Alopecia areata in childhood, clinical manifestations and therapeutic approaches

Alopecia areata na infância, manifestações clínicas e abordagens terapêuticas

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ABSTRACT
Introduction: Childhood alopecia areata is an autoimmune condition that causes hair loss in specific areas. Although it is not physically harmful, it can affect children's self-esteem. Treatment involves topical approaches, such as corticosteroids, with variable prognosis. Objective: The objective of this study is to expose the clinical manifestations and therapeutic approach briefly and clearly to alopecia areata in childhood. Materials and Methods: A synthesis of scientific articles and medical literature related to pediatric alopecia was carried out, and the PubMed and SciELO databases were searched using the keywords: Pediatric Alopecia; Clinical

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Manifestations; Diagnosis and Management and 1390 articles were located. After adding the filter: "since 2019", 641 articles were found. After selecting based on relevant titles, methodology, objectives and results, a compilation of 4 articles was obtained to be analyzed. Information was collected on the clinical manifestations of this condition, diagnosis and treatment options, as well as approaches to the management of alopecia in children. Results: Infantile alopecia can present in several forms, with alopecia areata being the most common, characterized by hair loss in specific areas of the scalp. Symptomatic manifestation is more common in the first decade of life. Diagnosis is clinical, with medical history and tests if necessary. The regulation of immune cells plays an important role in alopecia areata, its dysfunction can lead to the interruption of the hair growth cycle, in addition, alopecia areata can be associated with other autoimmune diseases, and its management may require multidisciplinary approaches. Treatment depends on the cause and extent of hair loss and may include laser therapies, corticosteroids, immunotherapy, hair transplantation, among others. Emotional support for the child and family is also important to cope with the emotional and social impact of alopecia. Conclusion: Proper diagnosis and management are essential to ensure appropriate treatment and minimize the emotional and social impact on affected children. Treatment should be individualized, taking into account the underlying cause, the child's age, and other clinical factors. Psychosocial approaches are key to ensuring the emotional well-being of affected children. It is essential that healthcare professionals who specialize in dermatology or pediatrics are involved in the diagnosis and management of pediatric alopecia, with long-term follow-up to monitor response to treatment and ensure the best possible care for affected children.

Keywords: Alopecia, Pediatric, Clinical manifestations, Diagnosis, Management.

INTRODUCTION

Childhood alopecia areata is a dermatological condition characterized by hair loss in localized areas, resulting from an autoimmune response that affects the hair follicles.

This phenomenon, although rare, can have significant implications on the emotional and social health of affected children. This article will address the clinical manifestations of this condition, as well as various therapeutic approaches.

Alopecia in children is a topic of considerable clinical importance. They highlight the need to understand the underlying causes and specific manifestations of childhood alopecia. Alopecia areata, in particular, has been associated with dysfunctional immune responses, as has been observed when exploring cases that analyze the regulation of immune cells in the hair cycle.

Alopecia can also, according to Anda, De Bedout and Miteva (2019), be seen as a systemic disease, highlighting the importance of the individual approach in its management, after all, although the clinical manifestation is the same, often the etiological agent may not be. Thus,

a broader perspective highlights the need to consider not only the physical manifestations, but also the possible psychosocial impacts associated with the condition.[3]

The severity of hair loss can have significant implications on mental health, especially in childhood, and the importance of a clinical approach that takes into account not only the physical aspect, but also the psychological consequences of childhood alopecia should be highlighted.[4]

The common forms of pediatric alopecia are extremely comprehensive, and may be triggered due to genetic factors, being manifested after episodes of stress and/or anxiety, endocrine changes, and even infections of a different nature, such as chickenpox, pneumonia. Alopecia can also be associated with traction, telogen effluvium, among other agents. Understanding these factors is essential for an accurate diagnosis and an effective treatment plan.[Question 5.15.]

It is also important to consider related conditions, such as trichotillomania, this condition can present distinct hair loss patterns, requiring specific therapeutic approaches.[6,7.]

In short, alopecia areata in childhood is a dermatological condition that requires treatment aimed not only at the apparent manifestation, but also at the psychological manifestation of the child. Understanding the clinical manifestations, underlying causes, and consideration of emotional aspects are crucial for effective management. Through this, it aims to present a detailed exposition of the physical and psychological aspects of children who present the diagnosis of Alopecia Areata, being based on the evidence provided by the studies selected for analysis.

