CASE REPORTS

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THE EFFECTIVENESS OF THE MULTIPROFESSIONAL APPROACH IN THE PEDIATRIC REHABILITATION OF CHRONIC GVHD: THE SPECIFIC CONTRIBUTION OF OCCUPATIONAL THERAPY

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ABSTRACT

This study reports the rehabilitation process in occupational therapy of a two-year-old child with Chronic Graft-versus-Host Disease (cGVHD), affecting multiple organs and joints, impacting their neuropsychomotor development (NPMD) and functionality. The method used was a case report, respecting ethical protocols. The assessment included the Observational Analysis of NPMD Milestones and the Functional Assessment Scale for Chronic GVHD (NIH). Based on the results, we utilized the International Classification of Functioning, Disability, and Health for Children and Youth (ICF-CJ) to categorize the objectives of therapeutic interventions. The intervention followed four stages: initial assessment, definition of objectives, application of the Therapeutic Toy Enabling Physiological Functions (TP) and periodic reassessments. After 27 sessions, there was an improvement in the range of motion of the affected joints, an increase in respiratory endurance, and advances in NPMD, including ambulation and fine motor skills such as feeding. The results demonstrate the efficacy of occupational therapy in functional recovery and in promoting quality of life. It is concluded that early intervention, integrated with a multidisciplinary team, is essential to minimize the impacts of cGVHD, prevent sequelae and favor child development.

Keywords: Pediatrics; Occupational therapy; Rehabilitation; Hematopoietic Stem Cell Transplantation.

Ethical considerations: In view of the above, the Human Research Ethics Committee of the Hospital de Clinicas Complex of the Federal University of Paraná (HC-UFPR), in accordance with the attributions established by CNS Resolution 466/2012 and Operational Norm No. 001/2013 of the CNS, approves the Case Report as proposed.
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INTRODUCTION

Severe Combined Immunodeficiency Syndrome (SICD) is characterized as a disease of severity, due to the drastic decrease in the immune response to infections[1].

Newborns are usually healthy until they are three months old, due to maternally inherited antibodies, transmitted during pregnancy through immunoglobulin G (IgG). After some time, your immune system reduces lymphocyte maturation and does not replace these immune cells[2]. As the child grows, exposure to potential contamination increases, intensifying the incidence of serious infections.

In the national territory, there is already the incorporation of neonatal tests for early diagnosis, significantly impacting the survival of these patients[3]. The tests are carried out through screenings such as "*T-cell receptor excision circles (TRECs)",* markers that verify the development of lymphocyte lineages, as well as whether the cells have deficits and mutations. In addition, complementary tests such as laboratory and genetic tests are also used[4].

After the diagnosis of SCID, the only therapy defined for the management and increase of the child's survival is Hematopoietic Stem Cell Transplantation (HSCT), with the best prognosis in the allogeneic modality[1]. The disease, if left untreated, can progress fatally in all patients in the first two years of life, reinforcing the indication of early HSCT and appropriate care of infections.

HSCT is a treatment for hematological, autoimmune and immunodeficiency diseases, in which there is correction of some defect in the functioning of the bone marrow[5]. Patients with immunodeficiencies underwent transplantation with an allogeneic donor, that is, they receive cells from another person who has compatibility of the human leukocyte antigen (HLA) genes. The compatibility between the haplotypes of the HLA genes favors the success of the treatment and the prevention of the development of Graft-versus-Host Disease (GVHD)[6].

GVHD is characterized as a multisystemic, multiorgan disorder in which transplanted cells begin to attack the patient's graft cells, developing an immune reaction. It is one of the post-transplant complications of constant concern among transplanters[7].

Allogeneic transplants have a higher risk of presenting the symptoms and signs of acute or chronic GVHD. Acute GVHD usually begins before one hundred days, after the graft is taken, and its manifestations can occur in the skin, intestine and/or liver[8]. The diagnosis is made through symptoms, and the main characteristics are: maculopapular erythema, weight loss, nausea, emisis, diarrhea and increased bilirubin. To confirm the disease, biopsy of the organs that manifest these aspects is performed The first-line treatment for GVHD is systemic corticosteroids and adjustment of serum cyclosporine levels and control of signs and symptoms[9].

Chronic GVHD (cGVHD) can develop concomitantly with acute manifestations or after symptom control and progresses with involvement of more organs that can evolve to fibrosis. Despite all treatment efforts, progression to cGVHD is considered one of the main causes of morbidity and mortality[10].

