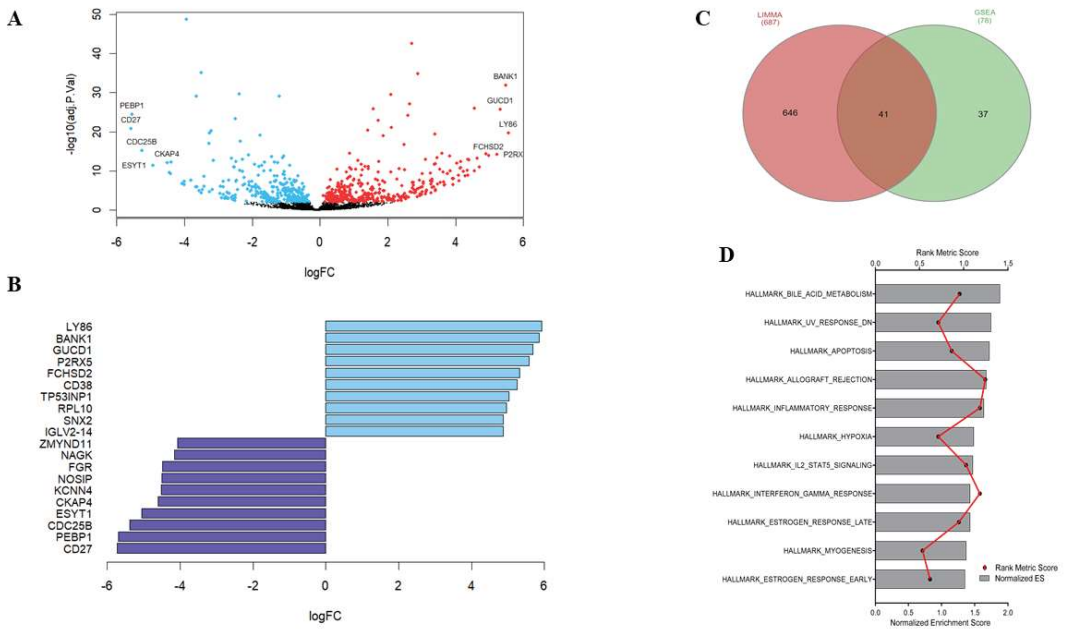


Figure 2 - Transcriptome analysis filtered to identify only cell membrane overexpressed genes in CLL.

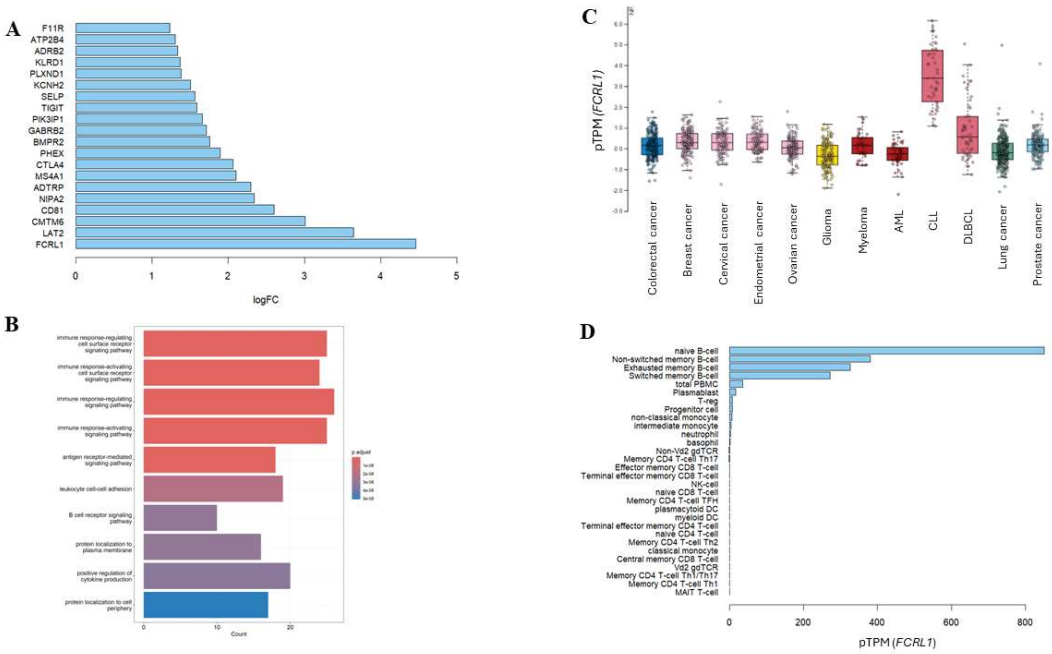


Figure 3 - *FCRL1* protein expression in different cancer cell lines (Human Protein Atlas).

