INTERNATIONAL JOURNAL
OF PHARMA AND BIO SCIENCES

Internationally Indexed Journal

Indexed in Chemical Abstract Services(USA),Index Coppernicus ,Ulrichs Directory of Periodicals,Google scholar ,Cabi ,DOAJ ,PSOAR, EBSCO ,SCOPUS, EMBASE etc.

Rapid Publishing

The International Journal of Pharma and Bio Sciences (IJPBS) is an international journal published quarterly. The Aim of IJPBS is to publish peer reviewed research and review articles in less time without much delay in the developing field of Pharmaceutical and Biological sciences. One week from the date of manuscript submission author gets the decision of acceptance and if accepted the manuscript will be processed within 3 weeks (approx.) for publication.

Pharmaceutical Sciences

Branches

- Pharmaceutics
- Novel drug delivery sys
- Nanotechnology
- Pharmacology
- Pharmacognosy
- Analytical chemistry
- Pharmacy practice
- Pharmacogenomics
- Polymer sciences
- Biomaterial sciences
- Medicinal chemistry
- Natural chemistry
- Biotechnology
- Pharmacoinformatics
- Biopharmaceutics

Biological Sciences

Branches

- Biochemistry
- Biotechnology
- Bioinformatics
- Cell biology
- Microbiology
- Allied Sciences
- Molecular biology
- Neurobiology
- Cytology
- Pathology
- Immunobiology

ELSEVIER

Impact Factor 0.47*

**Refer Instruction to authors available at www.ijpbs.net*

Indexed In Elsevier Bibliographic Database (SCOPUS, EMBASE and Sciverse)

Journal Home page
www.ijpbs.net

FOR INSTRUCTION TO AUTHORS VISIT
www.ijpbs.net
FOR ANY QUERIES EMAIL TO

- editorofijpbs@yahoo.com
- editorijpbs@rediffmail.com
- prasmol@rediffmail.com

Int J Pharm Bio Sci 2013 Jan; 4(1): (B) 978 - 982

Review Article **Pathology**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

ALOPECIA AREATA AND DENTAL DISEASE ASSOCIATION – A REVIEW

R.MATHAN RAJAN *[1], R. PRATIBHA RAMANI [2], VIJAY KARTIK V [3] AND D.KANDASAMY [4]

[1] *Department of Conservative dentistry and endodontics Faculty of Dental Sciences,Sri Ramachandra University, Porur, Chennai , Tamilnadu, India*
[2] *Consultant Dermatologist , Maruti Skin clinic ,Chennai*
[3] *Department of Oral and Maxillofacial Pathology, Saveetha Dental college, Saveetha University, Chennai.*
[4] *Department of Conservative dentistry and endodontics Faculty of Dental Sciences, Sri Ramachandra University,Porur, Chennai .*

ABSTRACT

Alopecia areata (AA) is a non-scarring, inflammatory, hair loss disease that can affect men, women and children. The factors that activate the onset of alopecia areata and the mechanisms of its development are not fully understood.The association of alopecia areata and infectious foci of dental origin may be explained by the autoimmune nature of the disorder. This article reviews this association and suggests that patients with localized alopecia should be subjected to careful exploration of the oral cavity in search of possible dental infections.

KEY WORDS : **Alopecia areata ,pathogenesis ,dental infection**

DR. R.MATHAN RAJAN
Professor, Department of Conservative dentistry and endodontics Faculty of Dental Sciences, Sri Ramachandra University,Porur, Chennai , Tamilnadu, India