Patients diagnosed with cGVHD have physical, functional, psychological, and social impairments that are unfavorable to their quality of life. With this assumption, multiprofessional interventions become essential to manage the implications and promote their general well-being[11].

This article aims to report the functional rehabilitation process, from the perspective of occupational therapy, of a two-year-old child diagnosed with chronic GVHD in the skin, mouth, lungs, and joints, presenting impaired joint mobility, functional loss, and delayed neuropsychomotor development (NPMD).

CASE REPORT

The child, six months old, was born vaginally without complications. The mother says that when she was one month old, the child had recurrent respiratory infections and a diagnosis of Covid-19, requiring a long period of hospitalization.

After laboratory tests, the diagnosis of SCID classified by CD3 delta T-B+NK+ deficiency was confirmed. He immediately started treatment with the use of immunoglobulin and obtained the transfer of care to a reference university hospital.

At the child's first contact with the specialty, the child was in good general condition (BEG), ruddy, acyanotic, anicteric, hydrated, eupneic, with stable vital signs and no complaints. He was hospitalized for pre-transplant tests and choice of a donor compatible with HLA. Compatibility was attested with the mother, and a haploidentical hematopoietic stem cell transplant was determined.

The programmed conditioning consisted of busulfan (Bu) 10.4 mg/kg + fludarabine (flu) 6.5 mg/kg + Antithymocyte globulin (ATG) 7.3 mg/kg and the immunoprophylaxis contained cyclophosphamide (CY) post 100 mg/kg + cyclosporine A (CSA) + mycophenolate mofetil (MMF).

The child presented some complications in the transplant such as the activation of cytomegalovirus (CMV) right in the pre-transplant and during the conditioning phase, being treated and resolved until D-1 with Immunosuppression of Ciclosporin (CSA) 0.3 + 0.3 ml; and severe Veno-Occlusive Disease (VOD), requiring peritoneal dialysis and medications such as Methylprednisolone 500mg/m^2 6 doses, Ursacol + Prednisolone in reduction 0.4 mg/kg, being solved.

Neutrophilic uptake was on D+13 and platelet onto D+28, and he was discharged from the ward to the day hospital, undergoing follow-up and uneventful medication. He was discharged to his city of origin at nine months, remaining in outpatient follow-up.

From day D+91 onwards, the child began to present some symptoms that proposed the suspicion of GVHD, such as worsening bilirubin tests, liver function and frequent episodes of diarrhea per day. On D+102, the patient presented with grade III cutaneous erythema in 30% of the skin, and the diagnosis of acute GVHD was confirmed on D+119 by biopsy.

Seven months after HSCT, the child has grade 2 acute skin GVHD, grade 3 intestine and liver, with MAGIC 3 classification, and oral corticosteroid (CTC) 2mg/kg/day and oral cyclosporine (CSA) were initiated. Unfortunately, after the conduct, it was found that the recommended serum level of Cyclosporine (CSA) was not reached.

It progresses to chronic grade 3 GVHD of the skin, grade 1 mouth, and grade 2 lung, according to the National Institutes of Health (NIH) consensus for the evaluation of GVHD, of severe level. The established approach was to be admitted to a day hospital for AAC and intravenous methylprednisolone, 1mg/kg, until reaching the recommended level.

The child's first contact after hospitalization with the occupational therapy service was in the playroom of the outpatient clinic of the Bone Marrow Transplant (BMT) service, when the child was two years old. Occupational therapeutic evaluation was carried out with the mother through an informal interview, addressing aspects related to the child and the routine of both. When questioned about functional issues and neuropsychomotor development (NPMD), she reported that the patient was totally dependent on care and daily activities such as self-care, feeding and clothing, and noticed signs of functional physical effort in playing, such as fatigue, reduced mobility and respiratory distress, presenting dyspnea.