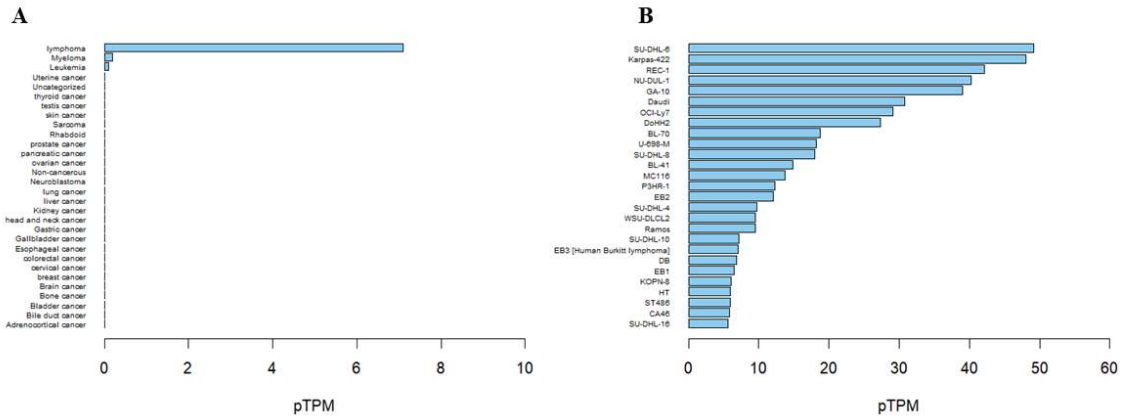
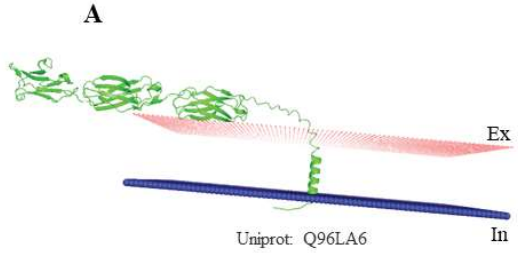
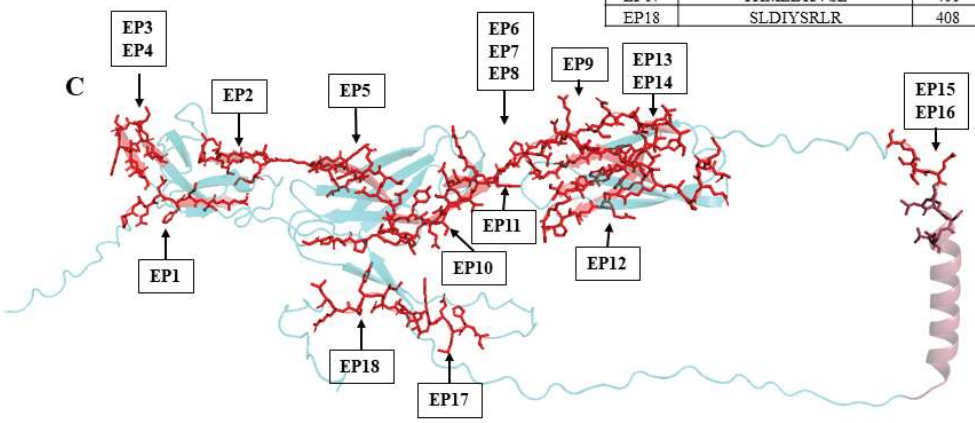


Figure 4 – *FCRL1* protein modelling and epitope identification.



B

ID	Epitope	Starting Position	Ending Position
EP1	PAELFLIAS	16	24
EP2	SPKLQIAAM	29	37
EP3	EAQTMASKVLR + OX(M5)	87	97
EP4	EAQTMASKVLR	87	97
EP5	VGLNLQSKTQRSLT	113	126
EP6	IPVSRPILMLRAPRAQ	164	179
EP7	IPVSRPILMLRAPRAQA	164	180
EP8	IPVSRPILMLRAPRAQAA	164	181
EP9	SRPILMLRAPRAQA	167	180
EP10	RESDAEQYY	174	182
EP11	GPSPSGLVSITVRIPVSRP	190	208
EP12	ILYWFYHEDITLGSRSAPSGG	238	258
EP13	EANNGLGAQR	277	286
EP14	AQRSEAVTL	284	292
EP15	SGVIEGLLSTL	307	317
EP16	GVIEGLLSTL	308	317
EP17	THMEDKVSL	401	409
EP18	SLDIYSRLR	408	416



ACUTE MYELOID LEUKEMIA POST KIDNEY TRANSPLANT: HOW TO INDICATE HEMATOPOIETIC CELL TRANSPLANTATION?

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INTRODUCTION

Skin cancer and post-transplant lymphoproliferative diseases (PTLD) account for up to 80% of all cases of post-solid organ transplant malignancies, but much less is known about the risks for hematologic malignancies of myeloid origin. The physiopathology of post-transplant AML (PT-AML) is probably multifactorial (immunosuppression, antigenic graft stimulation and direct drug mutagenicity), which can act in combination to help AML cells evade attack by the immune system. Donor-derived cancer transmission is reported in about 0.01% to 0.2% of solid organ recipients. Our literature review focusing on PT-AML found only 2 multicenter studies and 4 case series.