INTRODUCTION

Hippocrates first used the term alopecia (literally translated as "fox's disease"), the characteristics of the hair loss disease we now know to be alopecia areata (AA) were first described by Cornelius Celsus in 30 A.D. However, the actual term "alopecia areata" was first used by Sauvages in his "Nosologica Medica", published in 1760 in Lyons, France [1]. Alopecia areata (AA) is a non-scarring, inflammatory, hair loss disease that can affect men, women and children. The factors that activate the onset of alopecia areata and the mechanisms of its development are not fully understood. Circumstantial evidence suggests alopecia areata is an autoimmune disease where cells of an individual's own immune system prevent hair follicles from producing hair fiber. From the 1800's onwards there was considerable debate about the cause of alopecia areata. Two main hypotheses were put forward, one based on parasitic infection (Gruby 1843, Radcliffe-Crocker 1903), the other based on a nervous disorder (Von Barensrung 1858) [2]. One of the more unusual variations on the neuropathic origin of alopecia areata was put forward by Jacquet (1902) who suggested alopecia areata was initiated by sources of nerve irritation such as defective and diseased teeth [3]. Jacquet's hypothesis was apparently confirmed by others (Decelle 1909). It is now widely believed that alopecia areata is an autoimmune disease. Even though studies more than 100 years old showed that alopecia areata affected hair follicles were invaded by inflammatory cells (Giovannini 1891), the inflammatory autoimmune disease hypothesis did not become popular until the 1960s. The idea was first proposed by Rothman in a discussion of a paper by Van Scott (1958)[4,5,6]. The association of alopecia areata and infectious foci of dental origin may be explained by the autoimmune nature of the disorder. This article reviews this association and suggests that patients with localized alopecia should be subjected to a careful exploration of the oral cavity in search of possible dental infections.

DEFINITION

Alopecia areata (AA) is considered to be a nonscarring, inflammatory, cell-mediated autoimmune disease characterized by spontaneous reversible hair loss that most frequently affects the scalp. The presence of peribulbar lymphocytic inflammatory infiltrate is a histopathologic characteristic, found in most of the terminal hair in one evolutionary stage: catagen or telogen. The follicles become smaller during the course, forming miniaturized hair and are substituted by fibrous tracts. Eosinophils are also found in all the stages of alopecia areata, both in the peribulbar infiltrate and in the fibrous tract [7,8]. It has been demonstrated by immunohistochemistry that the cellular infiltrate is composed above all by T lymphocytes with CD4 T lymphocytes in greater number than CD8 T lymphocytes. There is an increase in the expression of HLA-DR. The CD4 and CD8 lymphocytes are in a varied proportion, from 2:1 to 8:1, and the CD4/CD8 ratio is slightly higher in the acute phase in relation to the chronic phase. Both CD4 and CD8 lymphocytes invade the follicular epithelium. There is also an increase in the expression of ICAM-1 in the dermal papillae, in the keratinocytes and in the external sheath of the hair root[9]. The hair follicle is a frequent target of immune-mediated tissue injury, leading to the development of alopecia areata. Under normal conditions, the hair follicle is considered an area of relative immune privilege during the anagen stage of hair growth. Thus, autoantigens are not recognized by CD8+ T-cells, allowing normal hair growth. MHC class I antigens demonstrate very low expression during this phase, something which is mediated by locally produced cytokines, such as TGF-b1, ACTH, a-MSH, and IGF-1, all of which serve as very potent immunosuppressants, produced by anagen hair bulbs . Also, anagen hair bulbs show very

