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Outcomes and impact of multidisciplinary team care on immunologic and hemato-oncologic pediatric patients

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Abstract
Introduction: Immunologic and hemato-oncologic disorders in the pediatric population represent an interrelated and complex group of conditions whose approach, diagnosis, and management could be difficult. Multidisciplinary teams have been proved beneficial in treating such complexities.
Methods: We conducted a retrospective observational study at a tertiary hospital in Madrid, Spain, which is a pediatric immunology and onco-hematology referral center. We included all patients of multidisciplinary outpatient consultation, comprising a working group of pediatric oncohematologists and immunologists, between April 2016 and December 2019. Epidemiologic, clinical, and laboratory data were collected. We analyzed these data and established a relationship between age and findings of final diagnosis as well as variance on diagnoses prior to their multidisciplinary assessment and number of visits to the consultation.
Results: In all, 93 children and adolescents were included in this study. Laboratory abnormalities were the most frequent reason for being referred to our unit (87.2%); 78% of children had a previously diagnosed comorbidity. Before starting follow-up in the multidisciplinary consultation, 14% of patients were diagnosed, and after the study by the multidisciplinary team, the final diagnosis was reached in 58.1% of patients. No correlation was discovered between final diagnosis and gender (P = 0.29), age (biserial correlation coefficient, r = 0.036, P = 0.70), and number of visits (P = 0.07).
Conclusion: A multidisciplinary approach to immunologic, hematologic, and oncologic pediatric diseases is feasible. It can be a powerful and useful tool for diagnosis and treatment, especially in complex pediatric patients.

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Introduction

Immunologic disorders in the pediatric population represent a complex and heterogeneous group of conditions that cause disturbances in different organ systems and whose approach, diagnosis and management could be difficult. Bone marrow is usually affected by immunologic diseases, and a lot of these disturbances can have hematologic impact. On the other hand, onco-hematologic disorders and their treatments frequently impact the immune system.[1]

Owing to the complexity of these diseases, collaboration between different specialists and medical teams is necessary in order to make correct diagnosis, take adequate clinical decisions, and for successful management and treatment of these patients.[2] Multidisciplinary teams are formed from collaboration between these specialists, with the aim of coordinating health services and removing barriers to meet the needs of patients with complexities. Multidisciplinary teams are composed of different specialists, bringing together their expertise and skills to assess, plan, and manage patient treatment and care collectively. These teams facilitate communication between different levels of care and specialties, ensure continuity of care, promote effective use of resources, and provide opportunities for learning and development.[3]

The benefits of this kind of holistic approach have been proved in different fields, largely in adult oncologic settings.[3,4] The benefits include better treatment compliances, reduced hospital admissions and emergency visits, improved continuity of care, and achieving better patient satisfaction.[2] However, despite these benefits, to date no study has described the use of holistic approach in pediatric patients presenting with immunologic and onco-hematologic diseases, whose complexity makes them suitable candidates for this clinical approach.

The aim of this study was to present the implementation of a multidisciplinary team for treatment of immunologic, hematologic, and oncologic diseases in a pediatric setting. The study evaluated a sample of patients and demonstrated the impact of holistic approach in their diagnosis and management.

Methods

Study design

We conducted a retrospective observational study at a tertiary hospital in Madrid, Spain, which is a pediatric immunology and onco-hematology referral center. The study included all patients from birth to 18 years of age and discussed in the multidisciplinary immuno-onco-hematology outpatient consultation between April 2016 and December 2019. We excluded the patients who were appointed for the clinic but failed to attend joint consultation as well as the patients whose electronic records were not accessible.

Epidemiologic, clinical, and laboratory data were collected. We screened records for previous illnesses, reasons for consultation, and requirement for hospitalization as well as diagnosis resulting from multidisciplinary approach, number of visits, different treatments, and time of discharge. We recorded results of performed immunologic and hematologic laboratory tests as well as requirement for other complementary studies.

For analysis of the results, we first described our data using frequencies and proportions for categorical variables, and median and interquartile range (IQR) for continuous variables. A biserial correlation was calculated to establish a relationship between age and the final diagnosis. Two-sided tests were performed, and $P < 0.05$ was considered statistically significant.

Analysis of variance (ANOVA) was performed for the categories of diagnoses prior to their multidisciplinary assessment and the number of visits to the consultation. Statistical analysis was performed using XLSTAT, version 2021.

The research project was approved by the Hospital's Institutional Review Board, with waived informed consent. The study did not imply any intervention on the included subjects, and it was conducted according to the ethical principles of the Declaration of Helsinki (DoH).