OBJECTIVE - To present a clinical case of AML in a patient post kidney transplant.

METHOD: Case report and literature review.

CASE REPORT

A 32-year-old woman who received a kidney transplant and immunosuppressed with mycophenolate sodium and tacrolimus developed progressive cytopenias. Bone marrow aspiration and immunophenotyping showed leukemic infiltration with 51% blasts, suggestive of Acute Myeloid Leukemia. Our patient was stratified as an adverse risk due to complex karyotyping and underwent induction chemotherapy with cytarabine and daunorubicin, and the immunosuppression was reduced, with no renal graft rejection. On the 28th day post-induction, achieved complete remission (CR) and on day 30 post-consolidation the measurable residual disease (MRD) was negative. She was referred for evaluation by the bone marrow transplant team and has an alternative donor (haploidentical).

DISCUSSION

Diagnosis of PT-AML was incidental in 40% of reported cases and median overall survival was 3-6 months. The two multicenter studies showed a standardized incidence ratio for the development of AML among kidney transplant recipients of 1.90, suggesting that immunosuppression severe and prolonged increases this risk and that azathioprine is the highest known risk immunosuppressive. Ineffective immune surveillance is part of the immunopathology of PT-AML. Immunosuppressive microenvironment and leukaemia cells mediate immune suppression to promote immune evasion, including altered antigen presentation, inhibitory ligands/receptors and immunosuppressive molecules. These mechanisms are reinforced, for example, by the fact that allogeneic T-cell-depleted hematopoietic cell transplant recipients (allo-HCT) and recipients without graft-versus-host disease (GVHD) have higher risks of AML recurrence than those receiving T-cell-filled grafts and those with GVHD. Gradual reduction of immunosuppression is necessary for treatment, but it is often insufficient. However, although allo-HCT is indicated in patients with high-risk therapy- or cytogenetics-related AML, the treatment of these cases have been heterogeneous with or without allo-HCT.

CONCLUSION

PT-AML is a rare entity and the optimal treatment approaches are not known yet.

KEYWORDS- 'Acute myeloid leukemia', 'myeloid neoplasms', 'kidney transplantation'.

LITERATURE REVIEW: BONE MARROW TRANSPLANTATION IN LYMPHOMA

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INTRODUCTION

Bone marrow transplantation or hematopoietic stem cell transplantation consists of the intravenous infusion of hematopoietic progenitor cells. Lymphomas originate from cells of the immune system. For patients with relapsed Hodgkin's lymphoma, autologous bone marrow transplantation (ABMT) is the main therapeutic option. The response to pre-transplant chemotherapy is the main prognostic factor, so patients with stable disease or minimal response to salvage therapy have less than 20% chance of achieving durable remission with ABMT. Bone marrow transplantation is a treatment indicated for diseases related to the production of blood cells and deficiencies in the immune system.

OBJECTIVE

This study seeks to understand the importance of bone marrow transplantation in lymphoma through a systematic literature review.

METHOD

A literature review was conducted in the Lillacs, PubMed, Scielo, and Google Scholar databases, focusing on articles published between 2020 and 2022, in Portuguese and English. Inclusion criteria involved works addressing articles up to 2022, excluding articles prior to 2020.

RESULTS

Searches in the different databases resulted in 2,490 publications, which were reduced to 57 after the first stage of analysis (title and abstract), 26 after the second stage (removal of duplicates), and finally, 10 publications after the third stage (analysis of the full content of articles), which met the established inclusion and exclusion criteria. Transplantation is an old treatment strategy, but still with very established results and worldwide use. Allogeneic transplantation is still reserved for refractory cases, as an attempt for a possible cure. Autologous transplantation remains a standard part of second-line therapy, even with the current treatment options.

CONCLUSION

We can consider, therefore, transplantation using hematopoietic stem cells as one of the greatest advances in modern medicine, although it does not provide absolutely normal survival to all patients, it represents a possibility of greater survival for patients who would not have any chance with any other type of treatment and prevents the patient from dying.

KEYWORDS

Allogeneic Transplantation, Lymphoma, Literature review.

PATIENT BLOOD MANAGEMENT (PBM) STRATEGIES IN BONE MARROW TRANSPLANTATION UNIT - IMPACT ON PRIMARY OUTCOMES

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Transfusion of blood components is a measure widely used to treat and control symptoms related to anemia and hemorrhage, but it is not a risk-free procedure for the patient. In this context, blood components must be used in the most rational way possible. Patient blood management (PBM) consists of a multidisciplinary, preemptive and evidence-based strategy to reduce the indiscriminate use of blood components based on reducing blood loss, correcting anemia and treating coagulopathies.

The principles of PBM are commonly used, however, when it comes to onco-hematological patients and, especially those undergoing bone marrow transplantation since cytopenias occur routinely this strategy becomes even more challenging.