The evaluation process with the child was through the observational evaluation of the expected milestones of child development. A protocol was structured that included direct observation of the activities and games performed in the playroom ddressing motor, cognitive and social aspects. In the evaluation, a delay in the NPMD was observed, as shown in Table 1:

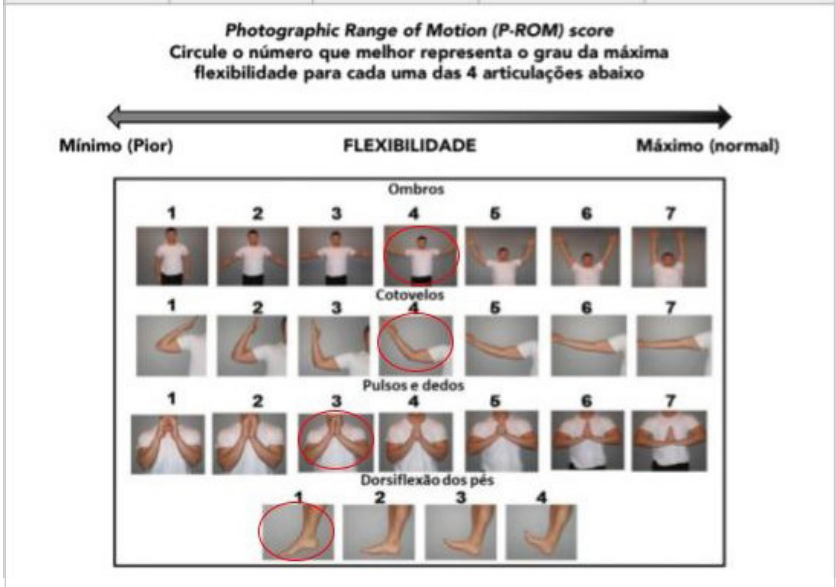
TABLE 1 - Assessment Of Neuropsychomotor Development 2 To 3 Years[12]

COGNITIVE SKILLS	APRIL
Knows the concepts of big, small, up and down	It does not perform
Play make-believe	It does not perform
Groups similar objects	Performs
SOCIAL INTERACTION SKILLS	
Improves your ability to give and share	It does not perform
It corresponds to the demonstration of affection	Performs
Learn to wait your turn	It does not perform
Independence in relation to food and clothing	It does not perform
Interact with others	Performs
MOTOR SKILLS	
Wanders	It does not perform
Desce stairs alternating feet	It does not perform
Runs and adapts your body in terms of speed and positioning	It does not perform
Pedal tricycle	It does not perform
FINE MOTOR SKILLS	
Manipulates everyday objects e.g. spoon	It does not perform
It makes firm horizontal, vertical and oblique strokes.	It does not perform
Models figure with modeling clay	It does not perform

In a discussion of the case with the pediatrics team, it was found through the NIH that cGVHD was affecting body functions and structures, such as respiratory capacity, epidermis and joint motor character, which interfered with its functionality, mobility, NPMD, performance of activities and play. In addition, the deficits of the disease interfered with the achievement of expected milestones and caused the regression of milestones already achieved, in addition to the child's quality of life, as shown in image 1 below:

FIGURE 1: Dechc Nih Assessment[13]

Avaliação	Pontuação 0	Pontuação 1	Pontuação 2	Pontuação 3
Gravidade geral da DECH (parecer do avaliador)	☐ Sem DECH	☐ Leve	☐ Moderado	☐ Grave



The child's functional diagnosis, according to the International Classification of Functioning, Disability and Health for Children and Young People (ICF-CJ), showed that cGVHD affected body functions and systems (respiratory function and joint structure), due to lesions of the epithelial tissue that progressed successively to fibrosis of the skin and lung organs, causing a pattern of immobility in the child, resulting in functional, postural and movement limitations, interfering with the performance and participation of daily activities, requiring rehabilitative approaches.

Based on the results obtained by the evaluations carried out, a rehabilitation plan was developed for the child, with the following objectives: recovery of the functions and structures of the body that were affected by cGVHD, maintenance of functionality, prevention of injuries (e.g., joint contracture), recovery of the child's functional independence and achievement of the milestones expected from the NPMD for performance and participation in activities.

The approach for the implementation of therapeutic interventions for functional rehabilitation was developed through the strategy of the Therapeutic Toy Enabling Physiological Functions (TP) and free and exploratory play for its NPMD, using play as a therapeutic tool mediated by the occupational therapist.

The interventions were carried out in a playful environment, in the hospital playroom and at times in the ward of the bone marrow transplant service, over a period of five months, totaling twenty-seven sessions, lasting one hour and ten-minute breaks and continuous monitoring of the child.

During the interventions, joint release of the upper limbs (UL) and lower limbs (LL) was first performed, through games and dances, to facilitate the movements and functions of the limbs. The application of the therapeutic toy capacitor of physiological function was inserted addressing the active movement of the joints, stimulating through fitting toys, tricycle, modeling clay, among others,

increasing the range of motion of the shoulders, elbows, wrists and ankles joints. The therapist performed the passive movement of the joints and performed the movement and function in which the game stimulated, applying the hand-over-hand technique with the patient and encouraging the child to move actively.