MATERIALS AND METHODS

A literature review was carried out with the objective of investigating the clinical manifestations and therapeutic approaches of alopecia areata in childhood. Articles published in scientific journals were reviewed to provide a comprehensive view of the topic.

Data were searched in the MEDLINE database, using the PubMed search platform. Search terms included keyword combinations related to alopecia areata, children/pediatrics, and clinical manifestations/treatment. The search was restricted to studies published in the last 10 years to ensure the relevance and timeliness of the data and conducted with the following inclusion and exclusion criteria:

INCLUSION CRITERIA

- Studies addressing alopecia areata in paediatric patients (up to 18 years of age).

- Articles describing the specific clinical manifestations of alopecia areata in childhood.

- Studies looking at the treatment options available for paediatric alopecia areata.

- Research published in peer-reviewed scientific journals.

- Studies available in English, Spanish, Portuguese or French.

EXCLUSION CRITERIA

- Studies that do not focus on alopecia areata or that do not specifically address childhood alopecia.

- Isolated case reports that do not provide relevant information on the clinical manifestations or treatment of pediatric alopecia areata.

- Duplicate or repeated studies.

- Articles not available in full or without free access.

The search strategy was developed using a combination of search terms related to alopecia areata in childhood, clinical manifestations, and therapeutic approaches. Boolean operators were used to optimize search accuracy and ensure that all relevant articles are identified. The descriptors used were: "Pediatric Alopecia"; "Clinical Manifestations"; "Diagnosis" and "Management" and 703 articles were found. After adding the filter: "since 2014", 406 articles were found. After selecting based on relevant titles, methodology, objectives and results, a compilation of 18 articles was obtained to be analyzed. The identified studies were initially reviewed based on their titles and abstracts to determine their relevance to the topic in question. The selected articles were then analyzed in full to confirm their inclusion in the literature review. Relevant data were extracted from the selected articles, including information on the clinical manifestations of alopecia areata in childhood and the different therapeutic approaches studied. The extracted data were analyzed qualitatively and synthesized in a narrative way. Patterns and trends in clinical manifestations and treatment options were identified, and the results were presented in an organized and understandable manner. The methodological quality of the included studies was assessed using specific criteria for each type of study. Aspects such as the study design, the representativeness of the sample, and the analysis methodology were considered. This literature review is based on the analysis of previously published data and does not involve the collection of information directly from human participants. Therefore, no

additional ethical considerations are required. The results of this literature review will be presented in a scientific manuscript for publication in a peer-reviewed journal. The findings may also be shared at relevant scientific conferences and disseminated to health professionals interested in the topic.

RESULTS AND DISCUSSION

Infantile alopecia is a complex dermatological condition that can be triggered by a variety of factors, including genetic predisposition, autoimmune conditions, and environmental factors. Silverberg (2022) discusses the genetic basis of cutaneous autoimmune diseases in children, including alopecia areata. One of the key findings of the study is the identification of common genetic patterns between alopecia areata and other cutaneous autoimmune diseases, such as vitiligo. This finding suggests a shared genetic predisposition to these conditions, which may help explain the concomitant occurrence in some patients and provide clues about the mechanisms underlying cutaneous autoimmunity. The study also highlights the importance of understanding the genetic mechanisms involved in the development and progression of alopecia areata, with the identification of specific genes and signaling pathways associated with the disease. Among the genes identified are those related to the immune system, such as the major histocompatibility complex (MHC) genes, especially the MHC class II genes. It is also important to highlight the importance of genes involved in the regulation of the immune response, such as genes that encode pro-inflammatory cytokines, such as interferons and interleukins. These cytokines play a central role in activating and recruiting immune cells into the hair follicle, triggering the inflammation and subsequently hair loss characteristic of alopecia areata. Other genes identified in the study are involved in the regulation of the hair cycle and the differentiation of hair follicle cells. Changes in these genes can directly affect the function and viability of hair-producing cells, leading to disruption of the hair cycle and hair loss. In addition to the specific genes, the study also identifies several signaling pathways associated with alopecia areata. Among these pathways, the JAK-STAT (Janus kinase - Signal transducers and transcription activators) pathway stands out, which plays a crucial role in the transduction of pro-inflammatory cytokine signals and the activation of genes involved in the immune response. Another relevant signaling pathway is the NF-κB (nuclear factor kappa B) pathway, which regulates the expression of pro-inflammatory genes and is involved in the activation of immune cells and inflammation of the hair follicle in alopecia areata.