This study aimed to evaluate restrictive transfusion strategies and their impacts on patients undergoing bone marrow transplantation (BMT) from January 1, 2018, to December 31, 2022, at a tertiary hospital, with support from the Blood Center of State. This is a descriptive and retrospective observational study. Data collection was performed by reviewing medical records and the Blood Bank System (SBS).

The sample consisted of 333 patients with a mean age of 45 years, of whom 168 (50.5%) were male and 135 (49.5%) were female. Sixty percent of the total patients had some comorbidity, with arterial hypertension being the most frequent (21%). Regarding the type of transplant, 62.8% were autologous and 37.2% allogeneic. The main diagnoses of patients undergoing BMT were plasma cell neoplasia (36.3%), Hodgkin's lymphoma (13.8%), non-Hodgkin's lymphoma (10.8%), acute myeloid leukemia (9%), and acute lymphoid leukemia (10.5%).

Restrictive strategies are adopted in the studied center, and transfusion triggers during BMT hospitalization were: Hemoglobin (Hb) < 7g/dL, platelets <50,000 µL if bleeding or lumbar puncture, <20,000 µL in the presence of fever or central venous access puncture, and <10,000µL prophylactically. There was no evidence of correlation between the number of transfusions, pre-transfusion hemoglobin, and platelet count with age or patient survival after hospital discharge, demonstrating that elderly patients did not require more transfusions.

The number of transfusions during this period did not impact survival, which was expected because post-hospital discharge survival is influenced by many other factors. In the analysis of in-hospital mortality, there was higher mortality in patients who received more transfusions and in those undergoing allogeneic transplantation. However, this is a study bias because some patients, especially those undergoing allogeneic BMT, tend to undergo more tests and transfusions due to their severity, and causality cannot be attributed. This study suggests that restrictive strategies are effective in reducing blood component transfusions in BMT, as well as reducing patients' exposure to transfusion risks, and reducing costs, without harming patients.

HEMORRHAGIC CYSTITIS DUE TO ADENOVIRUS INFECTION IN ALLOGENEIC TRANSPLANT RECIPIENT

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INTRODUCTION

Hemorrhagic cystitis (HC) is a common complication following allogeneic hematopoietic cell transplantation (HCT), occurring in approximately 30% of recipients. It is a cause of prolonged hospitalization and reduced quality of life due to symptoms such as urgency, polyuria, and dysuria. Risk factors for hemorrhagic cystitis include alternative donor, donor age, use of busulfan, ATG and cyclophosphamide (rare cause due to mesna prophylaxis), total body irradiation, and identification of CMV and BKV (detected in approximately 80% of HC) in urine.

OBJECTIVE

To describe a case of hemorrhagic cystitis due to adenovirus infection in a patient undergoing allogeneic HCT.

METHODS - Review of medical records and local databases.

RESULTS

A 20-year-old male patient diagnosed with T-cell lymphoblastic lymphoma in first remission underwent allogeneic HCT with matched-unrelated donor. Myeloablative conditioning with busulfan and cyclophosphamide (BUCY) was used. GVHD prophylaxis consisted of cyclosporine and methotrexate. Anti-thymocyte globulin (ATG) was used at a total dose of 4.5 mg/kg.

During hospitalization, he presented febrile neutropenia, viral infection with Parainfluenza 3 and coronavirus OC43, and grade 3 mucositis. On day +24 post-transplant, cytomegalovirus reactivation was identified, and preemptive treatment was initiated. On day +45, he developed symptoms of dysuria, polyuria, and hematuria.

He was admitted for supportive measures with bladder irrigation and tapering of immunosuppression, leading to resolution of hematuria. Further investigation revealed undetectable CMV and BK virus, and detectable adenovirus in both serum and urine.

CONCLUSIONS

The differential diagnosis of hemorrhagic cystitis in the context of post-allogeneic transplantation includes adverse drug effects, acute GVHD, viral (BKV, JCV, CMV, and AdV), and bacterial infections. Hemorrhagic cystitis due to viral infection still lacks effective methods for prophylaxis and treatment in order to mitigate its high morbidity.

FIGURE 1- Urine amplification plot. Kit Multiplex Neuro 9 (Xgen, Mobius)/QuantStudio 5