Multidisciplinary consultation

A multidisciplinary team was created in 2016 comprising pediatric oncohematologists and immunologists, with the aim to evaluate collectively patients with acute or chronic diseases, which may involve both immune and hematologic systems, or may be related to an onco-hematologic disease that impairs the immune response. The consultation was designed as a weekly audience with at least one consultant from each field. Patients were referred by any pediatric immunologist, oncologist, or hematologist when they think this joint approach would benefit the patient. Consultations with three different oncohematologists and an immunologist were also scheduled every 3 months for complex cases. Treatment and diagnostic decisions were agreed upon after patient visits, and in case of admission, immunologists and oncohematologists would jointly check the patient during clinical rounds.

Results

In all, 93 children and adolescents were included in the multidisciplinary immune-onco-hematology consultation, 50 of them (53.7%) were females. Mean age at start of follow-up was 10.25 years; SD: 5.42). Mean follow-up time in the consultation was 2.13 years (SD: 1.16), and each patient attended a median number of eight medical appointments (IQR: 4–20).

Abnormal laboratory findings were the most frequent reason why the patients were referred to our unit (87.2%), with leukopenia/neutropenia diagnosis in most of the cases (54.8%). Other reasons for consultation were recurrent infections (11.8%) and suspicion/diagnosis of a complex pathology (10.75%).

Around 78% of the patients had a previously diagnosed comorbidity before beginning follow-up in the consultation. The most frequent previously diagnosed diseases were congenital diseases or syndromes (26%), congenital

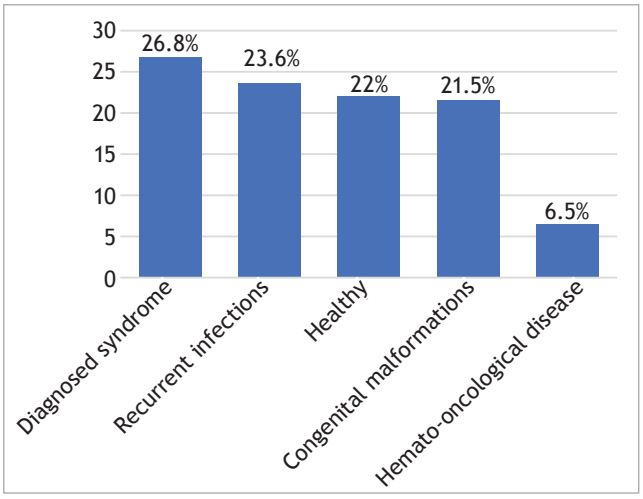

Figure 1 Comorbidities diagnosed before start of joint consultation. Results are given as percentage of total patients.

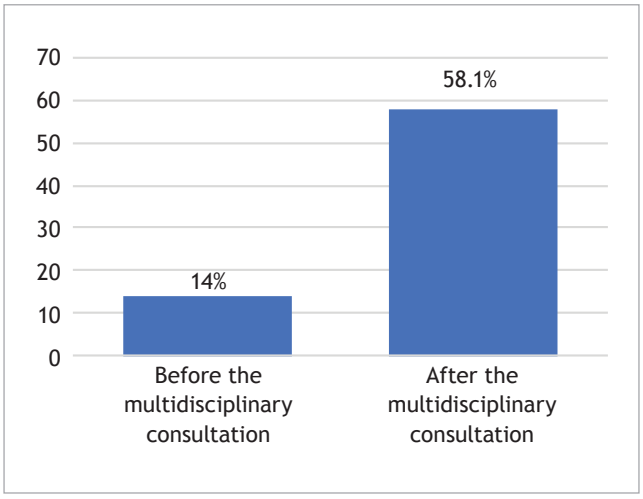

Figure 2 Percentage of patients with diagnosed disease before and after multi-disciplinary consultation.

malformations (23.6%), and recurrent or serious infections (23.6%). Diagnosed comorbidities are summarized in Figure 1.

As a part of the study, blood tests were performed on all patients, including complete blood count, biochemistry, and immunoglobulin A (IgA), M (IgM), and G (IgG). Complement studies (88%), lymphocyte populations (54.8%), double negative lymphocytes (37.6%), and anti-neutrophil antibodies (23.6%) were also carried out. In 32 patients (30.8%), a bone marrow biopsy was performed. In 54 patients (51.9%), a genetic study was carried out, either a genetic panel sequence test for immunodeficiencies or autoinflammatory diseases (48.3%) or a specific gene mutations study in 51.7% cases.

No differences in total number of visits were found between genders (P = 0.45 for Student's *t*-test) and age groups (P = 0.20 for Pearson's correlation). Patients with a previous hemato-oncologic disorder had a mean higher number of visits than rest of the patients (13.1 vs. 10.2 visits), but the difference was not statistically significant (P = 0.14 for Student's *t*-test). In 24 cases (25.8%), consultation with another pediatric specialist was required; most frequent consulted specialists were dermatologists (14 patients, 15.0%) and endocrinologists (6 patients, 6.4%). In all, 26 patients required hospital admission during their follow-up in the joint consultation.