The role of the immune system in regulating the hair cycle has been widely investigated, as discussed by Wang and Higgins (2020), who address how a dysfunctional immune response can trigger alopecia areata in children. Researchers investigated the complex interaction between the immune system and hair follicles, exploring how a dysfunctional immune response can trigger alopecia areata in children. They examined the cellular and molecular mechanisms involved in the pathogenesis of the disease, highlighting the interaction between immune cells, such as T lymphocytes, and follicular cells in the scalp. The study addressed the factors that can trigger an abnormal immune response, including genetic predisposition, exposure to environmental agents, and psychosocial stress. The researchers also investigated the specific signaling pathways involved in the regulation of the hair cycle and how these pathways can be disrupted in patients with alopecia areata. Understanding how the immune system contributes to the disease could lead to the development of targeted therapies that aim to restore normal immune function and prevent hair loss in affected children.

Cranwell and Sinclair (2018) and Cortés et al. (2015) highlight a variety of underlying conditions that can contribute to hair loss in children, including genetic disorders, hair traction, and scalp infections. The study by Zímová and Zímová, 2016 focused specifically on trichotillomania, a behavioral disorder that can result in peculiar patterns of hair loss in children. Trichotillomania is characterized by the repetitive and compulsive habit of pulling one's own hair, leading to areas of localized alopecia. This condition can be challenging to diagnose, as it is often associated with feelings of shame and embarrassment, leading patients to hide or deny the behavior. The researchers explored the clinical presentation patterns of trichotillomania in children, highlighting the signs and symptoms that healthcare providers should look for during diagnostic evaluation. They noted that trichotillomania can manifest in a variety of ways, from localized areas of hair loss to more diffuse patterns, and that early recognition of these signs is critical for accurate diagnosis and timely intervention. The study further addressed the risk factors and underlying causes of trichotillomania in children, including genetic, environmental and psychosocial influences.

Research has further explored the causes and potential treatments for childhood alopecia. The study by Zuo et al. (2015) explored environmental and behavioral factors that may play a role in the development of alopecia in children. For example, exposure to certain environmental agents, such as toxins or chemicals, has been investigated as a possible trigger for alopecia in pediatric patients. Similarly, as discussed by Zímová and Zímová, specific behaviors, such as the habit of pulling out hair (trichotillomania), have been examined as potential contributors to hair

loss in children. They investigated the possible association between immune system disorders and the occurrence of alopecia in children, taking into account immunological aspects related to the disease.

On the other hand, accurate diagnosis of childhood alopecia is essential to guide appropriate and effective treatment. Castelo-Soccio (2014) highlights the need for a comprehensive approach to the diagnosis and management of childhood alopecia, emphasizing the relevance of considering a variety of possible causes and contributing factors. The author also reviewed the therapeutic options available for the treatment of childhood alopecia, discussing the use of different therapeutic modalities, such as topical and systemic corticosteroids, immunosuppressive agents, light therapies, and specific topical treatments. She examined the efficacy and safety of each therapeutic option, as well as important considerations such as the patient's age, severity of alopecia, and the presence of underlying medical conditions. Another relevant aspect addressed in the study was the importance of psychosocial support for children with alopecia and their families. Castelo-Soccio acknowledged the significant emotional and psychological impacts associated with hair loss in children and highlighted the importance of a sensitive and compassionate approach to the care of these patients. This included providing resources and emotional support to help children cope with the emotional challenges associated with alopecia.

Case studies, such as those presented by Fialho and Medeiros Quirino (2023), highlight the therapeutic challenges and the importance of an individualized approach in the management of childhood alopecia. One of the aspects highlighted in the study is the importance of differentiating between alopecia areata and other forms of hair loss in children, such as traumatic alopecia or traction alopecia. Such a distinction is crucial to ensure an accurate diagnosis and, consequently, an effective and targeted treatment. The study also emphasizes the different challenges faced in the management of alopecia areata in children under 2 years of age, including the selection of appropriate therapeutic options and the need for careful monitoring due to immature immune systems and other physiological considerations.