few antigen-presenting cells that appear to be functionally impaired since they do not express MHC class II antigens. Several triggers, such as emotional factors, skin microtrauma, or infectious agents aided by a possible underlying immune predisposition, lead to intrafollicular rise in IFN-*γ*, that causes MHC class Ia upregulation in the proximal hair follicle epithelium . Also, HLA class II antigens and ICAM-1, both implicated in lymphocyte trafficking and antigen presentation, increase their expression in response to stimuli by IFN-*γ* and TNF-*α* in cultured hair follicles[10] . Several studies have shown that within the cascade of pathogenesis of alopecia areata, cytokines and other molecules that coordinate cyclical hair growth play a crucial role. IFN-*γ* is the main cytokine known to be aberrantly expressed in alopecia areata through a CD4+ Th1 mediated response. The elevated serum levels of IFN-*γ* in alopecia areata patients may reflect the state of inflammation. MIG (monokine induced by IFN-*γ*) is a cytokine that is elevated in human alopecia areata and its level correlates with disease activity, increasing in expanding lesions and vice versa, making it a useful marker of monitoring of the disease status and response to treatment. Also, another chemokine leading to recruitment of mononuclear cells is IP-10 (interferon inducible protein-10), which is also induced by IFN-*γ*. An Experiment in IP-10 is much less expressed compared to MIG but accounts for the persistence of Th1response in alopecia areata, perpetuating the recruitment of lymphocytes Serum levels of IL-1*α* and IL-4 are significantly elevated in patients with localized alopecia areata, while IL-2 and IFN- *γ* are mainly elevated in extensive disease states, possibly implying that the progression to the extensive form may be mediated by Th1 cytokines . Macrophage Migration Inhibitory Factor MIF levels are significantly elevated in alopecia areata patients. This molecule stimulates the production of IL-1 and TNF-a by macrophages, while the latter exert a positive feedback effect on MIF. The cycle endpoint is an on-going inhibition of hair growth, [11,12,13]. In studies by Carroll and colleagues, the kinetic progression of gene expression in the induced model of AA was consistent with an autoimmune mechanism of disease progression. The earliest markers suggested that onset of disease involves tissue inflammation and vasodilation, Proceeding to activation of macrophages and T helper 1 (TH1) lymphocytes, followed by alterations in expression levels of genes regulating immunoglobulin responses during later disease development. Downregulation of hair keratins and hair follicle associated genes was coincident with activation of macrophages and T cells, and suggested that disintegration or collapse of hair follicle integrity is initiated by a immune system attack, rather than by an immune response being invoked by hair follicle damage. Genes that were upregulated in studies of human skin biopsies from individuals with chronic, nonresponsive AA were suggestive of changes associated with chronic, innate immunity and infiltration of TH1 T cells. Genes involved in a variety of metabolic, adhesion, and signaling processes that previously had not been associated with AA were also upregulated. Of the 64 genes that was downregulated, 15 are associated with human keratins or hair follicles demonstrating the importance of cell-mediated immunological disease in AA and provide an important example of how new insights into the pathogenesis of autoimmune disease obtained through microarray technology[14,15,16].

Alopecia areata and dental disease association

Autoimmune mechanisms may be cited to explain AA of dental origin occurring at a distance from the site of infection. In effect, infections of dental origin arise as a result of chemical, mechanical or bacterial irritation, which causes an inflammatory reaction in the dental root canals followed by pulp tissue necrosis and the migration of germs towards the periradicular zone, external to the tooth. Depending on the stage of the infectious process, histological examination may reveal

the presence of numerous inflammatory cells such as polymorphonuclear leukocytes, macrophages, lymphocytes, plasma cells, basophils and eosinophils Interaction between the external irritants and the host defense cells may in turn induce the appearance of endogenous chemical mediators including neuropeptides, fibrinolytic peptides, kinins, complement fragments, vasoactive amines, lysosomal enzymes, cytokines and immune response mediators. These immune responses are divided into antigen-antibody and cell-mediated immune reactions. Some studies have demonstrated the presence of systemically circulating immune complexes, fundamentally in acute dental infections. Although the presence of lymphocyte populations appears to have been demonstrated in acute and chronic infections in the tissues surrounding the teeth of animals, their presence in humans remains to be fully confirmed. Thus, the presence of common immune mediators in the pathogenesis of both dental infection and AA could explain the dental origin of the latter. In many cases the resolution of AA requires combined therapy involving topical or intralesional corticosteroids, immunotherapy with diphenyl-cyclopropenone , or even psychotherapy[17]. In other cases treatment consists of simply eliminating the dental infectious process of variable origin (i.e., caries, chemical or mechanical damage, etc.) or retained teeth causing infection or mechanical stimulation of nerve fibers[21] .Alopecic patches of dental origin are generally located on the same side as the infectious process. In the case of upper maxillary teeth, these locations are typically found above a line traced along the lip commissures, scalp, beard and even eyebrows. When located below this line, the cause usually corresponds to the mandibular teeth, as confirmed by a review of the most recent cases published in the literature. Lesclous et al. reported a case of AA involving the beard and caused by the proximity and possible stimulation of the fibers of the inferior alveolar nerve due to the presence of a retained lower molar. However, in yet another case report , the bald patch was located on the contralateral side. Attempts have long been made to define an AA distribution map as a function of the causal teeth though with little success, in the light of the above mentioned cases[18,19,20].