In order to improve occupational performance in play, achievement of the milestones expected for their age and the feasibility of experiencing daily activities considering the child's age group, free activities and games, environmental exploration, learning and stimulation of skills for brain neuromodulation and achievement of NPMD milestones were applied.

In some games, the simulation of daily and instrumental activities, such as supermarket and food, stimulated the patient to develop specific skills and functions, such as manipulation of objects and ambulation. During the plan, the same day-to-day simulation activities were performed. It was observed that the child showed independence in the execution of skills required for occupational performance.

During the interventions, continuous evaluations were carried out by the pediatrics and occupational therapy teams. Favorable gains were observed, such as increased range of motion of the shoulders, elbows, wrist and ankle joints, greater respiratory endurance and the achievement of some of the neuropsychomotor development milestones expected for the child's age group, in particular ambulation and fine motor skills, as demonstrated in the following evaluations (Table 2 and Figure 2):

TABLE 2 - Evaluation of Neuropsychomotor Development 2 to 3 Years During the Sessions[12]:

COGNITIVE SKILLS	MAY	JUNE	JULY	AUGUST
Knows the concepts of big, small, up and down	It does not perform	Performed after intervention	Performed after intervention	Performed after intervention
Play make-believe	Performed before	Performed after intervention	Performed after intervention	Performed after intervention
Groups similar objects	Performed before	Performed after intervention	Performed after intervention	Performs
SOCIAL INTERACTION SKILLS	MAY	JUNE	JULY	AUGUST
Improves your ability to give and share	It does not perform	Performed after intervention	Performed after intervention	Performed after intervention
It corresponds to the demonstration of affection	Performed before intervention	Performed before intervention	Performed before intervention	Performed before intervention
Learn to wait your turn	It does not perform	It does not perform	Performed after intervention	Performed after intervention
Independence in relation to food and clothing	It does not perform	Performed after intervention	Performed after intervention	Performed after intervention
Interact with others	Performed before intervention	Performed before intervention	Performed before intervention	Performed before intervention

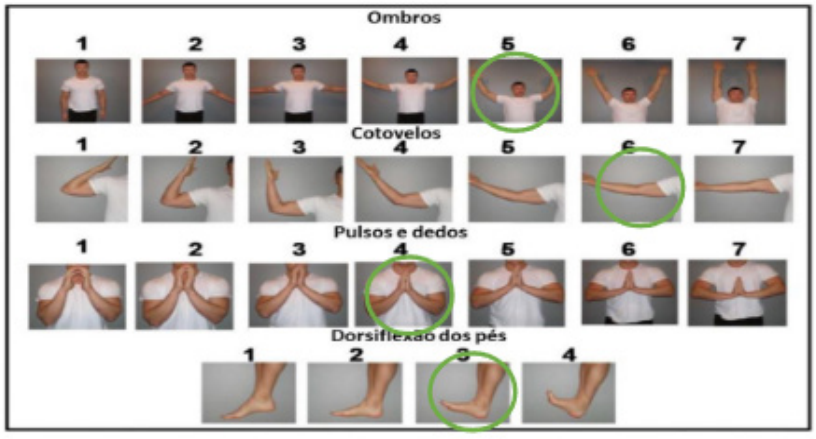
MOTOR SKILLS	MAY	JUNE	JULY	AUGUST
Wanders	It does not perform	It does not perform	Performed after intervention	Performed after intervention
Desce stairs alternating feet	It does not perform	It does not perform	Performed after intervention	Performed after intervention
Runs and adapts your body in terms of speed and positioning	Performed before intervention	Performed before intervention	Performed before intervention	Performed before intervention
Pedal tricycle	Performed before intervention	Performed before intervention	Performed before intervention	Performed before intervention
FINE MOTOR SKILLS	MAY	JUNE	JULY	AUGUST
Manipulates everyday objects e.g. spoon	It does not perform	Performed after intervention	Performed after intervention	Performed after intervention
It makes firm horizontal, vertical and oblique strokes.	It does not perform	It does not perform	Performed after intervention	Performed after intervention
Models figure with modeling clay	It does not perform	Performed after intervention	Performed after intervention	Performed after intervention

FIGURE 2: CSHD NIH ASSESSMENT AFTER SESSIONS[13]