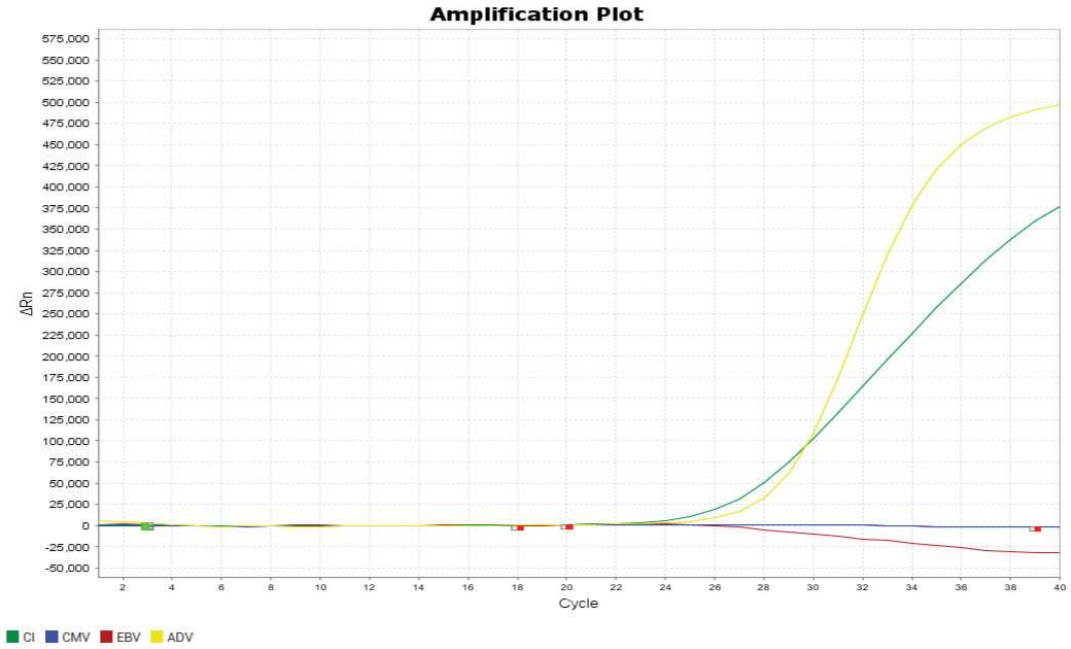
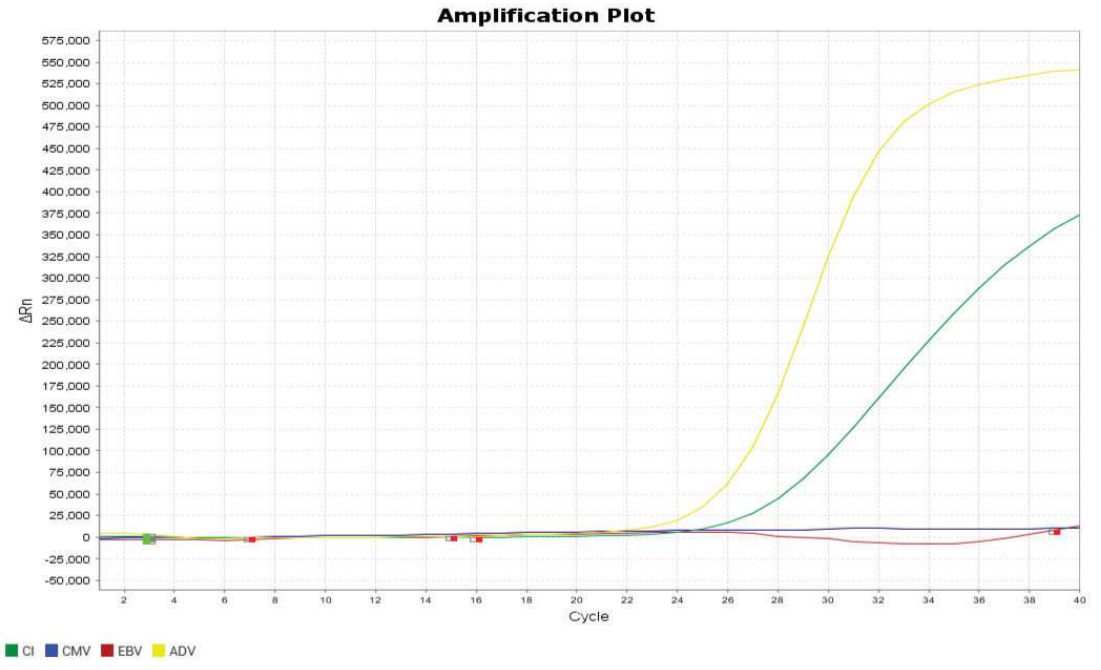


FIGURE 2 - Serum amplification plot. Kit Multiplex Neuro 9 (Xgen, Mobius)/QuantStudio 5



MEDICATION RECONCILIATION IN THE TRANSITION OF CARE FOR PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: THE CONTRIBUTION OF THE CLINICAL PHARMACIST

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is therapy widely used in the treatment of hematological diseases and requires the work of a multidisciplinary team for its successful execution. In this context, the clinical pharmacist has played an extremely important role through drug reconciliation services, which consist of a review of the patient's medication at the moment of the admission and hospital discharge, promoting individualized care and preventing medication errors by identifying discrepancies.

OBJECTIVE

To describe the main discrepancies in medication reconciliation as well as the sociodemographic and clinical profile of patients undergoing HSCT.

CASUISTRY

Patients who underwent hematopoietic stem cell transplantation during the study period.

METHODS

The study was based on the medication reconciliation records and pharmacotherapeutic follow-up carried out by the unit's clinical pharmacy team between July and December 2023 at a teaching hospital. The data collected was distributed in a padronized table of the unit of clinical pharmacy, made in Excel®, in which was describe the following information: age, gender, underlying disease, type of transplant and discrepancy between previous pharmacotherapy and current pharmacotherapy upon hospital admission. The present study was approved by the Research Ethics Commitee under opinion number 5.409.579.

