Familial Alopecia Areata and Overview of Alopecia Areata at Lagos University Teaching Hospital

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ABSTRACT

Introduction: Alopecia areata (AA), an asymptomatic, non-scarring, hair loss on the scalp and/ or body is now regarded as an autoimmune inflammatory disorder. The aetiology and pathogenesis of alopecia areata is not known; factors implicated include patient's genetic constitution, the atopic state, emotional stress, organ specific and nonspecific immunity.

Aim: This is a report of 2 female siblings with AA of early onset (two years); and review of dermatology clinic data of patients to determine the frequency, sex and age distribution of patients with alopecia areata.

Case Summary and Result: Two female siblings presented with alopecia areata with onset at age 2 years. The older sibling who presented at age 9 with 7 years history of progressive loss of hair (alopecia totalis); while the younger sibling who was 2 years presented with 6 month history of alopecia areata (ophiasis pattern). The male siblings were not affected and no family or personal history of atopy, thyroid disorders and autoimmune disorders. Patients defaulted treatment because of parents' dissatisfaction with hair growth.

Alopecia areata accounted for approximately 1.7% of the total clinic attendance at the dermatology outpatient of the Lagos University Teaching Hospital (LUTH). There was a female preponderance with a male to female ratio of 1:1.6. Most of the patients presented in the third and fourth decades of life.

Conclusion: Severity of AA at first consultation is an important prognostic factor. The prognosis is worse in children and with increased duration. Studies to determine the efficacy of therapeutic options and genetics of alopecia areata

INTRODUCTION

Alopecia areata, an asymptomatic, non-scarring, hair loss on the scalp and / or body is now regarded as an autoimmune inflammatory disorder[1, 2]. It is classified according to the extent of hair loss. Patch alopecia areata describes patchy hair loss; alopecia totalis involves total loss of scalp hair; and alopecia universalis involves loss of all scalp and body hair[1,3]. The aetiology and pathogenesis of alopecia areata is not known; factors implicated include patient's genetic constitution, the atopic state, emotional stress, organ specific and nonspecific immunity[1].

This is a report of 2 female siblings with alopecia areata of early onset; and review of dermatology clinic data of patients to determine the frequency, sex and age distribution of patients with alopecia areata between January 2006 and December 2009.

CASE 1

A 9 year old girl presented at the dermatology clinic of Lagos University Teaching Hospital (LUTH) on 5th June 2010 with a 7 year history of progressive loss of scalp hair. This started at the periphery, in patches and extended to involve all parts of the scalp. The parent shaved off the remaining patches of hair and the hair failed to regrow giving a total loss of scalp hair. There was no fever, no abnormal behavior like pulling of hair or child abuse. She was not on cytotoxics or radiotherapy. There was no personal or family history of atopy. She was born with full hair on the scalp and had normal developmental milestones. She had no obvious congenital abnormalities and genetic disorder. There was no hair loss in parents or extended family member. However, the younger sister who was 2 year old suddenly developed similar pattern of hair loss, while other siblings which are boys did not have any hair loss (Figure 1). She had used several medications (names unknown to the parents) and herbal medications with no improvement.

On examination, we found a young girl with total loss of scalp hair; the eyebrow, eyelashes and body hair was intact. There was no erythema, infiltration or desquamation of the scalp; no abnormality of the nails, oral mucosal and other systems of the body. Investigations revealed normal blood sugar, ESR 8mm/hr, PCV 35%, total white blood count – 4,100 cells/m^3, with normal differentials. A diagnosis of alopecia totalis was made. Parents declined scalp biopsy,

so she was started on steroid shampoo, steroid creams and later minoxidil. She had an initial scanty hair growth which was lost after 3 months. Parent of patients declined further investigations and treatment, and defaulted from the clinic following further loss of hair after commencement of minoxidil.

CASE 2

2 year old girl presented along with older sibling with a 6 months history of progressive patchy hair loss, started at the occipital margin of the scalp and progressed to involve other parts of the scalp. Earlier attempts by parents to plait her hair resulted in pulling off of the hair. The loss of hair was not associated with febrile illness. She was not on chemotherapy or radiotherapy for any illness. She had a normal developmental milestone; and no congenital abnormality. Family history is as noted in the previous case presented (Figures 2 and 3). There was no personal or family history of atopy and thyroid disorders. On examination there was patch hair loss with no scalp abnormality and skin lesions in other parts of the body. Parents declined scalp biopsy.