Avaliação	Pontuação 0	Pontuação 1	Pontuação 2	Pontuação 3
Gravidade geral da DECH (parecer do avaliador)	☐ Sem DECH	☐ Leve	☐ Moderado	☐ Grave

Photographic Range of Motion (P-ROM) score
Circule o número que melhor representa o grau da máxima flexibilidade para cada uma das 4 articulações abaixo

Mínimo (Pior) **FLEXIBILIDADE** **Máximo (normal)**



DISCUSSION

In the treatment of immunodeficiency drugs such as SCID and post-HSCT complications such as cGVHD, the child is subjected to long hospitalizations and invasive treatments. And these experiences can impact important aspects of childhood, as well as the functional capacity to perform and participate in daily activities and neuropsychomotor development (NPMD). As a result, the child begins to miss moments of his childhood and experience uncomfortable situations.

Hospitalization generates in the child what we call occupational deprivation in occupational therapy. It is determined when the child does not participate in activities, does not play significant roles or acquires skills that favor their performance, due to an external factor[14]. Being in an unknown and limiting environment causes a deficit in the exploration and acquisition of skills that favor their development and functionality.

When hospitalized, the child starts to play the role of a miniature adult. He experiences significant losses, symbolic and the rupture of his childhood, especially the occupational performance of playing. Their childhood is formulated through experiences that generate physical and mental suffering[15].

In hematopoietic stem cell transplantation, the patient is hospitalized for a long period and tends to require rehospitalizations due to post-HSCT complications, as was the case with the child in this study. They are subjected to invasive procedures, experience distressing situations that generate suffering and are exposed to a limiting environment. It causes the loss of their autonomy and independence from their activities, the deconstruction of occupational roles, living with strangers and a determined routine[16].

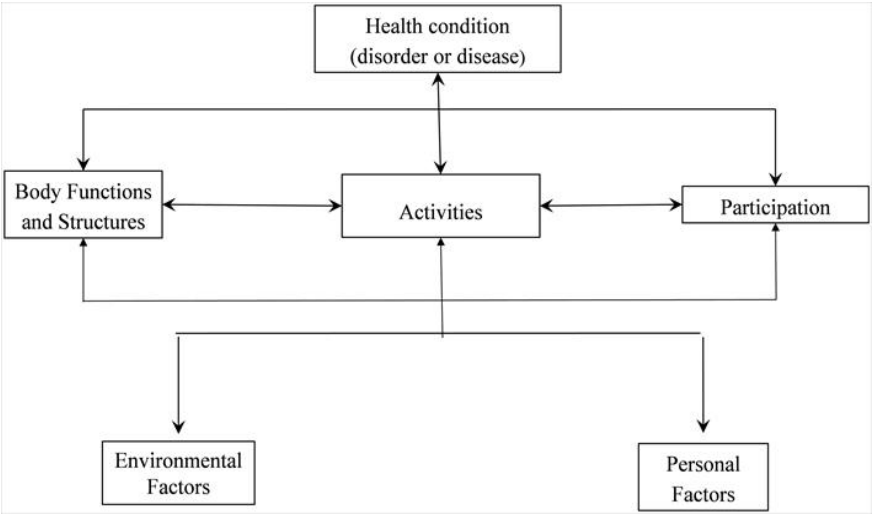
Occupational therapists consider these aspects of hospitalization, treatment, and their disease, addressing NPMD, functionality, occupational play performance, and participation in children's daily activities.

The occupational therapist performs his functional diagnosis in order to develop a treatment plan with the purpose of intervening in the clinical manifestations and external factors that imply in the child's daily life, such as cGVHD. To survey demands, the professional uses classifications to assist in his clinical reasoning.

One of the functional diagnostic classifications used by therapists is the International Classification of Functioning (ICF). Its objective is to classify the patient's level of functionality by addressing physiological, environmental and personal aspects, analyzing their ability to perform and participate in activities, considering their health condition[17].

To define the functional diagnosis, the therapist focuses his interest on functionality in daily activities. It seeks to investigate what are the internal and external factors that imply occupational performance, as shown in the following image:

FIGURE 3: International Classification of Functioning, Disability and Health (ICF)[18]



For children, the International Classification of Functioning, Disability and Health for Children and Young People (ICF-CJ) is aplied. The objective is to outline the child's functionality profile and performance in aspects related to childhood, considering their diagnosis, aiming at a rehabilitation plan[19].