RESULTS

During the time interval included in the study, a total of 68 admissions were made through medication reconciliation for 53 patients. Between these patients 45.6% were female and 54.4% male. About 61.8% of the patients were between 31 to 60 years old. The most frequent underlying diseases were as follows: 27.9% with Multiple Myeloma (MM), 17.6% of patients with Acute Lymphoblastic Leukemia (ALL), 13.2% with Acute Myeloid Leukemia (AML) and 41.3% of patients with other diagnoses. Regarding the type of transplants, the most common among the patients evaluated was autologous HSCT with (34/68) 50% of the cases, (25/34) 36.8% of related allogeneic transplants and (9/34) 13.2% of unrelated allogeneic transplants. Problems related to discrepancies between previous pharmacotherapy and current pharmacotherapy were identified, with 48.5% of patients having discrepancies, 60.6% of which were justified. Among the discrepancies, the problems related to the discontinuation of medication (30.3%) stood out, followed by failure to prescribe necessary medication (33.3%) and the substitution of medication (21.2%).

CONCLUSION

From the offering of this clinical service, it was possible to identify prescription errors and make the necessary prescription adjustments, promoting the safe use of medication in the transition of care and in relation with patients treatment, in addition to outlining a sociodemographic and clinical profile of these patients.

KEYWORDS

Drug reconciliation; Clinical pharmacy service; Patient safety.

PROFILE OF REPORTS OF ADVERSE DRUG REACTIONS IN BONE MARROW TRANSPLANT PATIENTS IN A SENTINEL HOSPITAL

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INTRODUCTION

Adverse drug reactions (ADRs) are any harmful or undesirable and unintentional response that occurs with drugs at the doses usually used, becoming a problem in healthcare. In order to monitor and reduce these events, reporting them to risk management services enables traceability with a focus on patient care. To facilitate this notification, it was created VIGIHOSP, a software for Health Surveillance and Hospital Care Risk Management, used in federal university hospitals, which facilitates voluntary notification and traceability.

OBJECTIVE

To analyze the notifications and describe the occurrence of adverse drug reactions in patients who underwent bone marrow transplantation in a public teaching hospital linked to the Ebserh Network.

CASUISTRY

Patients who underwent hematopoietic stem cell transplantation during the study period.

METHODS

This was a retrospective descriptive observational study. The research was carried out by collecting data on ADR notifications that occurred in a teaching hospital, related to hematopoietic stem cell transplant patients and that were notified through the VIGIHOSP system during the year 2023. The data collected was described using the following variables: gender, age, medication, symptoms after medication administration, risk classification and severity classification. This study was approved by the Research Ethics Committee under opinion number 5.409.579.

RESULTS

During the year 2023 there were 8 spontaneous notifications of ADRs, of these 75% (n=6) related to female patients and 25% (n=2) to males. The most prevalent age group was between 20 and 24 years old, with 37.5% (n=3). The most common medication was cyclosporine with 25% (n=2) of the cases, followed by thymoglobulin, meropenem, carmustine, teicoplanin, vinorelbine and etoposide, each with 12.5% (n=1) of the cases. The most frequent symptoms were pruritus and skin rash, followed by nausea, facial edema, facial paresthesia, facial heat, lower limbs heat, headache, injection site pain, crepitation, desaturation, vomiting followed by syncope and fall. The risk classification according to the WHO was 87.5% (n=7) mild and 12.5% (n=1) moderate. When assessing causality, according to Naranjo's algorithm, 100% (n=8) of the events were classified as possible.

CONCLUSION

The importance of voluntary reporting by all those involved in patient care is noteworthy. Under-reporting is the biggest challenge in identifying ADRs. Voluntary reporting should be encouraged for all health professionals, with a view to the safety and quality of life of patients who need bone marrow transplants.

KEYWORDS

Adverse Drug Reactions; Notification; Bone Marrow Transplant.

MANDACARU-T PROJECT: A JOURNEY IN IMPLEMENTING CAR-T THERAPY WITHIN A HEMOTHERAPY SERVICE IN BRAZIL

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INTRODUCTION

Chimeric antigen receptor (CAR) T-cell therapies targeting CD19 have shown promise in treating patients with relapsed/refractory diffuse large B-cell lymphoma (r/r DLBCL) and Acute Lymphocytic Leukemia (ALL). This innovative approach involves modifying a patient's own T-cells genetically to express a chimeric antigen receptor designed to recognize tumor antigens. Once reintroduced into the patient's body, these engineered CAR T-cells target and destroy cancer cells bearing the specific antigen. By 2020, regulatory bodies had approved two CAR T-cell therapies for select adult patients with r/r DLBCL. Axicabtagene ciloleucel (axi-cel) gained approval from the US Food and Drug Administration (FDA) in October 2017, followed by tisagenlecleucel (tisa-cel) in May 2018. Furthermore, ongoing research continues to advance in the development of new CAR-T cell treatments.