Altogether, 13 patients (14.0%) were diagnosed prior to starting follow-up in our consultation. After being assessed jointly, the final diagnosis was reached in 54 patients (58.1%; Figure 2); 39 patients (37.5%) received specific treatment for their diagnosis. No correlation was found between final diagnosis and gender (P = 0.29 for Chi-square test), age (biserial correlation coefficient, r = 0.036, and P = 0.70), or number of visits (P = 0.07 for Student's *t*-test).

By the end of the study, 25.8% of the patients were discharged; 56.0% were still monitored in our consultation; 5.8% were transferred to an adult consultation; and 3.2% were followed in another center. In 14.4% of the cases, follow-up of the patient was lost. One patient died during the study.

Discussion

In this study, we illustrated the feasibility and advantages of a joint approach toward the treatment of immunologic, hematologic, and oncologic pediatric disorders, describing a sample of patients evaluated during the first 4 years of a new multidisciplinary clinic at a tertiary hospital in Madrid.

Multidisciplinary teams have entered the scene during last few decades as a powerful tool to handle complex patients consulting different specialists. These joint approaches do not only facilitate reaching difficult diagnosis or finding treatments for difficult conditions but also have eased communication among different hospital teams and levels of care, led to use resources more efficiently, and to provide higher rates of evidence-based recommendations.[3] Multidisciplinary approach has been successfully implemented in the fields of gynecology, cardiology, neurology, endocrinology, and, most frequently, adult oncology.[3-7]

Pediatric care has evolved over last few decades with increasing prevalence of chronic diseases[8] and a substantial proportion of healthcare expenditure going to the management of chronic and complex children disorders.[9] Pediatric patients frequently need multiple consultations from pediatric specialists, and have an increased absence from schools and a psychologic impact on their quality of life and well-being. It is clear pediatric patients with complex disorders are greatly benefitted from holistic approaches because of fewer and shorter consultations, probably resulting in a better quality of life.[10]

Some authors have described the use multidisciplinary clinics in complex pediatric settings with great success. Ajarmeh et al. described their experience with children having chronic kidney disease; they established that nutritional, hematologic, and even disease progression outcomes improved with multidisciplinary approach.[11] Wren et al. described that a joint treatment approach to treat pediatric pain controlled both acute and chronic pain conditions.[12] Rove et al. reviewed evidences of pediatric surgical

recovery and found that multidisciplinary approaches could lessen postoperative recovery period.[13] Multidisciplinary teams described in this study have been utilized successfully in many pediatric settings as diverse and complex as neurocritical care,[14] difficult airway,[15] and hepatology.[16] However, this is the first study to describe a multidisciplinary team comprising immunologists, oncologists, and hematologists.

In pediatrics, immunologic, oncologic, and hematologic disorders constitute a complex environment of interrelated diseases,[17] with difficult differential diagnosis and requiring intervention of two or more pediatric specialists for management. It is often observed, as in our case, that these patients have pre-existing disorders or syndromes. We found that most of the patients in our clinic had congenital diseases or syndromes, some of them without a definitive diagnosis.

In almost half of the cases, diagnosis was reached with multidisciplinary approach and study (Figure 2). Previous studies have shown, as also pointed out by the results of the present study, that multidisciplinary teams lead to a higher rate of appropriate diagnosis and cancer stages,[18,19] showing how diagnostic challenges can benefit from communication and collaboration between different specialists.

Our study had some important limitations. As a single-center study, it described our experience in starting a multidisciplinary approach to immunologic, hematologic, and oncologic pediatric diseases; however, it might not be directly applicable to other settings with different resources and patient populations. We retrospectively reviewed patients' documents, and even though data were recorded thoroughly, retrospective studies are always subject of important bias. Some patients were simultaneously followed in the multidisciplinary consultation as well as individual immunologic/oncologic/hematologic consultations. Since this study describes an ongoing multidisciplinary consultation, some of the patients had not completed the study and these data could not be reflected in our study.

Conclusion

We have proved that a multidisciplinary approach to immunologic, hematologic and oncologic pediatric diseases is feasible and can be a powerful and useful tool to find diagnosis and treatment, especially in complex populations in which most of the patients have preexisting conditions.

Conflict of interests

The authors declared no potential conflict of interest with respect to research, authorship, and/or publication of this article.

Authors' contributions

Gonzalo Solís García and Alicia Domínguez Estirado contributed equally to this work. Both contributed to compile and analyze patient data and interpret results, and participated in the writing of final manuscript.

Jorge Huerta Aragonés and Carmen Garrido Colino contributed to compile and analyze patient data.

Elena Seoane-Reula and Cristina Mata Fernández contributed equally to this work. Both contributed to compile and analyze patient data and interpret results. They have also supervised and corrected the final manuscript.

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