Specific approaches to alopecia variants, such as childhood alopecia areata ophiasica, are discussed by Gozzano et al. (2016), providing valuable insights into the diagnosis and treatment of these conditions. This condition has distinct characteristics, with hair loss patterns that resemble the tracks of a snake (hence the term "ofiasica"). Typical clinical manifestations of ophiasic alopecia areata usually involve localized areas of hair loss in linear or curvilinear bands, often accompanied by inflammation and flaking of the scalp. Specific therapeutic approaches for

childhood alopecia areata ophiasis include options such as topical or injectable corticosteroids, topical immunotherapies, and even systemic therapies in more severe or recalcitrant cases. The discussion of treatment highlights the importance of an individualized approach, considering the severity of the condition, the patient's age, and other relevant factors.

However, infantile alopecia is not just limited to the physical manifestation of hair loss. Anda, De Bedout and Miteva (2019) point to a more comprehensive understanding of this condition as a systemic disease, with ramifications that go beyond the dermatological aspect. The authors explore the possible associations between childhood alopecia and other health conditions, such as autoimmune disorders and endocrine diseases, as well as highlight the psychosocial impacts of childhood alopecia, highlighting how the severity of hair loss can affect the self-esteem, quality of life, and emotional well-being of affected children. In the same vein, Segal-Engelchin and Shvarts (2020) explore the psychosocial impacts of alopecia in children, emphasizing how the severity of hair loss can be associated with negative mental health outcomes. They note that in some cases, hair loss can lead to psychological problems such as anxiety, depression, and eating behavior disorders. The study also highlights the need for psychosocial and emotional support interventions for children with childhood alopecia, through psychological counseling, peer support and education programs about the condition, aimed at strengthening children's resilience and adaptation to the challenges associated with hair loss. The importance of public awareness and education about childhood alopecia, in order to reduce stigma and promote greater understanding and acceptance of the condition, is another relevant point pointed out in the study.

Expert consensus statements were also reviewed and offer practical guidance for healthcare professionals in the management of childhood alopecia. The study conducted by Fatani et al. (2023) represents a significant contribution to the understanding and management of childhood alopecia, especially in the context of the Saudi context. This research stands out for being a consensus statement drafted by dermatology experts in Saudi Arabia, offering clear guidelines and recommendations for the diagnosis and treatment of alopecia in children in this specific context. The statement considers not only the available scientific evidence, but also clinical practices and the specific needs of pediatric patients in Saudi Arabia. The researchers brought together a panel of experienced experts in paediatric dermatology, who reviewed and synthesised international best practices and guidelines to adapt them to the local context. The consensus statement addresses a wide variety of topics related to childhood alopecia, including guidelines for the differential diagnosis, recommended therapeutic approaches, and special

considerations for the management of specific cases, including clear guidance on the use of topical, oral, and injectable therapies, as well as the management of complications and adverse effects associated with these interventions. The study also highlights the importance of education and psychosocial support for pediatric patients with alopecia and their families. Acknowledging the significant impact that hair loss can have on children's quality of life and emotional well-being, the researchers emphasize the importance of a holistic approach that takes into account not only the medical aspects but also the emotional and psychosocial aspects of the condition.

The systematic reviews reviewed provide a comprehensive overview of the therapeutic options available and their effectiveness in the treatment of childhood alopecia. In the study by Barton et al. (2022), analysis of treatment duration and dosage offers in-depth insight into the efficacy and safety of therapeutic interventions for alopecia areata in children. The duration of treatment is a crucial aspect, as it can vary considerably based on the extent and severity of the condition, as well as the individual patient's response to treatment. For mild to moderate cases, treatment protocols may involve topical medications, such as moderate-to-high-potency corticosteroids, regularly applied to the affected scalp. In general, these topical treatments are given once or twice daily and may be continued for several weeks to months, depending on the improvement seen in the patient's condition. For more severe or refractory cases, systemic therapies such as oral corticosteroids, immunosuppressants, or Janus kinase (JAK) inhibitors may be considered, depending on the patient's age, the extent of hair loss, and other clinical factors. The duration of these systemic treatments can vary considerably and is usually determined based on the patient's response to the drug and the need for maintenance of remission. As for the dosage, it is carefully adjusted to ensure maximum effectiveness with minimal side effects. In children, the dosage of drugs is often calculated based on the patient's body weight and age, with lower doses being preferred to avoid the risk of toxicity. Dosage may be gradually adjusted over time as needed based on patient response and clinical parameters monitored during treatment.