AIMS

This experience report aims to describe the main difficulties faced in the implementation of CAR-T therapy in a hemotherapy service in Brazil.

METHODS

This report provides an overview and analysis of presentations given during an internal meeting held at the Hematology and Hemotherapy of Ceará (Hemoce) in 2023, focusing on the integration of advanced therapies within the hemotherapy service.

RESULTS

The MandaCARu-T project was conceptualized in 2019, with plans for the clinical trial of CAR-T anti-CD19 therapy set to begin in 2025. The project has adhered to the requisite documentation processes outlined by Federal law and by the Brazilian Health Regulatory Agency (Anvisa). The existing regulatory framework for advanced cell therapy and gene therapy products is structured to navigate the complexities inherent in products involving multiple institutions. One of the challenges is that this framework entails multiple steps involving more than one institution, such as Anvisa, National Research Ethics Committee (Conep), and National Technical Biosafety Commission (CTNBio), each with its response deadlines and procedures, thereby extending the regulatory timeline. Also, the discrepancy between the regulatory framework, which is largely oriented towards commercialization, and the objectives of the MandaCARu-T project, which aims to provide CAR-T therapy through public healthcare services, poses a significant challenge. Typically, regulatory processes are adapted to assist commercial ventures, making navigating for initiatives focused on public service delivery challenging.

CONCLUSION

The complex network of institutions, combined with legal and constitutional factors, underscores Brazil's intricate nature of regulating advanced cell and gene therapies. Despite these complexities, ANVISA plays a crucial role and has made notable advancements in this domain. Over the past year, the MandaCARu-T project has also made substantial progress, with plans for the clinical trial slated to commence in 2025.

KEYWORDS

CAR-T; leukemia; lymphoma.

HEMATOLOGY OUTPATIENT CLINIC AT A HEMOCENTER: SUPPORTING BONE MARROW TRANSPLANTATION

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INTRODUCTION

The hematology outpatient clinic consists of a multidisciplinary team that provides scheduled/regulated and on-demand care. This care is provided comprehensively and humanely. It is a reference center for the diagnosis and treatment of patients with hematological diseases. It provides care for patients with sickle cell disease and other hemoglobinopathies, patients with hereditary coagulopathies throughout the state, hematology patients: outpatient care for general hematology patients residing in the interior of the state of Ceará, and specialized diagnostic tests: performing laboratory tests for diagnosis in general hematology, blood coagulation, hemoglobinopathies, flow cytometry, and bone marrow pathology and cytology.

OBJECTIVE

To evaluate the importance of the general hematology outpatient clinic in the interior of the state of Ceará for the indication of bone marrow transplantation.

METHOD

This is an observational, descriptive, quantitative, and retrospective study of the services provided in the year 2023 according to the spreadsheet of the Ambulatory Production Bulletin (BPA) of the service, in a general hematology outpatient clinic in a Hemocenter in the interior of the state of Ceará.

RESULTS

The medical services during the mentioned period totaled 1,879 consultations, of which 947 were general hematology consultations, and as support for this service, 3,222 laboratory tests were performed, including 2,719 blood counts, 390 reticulocytes, 96 myelograms, and 17 immunophenotyping. Among the patients seen in the outpatient clinic in 2023, one was referred for a bone marrow transplant. It is worth noting that in previous years, the Hemocenter has a history of two more bone marrow transplants, also contributing to the health of the population it serves.

CONCLUSION

The Hemocenter outpatient clinics are involved in providing outpatient care to hematology patients through specialized medical consultations and multidisciplinary team care. All units also have specialized laboratories for the diagnosis of hematological diseases, coagulopathies, and hereditary hemoglobinopathies. This demonstrates that the Ceará Blood Network is structured and organized to serve the population of Ceará throughout the entire state, even contributing to highly specialized services such as bone marrow transplantation.

KEYWORDS

Hemocenter, Bone marrow transplantation, Diagnosis.

HEMATOPOETIC STEM CELL HARVEST BY EFFICIENCY-GUIDED LEUKAPHERESIS AND ITS IMPACT ON PROCESSED BLOOD VOLUME AND ACD-A TO DONORS: A SINGLE-CENTER EXPERIENCE

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INTRODUCTION

Although processing a fixed number of donor total blood volumes (TBVs) is still a practice in resource-constrained settings, where peripheral CD34 count is not readily available, many centers are tailoring leukapheresis by their own eficiency data from previous procedures, rather than by manufacturer's standard efficiency rate.

AIM

We herein report our experience transitioning from processing a fixed number of TBVs to guiding processed volume (PV) by our efficiency data. Cohort: We retrospectively collected data from 734 leukaphereses performed between 2019 and 2023. Until 2020, 216 procedures were carried out using Spectra Optia (group 1) and 56 using COBE Spectra (group 2) both processing 6 TBVs. As of 2021, all 462 procedures were performed using Spectra Optia and PV was guided by mean efficiency rate from previous leukaphereses.