The functional diagnosis of the child in the study presented functional deficits that interfered with daily activities and caused delay in neuropsychomotor development (NPMD), due to the impairment of organic functions, caused by chronic inflammation that resulted in fibrosis[10]. This condition led to the progressive loss of physical capacities and function of the systems affected by the disease, manifesting itself through symptoms such as fatigue, difficulty breathing, muscle stiffness, decreased joint range of motion, significant changes in postural patterns and joint contractures, impacting their quality of life, justifying the choice and implementation of the rehabilitation approach.

In the Brazilian context, rehabilitation is part of a line of care integrated into the national priority health agenda for children. Child rehabilitation has as its main focus the formulation of therapeutic plans that seek to minimize or compensate for the compromised functions, according to the child's needs[20]. Pediatric rehabilitation in the hospital context with children with cGVHD should be early and employed as a continuous line of treatment with a multidisciplinary team in the Hematopoietic Stem Cell Transplantation service.

From the perspective of occupational therapy with this public, it seeks in the approach of pediatric rehabilitation, the promotion of the maintenance of functionality, functional rehabilitation and the prevention of injuries, caused both by the disease and by the period of hospitalization, favoring the quality of life, contributing to their child development and participation and performance in daily activities[21].

The rehabilitation process for cGVHD in pediatrics involves a series of steps, as already addressed the functional diagnosis, the treatment plan and the interventions. Therapists can select strategies for the application of their rehabilitative therapeutic interventions with children[22]. One to be used is the Therapeutic Toy (TP).

With three modalities, the main objective of TP is to promote the physical and emotional well-being of the child during the hospitalization process. Each modality has specific purposes for its application and are classified as: dramatic, instructional and the enabler of physiological functions[22]. The TP that enables physiological functions, used in this case, was intended to rehabilitate and recover the functions and systems of the body aggravated by cGVHD, through the occupational performance of playing, offered by the occupational therapist[23].

The implementation of the rehabilitation approach, in addition to having as its objective the recovery of functions, favors the achievement of aspects related to childhood, such as child development. According to the evaluations applied, the child in the study presented delay and regression of milestones in his NPMD.

Neuropsychomotor development is defined as a progressive follow-up in which the child masters and exercises motor, cognitive and social skills, from the most basic to the most complex, according to their age, allowing their brain neuroplasticity[24].

For brain neuroplasticity, the child needs to discover and experience external stimuli, corroborating the regeneration of neurons and the creation of synaptic connections, promoting the learning of new skills and reaching milestones in their development[25]. The child obtains this exploration through a favorable environment, with stimuli and during the performance of an occupation an occupational activity: playing.

In addition to being an occupation, it is shrewd in promoting stimuli and experiences. Playing is a necessary activity for the child. It corroborates brain neuroplasticity, sending stimuli to the brain, forming the learning of skills for the performance of daily activities and consequently contributing to its development.

Playing can be used in occupational therapy as a professional resource for the delimitation of playfull activities pertinent to the child's age group, when the objective is a therapeutic intervention[27], as was used in the present case from the perspective of the TP that enables physiological functions, being a training resource for the child, seeking its functionality in daily activities.

In addition, occupational therapy studies and employs free and exploratory play in a favorable environment, such as hospital toy libraries, or the offer inside the wards, favoring brain neuroplasticity, promoting the learning of skills for NPMD.

Taking into account the aspects presented, child rehabilitation from the perspective of occupational therapy with pediatric patients with cGVHD aims to prevent sequelae, treating functional and postural deficits, recovering functional capacity to perform daily activities, and non-pharmacological treatment of symptoms caused by the disease. In addition, we seek to minimize the emotional and functional impacts generated by hospitalization, in addition to the surveillance and stimulation of NPMD, favoring the child's quality of life.

CONCLUSION

cGVHD is one of the post-transplant complications that requires follow-up by a multidisciplinary team. When advanced, it interferes with aspects related to the patient's daily life, placing him in a position of incapacity and dependence.

Patients with cGVHD can have debilitating effects that directly impact their functionality. The results of occupational therapy interventions are favorable for the public, minimizing functional deficits, through the use of activities, aiming at the rehabilitation of body functions and systems, achieving the main objective of the profession: occupational performance in daily activities.

We reaffirm the relevance of monitoring by health professionals for patients who undergo HSCT, aiming at the strategy of preventive and rehabilitative interventions, contemplating the patient in all its spheres, favoring recovery, promoting the maintenance of functionality, aiming at preventing the evolution of diseases, favoring quality of life, health and physical well-being, and their social insertion.

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