In reviewing the existing literature, Waśkiel-Burnat et al. (2021) highlight the variety of therapeutic options available, including topical corticosteroids, immunotherapy, low-level light/laser therapy, Janus kinase (JAK) inhibitors, among others. Each therapeutic modality is carefully analyzed in terms of its clinical efficacy, safety, and side effect profile in children. The author also addresses issues related to the duration of treatment, dosage, and frequency of administration of different therapies. In the case of topical therapies such as corticosteroids, the duration of treatment can range from a few weeks to months, depending on the extent of hair loss

and the improvement observed. The dosage and frequency of administration of these drugs take into account the age and tolerance of the patient. For systemic therapies such as oral immunosuppressants (e.g., cyclosporine) or Janus kinase (JAK) inhibitors, the duration of treatment may be longer and may range from months to years, especially in cases of severe or recurrent alopecia areata. The dosage and frequency of administration of these drugs are determined based on the patient's clinical response, as well as monitoring for potential side effects such as immune suppression and liver toxicity. In the case of physical therapies, such as low-level light/laser therapy, the duration and frequency of treatment may vary depending on the specific protocol used, which may involve weekly or bi-weekly sessions over several weeks or months. The exact dosage and frequency of administration are adjusted to optimize the therapeutic response and minimize the risk of adverse reactions such as skin irritation.

Additional studies have focused on therapeutic approaches to childhood alopecia, aiming not only to treat hair loss but also to address the underlying causes and improve the quality of life of affected children. Lima et al. (2023) explore the use of corticosteroids in the treatment of alopecia areata, highlighting their effectiveness in controlling the associated inflammatory response, which can help reduce the progression of hair loss and promote hair growth. They discuss different forms of corticosteroid administration, including topical and intralesional applications, underscoring the specific benefits and considerations of each approach, as well as addressing issues related to the safety and tolerability of corticosteroid use in children. By considering the potential side effects and risks associated with corticosteroid use, clinicians can perform an individualized risk-benefit assessment for each patient, ensuring a safe and effective approach to the management of childhood alopecia.

Innovative treatment strategies, such as Janus kinase inhibitor therapy, are being explored as a promising approach, as discussed by Stefanis (2023), highlighting the continued potential for advances in the treatment of childhood alopecia. The author examines how JAK inhibitors interfere with the signaling pathways responsible for the inflammation and immune response associated with alopecia areata. These drugs specifically target Janus kinases, which play a crucial role in transmitting signals from pro-inflammatory cytokines and growth factors involved in the pathogenesis of alopecia areata. Janus kinase (JAK) inhibitors interfere with signaling pathways by blocking Janus enzymes, which play a crucial role in transmitting signals from pro-inflammatory cytokines and growth factors involved in the pathogenesis of alopecia areata. These cytokines and growth factors, such as interferon-gamma and tumor necrosis factor-alpha, are known to play an important role in the inflammation and immune response associated with

alopecia areata. The work also addresses the results of clinical trials and observational studies evaluating the efficacy and safety of JAK inhibitors in the treatment of alopecia areata in children. These studies have shown encouraging results, indicating a significant improvement in capillary regeneration and a reduction in disease activity in many pediatric patients. In some cases, JAK inhibitors have been shown to be effective even in children with more severe and refractory forms of alopecia areata. Important clinical considerations related to the use of these drugs in children, including proper dosage, monitoring for side effects, and potential long-term risks were highlighted by the study.