METHOD

Mean efficiency rates for autologous and allogeneic harvest were calculated separately. Statistical analysis was carried out with SPSS 20.0. At the physician's discretion, it was possible to process more TBVs than calculated by mean efficiency in order to avoid the need for a second or third leukapheresis.

RESULTS

In comparison to groups 1 and 2, group 3 showed inferior median processed blood volume (20.23 IQR=9.5L group 3 vs 23.07 IQR=8.12L, p<0.001 group 1; vs 25.49 IQR=7.02L; p<0.001 group 2), fewer processed TBVs (5 IQR=2 group 3 vs 6 IQR=1, p<0.001 group 1; vs 6 IQR=1, p<0.001 group 2) and less ACD-A to donor (1.64 IQR=0.77L group 3 vs 1.75 IQR=0.62L, p=0.007 group 1; vs 1.86 IQR=0.49L, p=0.006 group 2). Second or third leukaphereses to meet target CD34 represented 15.1% of procedures and were significantly rarer in group 3 than in group 1 (12.3% vs 21.8%, p=0.002) and in allogeneic than in autologous donors (3.6% vs 19.3%, p<0.001). As of 2021, allogeneic donors presented less processed volume (18.51 IQR=9.95L vs 20.87 IQR=9.32L, p=0.049), fewer processed TBVs (4 IQR=3 vs 5 IQR=2, p<0.001) and a tendency to receive less ACD-A (1.52 IQR=0.82L vs 1.70 IQR=0.76L, p=0.057) than autologous donors.

CONCLUSION

In our center, tailoring leukapheresis by mean effiency rate resulted in less processed blood volume and ACD-A to donors. This benefit seems to be greater to allogeneic donors.

USE OF CLASSICAL AND MOLECULAR CYTOGENETICS COMBINED WITH FLOW CYTOMETRY TO EVALUATE THE RESULTS OF BONE MARROW TRANSPLANTATION IN ONCOHEMATOLOGY PATIENTS AT A HEMATOLOGY AND HEMOTHERAPY CENTER IN NORTHEAST BRAZIL.

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Hematopoietic stem cell transplantation (HSCT) is an important part of curative therapy for oncohematological patients. However, the disease recurrence rate after HSCT is quite variable. Therefore, it is extremely important to analyze minimal residual disease (MRD) through flow cytometry and search for residual cytogenetic abnormalities in these post-HSCT patients for evaluation and monitoring of the transplant, enabling targeted and effective therapeutic conditioning. Therefore, this study aimed to evaluate the presence of residual cytogenetic abnormalities and MRD in oncohematological patients who underwent bone marrow transplantation, through karyotype analysis with G-banding, Hybridization in situ fluorescence (FISH) and flow cytometry. In the period from Oct/2021 to Feb/2024, 54 samples were received and analyzed from patients who underwent HSCT, with 35 (68.62%) receiving transplants from opposite-sex donors and 17 (31.3%) receiving transplants from donors of the same sex. The patients evaluated had a pre-transplant diagnosis of: myelodysplastic syndrome (MDS) (n=7), acute myeloid leukemia (AML) (n=20), B-lineage acute lymphocytic leukemia (B-ALL) (n=16), T-lineage acute lymphocytic leukemia (T-ALL) (n=1), chronic myeloid leukemia (CML) (n=4), chronic lymphocytic leukemia (CLL) (n=1), undifferentiated leukemia (n=1), leukemia biphenotypic (n=1), aplastic anemia (n=1), Hodgkin lymphoma (n=1) and myelofibrosis (n=1). The first cytogenetic analyzes after BMT by G-banding showed that 19 (40.6%) patients had complete chimerism, 11 (21.8%) had partial chimerism and 22 (34.3%) had an altered karyotype. Further analysis on D60 of 40 patients showed 14 patients with altered karyotype, 15 with complete chimerism and 5 with partial chimerism. Of these, 19 patients underwent further analysis (D90 or D120) and 7 presented altered karyotype, 7 presented complete chimerism and 5 presented partial chimerism. Evaluation by the FISH method, using the SHOX probe, was carried out in 15 cases that received transplants from donors of the opposite sex, showing agreement with the karyotype in 9 cases. Regarding MRD analysis by flow cytometry, five patients had positive MRD for AML (the patient's karyotype showed alterations), one case had positive MRD for B-ALL and one patient had inconclusive MRD. Of the cases that had an altered karyotype, 11 had negative MRD. B-ALL was the leukemia with the lowest response rate to HSCT, with nine of the 16 patients presenting a karyotype with residual genetic abnormalities after HSCT. Despite the still small sample size, the importance of performing combined techniques of classical and molecular cytogenetics with flow cytometry in the evaluation and monitoring of HSCT was highlighted. Furthermore, the importance of performing FISH in a scenario where there is no access to classical or even molecular chimerism (NGS) stands out. Therefore, this method used can be of great value when donors and patients are of different sexes.

KEYSWORDS - chimerism, cytogenetic, Hematopoietic stem cell transplantation