A clinical diagnosis of alopecia areata (ophiasis pattern) was made. Parents were counseled on the disease, management and prognosis and commenced on steroid shampoo (clobetasol) and creams and minoxidil. No hair growth was noted in 3 months of follow up with the institution of therapy. Parents defaulted treatment and follow up when they noticed the hair loss in the elder sister persisted.

Data on alopecia areata from the dermatology clinic of LUTH

Between January 2006 and December 2009, alopecia areata accounted for approximately 1.7% of the total clinic attendance (161/9,628) at the dermatology outpatient clinic of the Lagos University Teaching Hospital (LUTH). Sixty two patients were males while 99 patients were males giving a male to female ratio of 1:1.6. Most of the patients presented in the third and fourth decades of life (see table below). Mean age of patients was 22.26± 13.21; and age ranged between 4 months and 68 years. After the 4th decade of life, the frequency of alopecia was noted to have decreased and no patients presented after the 7th decade of life (table 1). One hundred and forty patients (86.9%) had patchy AA, while 14 patients (8.7%) and 7 (4.3%) had alopecia totalis and alopecia universalis respectively. Six patients had the ophiasis pattern of patchy alopecia, while 2 had affectation of the beard.

DISCUSSION

Epidemiology

All patterns and variants of Alopecia areata occur in all races, with equal sex distribution and the onset can be at any age. AA accounts for approximately 2% of new cases in dermatology clinics in UK and US[2]. In Singapore, it accounted for 3.8% of cases seen at the dermatology clinic[4]. Alopecia areata in the pediatric age group constituted 60% of all AA and 60% of patients have the onset before 20 years of age[2]. Various epidemiological surveys done in Nigeria suggested that the frequency of alopecia areata at dermatology clinics vary between <1% and 3.4% of dermatology clinics' attendance[5-7].

The frequency of alopecia areata at the dermatology clinic LUTH (1.7%) is similar to data from other dermatology clinics in other parts of the world which ranges between 0.7 and 3.8% [2]. The female preponderance of alopecia areata found at the dermatology clinic of LUTH may be related to the immense cosmetic significance of the disease[3]. Prevalence studies in various dermatology outpatients in Nigeria showed female preponderance for most dermatologic conditions[5-7]. The highest number of patients presented in the third and 4th decades of life. This is similar to the findings in other parts of the world were the peak incidence was found to be between the second and the fourth decades[2,3]. In a series done by Ekpudu on alopecias at LUTH, alopecia areata accounted for 15% (15/100) of consecutive patients who presented with various types of alopecias during the study period[8].

In the series done in Singapore, family history was found in 4.6% of patients with AA[4]. Systematic study of familial AA revealed estimated lifetime risks of 7.1% in siblings; 7.8% in parents and 5.7% in Offspring[9]. Age of onset of AA in index patients and first degree relatives was significantly correlated[9]. The similar age of onset in the two female siblings and the sparing of the male siblings are suggestive of the role of genetic factors in the development of alopecia areata[9]. Alopecia universalis and alopecia totalis are noted to be more common with younger age group than patchy AA and are most likely to have been associated with autoimmune disorders, severe disease and extensive family history[10]. Alopecia areata is also associated with rheumatologic conditions, hematologic disorders, gastrointestinal disorders and other dermatologic conditions like atopy, vitiligo, psoriasis and lichen planus[11]. Familial alopecia areata is associated with heredity thrombocytopenia (pseudo-von Willebrand disease)[12].

Pathology, Pathogenesis and Genetics

Aetiology of AA is thought to be interplay of both genetic and environmental factors resulting in final prototype[13]. The genetics of alopecia areata is not completely understood and the environmental factor triggering disease initiation and exacerbation is still speculative although pro inflammatory agents, stress and diet have been suggested to play a role[2,14]. Interleukin 1 receptor antagonist is associated with patchy alopecia areata; and interleukin 1 cluster genes

are associated with disease severity, other autoimmune and inflammatory diseases[14,15].

Genetic susceptibility to the development of AA has been found to involve specific alleles of the HLA region[2]. Some DQB and DR alleles have conferred high risk for disease in both case control and family- based studies[14]. Alopecia areata is associated with Down's Sydrome; MXI, a gene in the Down's syndrome chromosome 21 is associated with AA[14]. The mutations of the autoimmune regulator gene (AIRE) on chromosome 21q22.3 have been dissociated with high frequency of AA in autoimmune polyglandular syndrome type 1[14]. The evidences supporting the autoimmune mechanism of AA include the association with organ specific immunity, the presence of inflammatory lymphocytes around and within affected hair follicles and the ability to promote hair re growth with the use of immunosuppressive agents[2]. The CD8+ cells have been hypothesized to act as the effector cells and CD4 + T cell acts as the helper cells[16].