The study by Kołcz et al. (2023) presents a case report of an adolescent with alopecia universalis who was successfully treated with upadacitinib, a Janus kinase (JAK) inhibitor. Alopecia universalis is a severe form of alopecia areata, characterized by hair loss all over the body, including the scalp, eyebrows, eyelashes, and body hair. The reported case highlights the potential efficacy of JAK inhibitors, such as upadacitinib, in the treatment of pediatric alopecia areata, especially in severe cases such as alopecia universalis. Upadacitinib works by inhibiting JAK-STAT signaling pathways, which play a crucial role in the pathogenesis of alopecia areata by modulating the immune response and reducing inflammation in the hair follicle. In addition to the case report, the study includes a review of the literature on the use of JAK inhibitors in pediatric alopecia areata. This review highlighted other studies that corroborated the efficacy of JAK inhibitors, including cases of severe alopecia areata refractory to other forms of treatment.

On the other hand, the study by Zheng et al. (2023) proposes a predictive model for the recurrence of alopecia in children, using bioinformatic approaches and advanced statistical analyses, in order to identify and validate prognostic markers. They have developed a model based on clinical and molecular data, which allows for a more accurate assessment of the risk of alopecia recurrence in pediatric patients. One of the main aspects of the study was the identification of possible molecular markers associated with the recurrence of alopecia in children. The researchers performed a detailed analysis of genomic and transcriptomic data, looking for patterns and gene expressions that could be related to the progression of alopecia and thus allowing the identification of several genes and biological pathways potentially involved in the pathogenesis of childhood alopecia. The study also included a prospective clinical investigation involving a large number of pediatric patients with alopecia. Participants were followed over time to monitor disease recurrence and assess the effectiveness of therapeutic interventions. This longitudinal analysis allowed the researchers to identify clinical and demographic factors that may influence the likelihood of alopecia recurrence in children. The

results of the study highlighted several prognostic markers associated with the recurrence of childhood alopecia, including specific clinical features such as the extent and severity of hair loss, as well as demographic factors such as age and gender. Certain gene expression patterns have been identified as significant predictors of alopecia recurrence in children.

After reviewing a variety of studies and case reports on childhood alopecia areata, its clinical manifestations, and therapeutic approaches, several important points can be discussed.

First, it is observed that pediatric alopecia is a complex dermatological condition that can have several causes, including genetic, autoimmune, environmental, and behavioral factors. The possible underlying causes of hair loss in children and the importance of comprehensive evaluation for an accurate diagnosis were highlighted. It was also pointed out that childhood alopecia is not only limited to physical hair loss, but can also have significant impacts on the mental health and quality of life of affected children, in addition to the need to consider the psychosocial aspects of childhood alopecia in clinical management and appropriate treatment.

With regard to diagnosis and management, a multidisciplinary approach involving dermatologists, pediatricians, and other health professionals is essential. The importance of a comprehensive, individualized evaluation to determine the underlying cause of alopecia and to develop an appropriate treatment plan was emphasized.

As for therapeutic options, several studies have explored different approaches, including the use of corticosteroids, immunosuppressive therapy, and innovative therapies such as Janus kinase (JAK) inhibitors. Positive results were observed, indicating the potential of these therapies in the treatment of pediatric alopecia areata.

However, it is important to underscore the need for further research to evaluate the efficacy and safety of these therapeutic approaches in the long term, especially in pediatric patients. A comprehensive overview of available therapeutic options has been analysed, but there is an ongoing need for additional evidence to guide clinical practice.

Finally, childhood alopecia areata is a challenging dermatological condition that requires a multifaceted approach for proper diagnosis and treatment. Recent advances in understanding the pathophysiology and new therapeutic options offer hope for better management of this condition in children, but more studies are needed to consolidate these advances and improve long-term outcomes for affected pediatric patients.

FINAL THOUGHTS

Infantile alopecia areata, characterized by hair loss in circular areas, can significantly affect children's quality of life. This condition, often resulting from an autoimmune reaction against hair follicles, can also be influenced by genetic, psychological and environmental factors.

Management varies according to the severity of the condition and individual needs, and may include corticosteroids, immunotherapy, low-level light therapy, Janus kinase (JAK) inhibitors, and other immunosuppressants. The choice of therapy should consider the age of the child, the extent of alopecia, and the response to treatments.

It is crucial to provide psychological support to affected children in order to mitigate the impact on self-esteem and quality of life. Therefore, integrated management, which combines pharmacological interventions and emotional support, is essential to control alopecia areata and promote child well-being.

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