Thus, dental counseling is advised in all cases of AA of unknown origin in the absence of other possible causes. In this sense, a thorough examination is required, with X-ray exploration to detect possible infectious foci or sites of nerve fiber stimulation[21]. Such measures may contribute to resolve the hair loss by simply eliminating the cause without the need for unwarranted pharmacological treatments.

REFERENCES

1. Sauvages. Nosologica Medica, Lyons, 1760
2. Giovannini S. Recherches sur l'histologie pathologique de la pelade. Annales de Dermatologie et de Syphiligraphie 1891; series 3: 923-957
3. Jaquet L. Nature et traitment de la pelade - la pelade d'origine dentaire. Ann Dermatol et de Syph 1902; 3: 180-190.
4. Decelle. Bull et Mem Soc Med de Hop de Paris 1909; 21: 72
5. Van Scott EJ. Evaluation of disturbed hair growth in alopecia areata and other alopecias. Ann NY Acad Sci 1959; 83: 480-490.
6. R. Paus, N. Ito, M. Takigawa, and T. Ito, “The hair follicle and immune privilege,” Journal of Investigative Dermatology Symposium Proceedings, vol. 8, no. 2, pp. 188–194, 2003.
7. T. Christoph, S. M¨uller-R¨over, H. Audring, et al., “The human hair follicle immune system: cellular composition and

immune privilege," British Journal of Dermatology, , 2000 ,vol. 142, no. 5, pp. 862–873.
8. Pericin M, Trüeb RM. Topical immunotherapy of severe alopecia areata with diphenylcyclopropenone: evaluation of 68 cases. Dermatology1998; 196: 418-21
9. Ghersetich I, Campanile G, Lotti T. Alopecia areata: immunohistochemestry and ultrastructural of infiltrate and identification of adhesion molecule receptors. Int J Dermatol. 1996; 35:28-33
10. Vandenbark AA. Autoimmune Diseases: promising emerging therapies.J Invest Dermatol 1995; 104: 10-11.
11. Moreno GA, Ferrando J. Alopecia areata. Med Cutan Ibero Latina Americana. 2000; 28:294-312
12. Ackerman AB, Guo Y, Vitale O. Clues to diagnosis in dermatopathology II. Hong Kong: Everbest Printing; 1992. p. 330-2.
13. Madani S, Shapiro J. Alopecia Areata Update. J Am Acad Dermatol. 2000; 42:549-
14. Carroll JM, McElwee KJ, King LE Jr, et al: Gene array prooling and immunomodulation studies ,a cell-mediated immune response underlying the pathogenesis of alopecia areata in a mouse model and humans. J Invest Dematol, 2002;119:392-402.
15. Kathy L. Moser et al The Use of Microarrays to StudyAutoimmunity J Investig Dermatol Symp Proc 9: 18 ^22, 2004.
16. Stamatis Gregoriou, Dafni Papafragkaki, George Kontochristopoulos,Eustathios Rallis, Dimitrios Kalogeromitros, and Dimitris RigopoulosCytokines and OtherMediators in Alopecia Areata Mediators of Inflammation Volume 2010, Article ID 928030.
17. James d Grace . Extensive alopecia areata ofdental origin Arch Derm Syphilol. 1942;45(2):349-352.
18. Romoli M, Cudia G. Alopecia areata and homolateral headache due to an impacted superior wisdom tooth. Int J Oral Maxillofac Surg. 1987 Aug;16(4):477-9. -2.
19. Lesclous P, Maman An unusual case of alopecia areata of dental origin.Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997 Sep;84(3):290
20. Dental Origin of Alopecia Areata. JAMA. 2002;287:2330
21. S.Jayakumari et al evaluation of toothache activity of methanolic extract and its various fractions from the leaves *psidium guajava* linn International Journal of Pharma and Bio sciencesvol 3/Issue 2/April – June 2012 238-249.