Possible mechanism of disruption of the normal hair pathway in AA include inflammation of hair follicle and dystrophic anagen phase leading to inability to produce hair fibre of significant size; intense inflammation giving multiple anagen-telogen phases of short durations; and persistence of hair follicle in prolonged telogen phase[2].

The histologic features of alopecia areata depend on the stage of current episode; it is suspected in the presence of high percentage of telogen hairs or miniaturized hairs, even in the absence of peribulbar lymphocytic infiltrate[17]. In the early stage, histologic findings of AA includes premature telogen hair follicles with small anagen follicles, reduction in follicle density and mild peribulbar inflammatory cells infiltrate around small anagen follicles with no scarring[18]. At the expanding edge of the alopecia patch, most follicles are in late catagen and telogen phase. Large numbers of anagen follicles have peribulbar lymphocytic infiltrate (called swarm of bees) with occasional macrophages and plasma cells[18]. On direct immunoflorescent staining, C3, IgG and IgM are found along the basement membrane of the inferior segment of the hair follicles[17].

Clinical presentations

Alopecia areata is a form of non scarring alopecia which presents with single or multiple patches which expand with progression of the disease[2,19]. The pattern of hair loss varies and include band like hair loss along the posterior occipital and temporal margins (ophiasis), hair loss in the fronto-parieto-temporal area (ophiasis inversus) and diffuse thinning over part or all of the scalp[2,3]. Alopecia areata lesions are well demarcated round or oval patches. The skin may be normal initially but later becomes slightly peachy or reddened colour[2]. A characteristic finding frequently seen in and at the border of the patches is "the exclamation mark hairs": short hairs that are tapered proximally and wider distally[2]. A hair pull test may be positive at the periphery of the lesion[2,3]. Ikeda classified AA into 4: the common type, the atopic type, the prehypertensive and the combine type based on disease onset and associated disorders[11,20].

Nail changes found to accompany hair loss include trachyonychia, beau's line, onychorrhexis, thinning or thickening, onychomadesis, Koilonychias, punctuate or transverse leukonychia and red spotted lunula[3,19]. Alopecia areata is associated with high psychiatric comorbidity, anxiety and mood disorders which require psychiatric evaluation is the most common form[21]. In the series by Tan E et al in Singapore, 9.8% recalled stressful event preceding hair loss[4].

Bad prognostic factors in AA include male sex, family history, atopic diathesis, impaired immune state, involvement of >30% of the scalp; predominant occipital involvement; presence of pseudo comedones, nail involvement and duration of the disease greater than one year[11]. The patients presented had positive family history, involvement of >30% of scalp, predominant occipital involvement, and duration of disease greater than one year. Severity of AA at first consultation is also an important prognostic factor. The prognosis is worse in children and with increased duration[22].

Management

Management of AA is handled on individual basis with final outcome based on cosmetic regrowth of the hair[19]. Several agents have been considered for management of AA but none is preventive or curative and the aim of management is to suppress the disease activity[23].

In adults, intralesional corticosteroids particularly triamcinolone acetonide is regarded as gold standard in treatment of AA; regrowth is shown to be between 64% and 97% and it is advised that treatment should be stopped after 6 months if no response[23]. Oral prednisolone at a dose of 200mg once weekly pulse therapy has been found to be successful though needs standardization to optimize therapeutic efficacy and minimize side effects[24]. Topical treatment with clobetasol propionate 0.05% under occlusion has induced regrowth of AT and AU with long term benefit noted in 17.8% of patients[25].

Minoxidil at 5% has been noted to be effective as adjuvant therapy in the treatment of AA[23,26]. Mode of action of minoxidil is not fully understood but proposed action includes vasodilatation, angiogenesis, enhanced cell proliferation, potassium channel opening and immune suppression[23]. Topical immune therapy with diphenylcyclopropenone (DPCP) is used to treat for adults with more than 50% involvement[23]. A lag of 3 months can occur between initiation of therapy and

developments of significant hair regrowth[27].

PUVA is useful in the treatment of AA, though long term safety, side effects, increased risk of skin malignancies and high relapse rate has limited its use[23, 28]. The mechanism of action is not known but it is believed to be through immunosuppressive and anti inflammatory properties[3]. Hair regrowth of about 23% is noted with use of sulphasalazine which has both immunomodulatory and immunosuppressive actions[23]. The use of cytotoxics like cyclosporines and methotrexate alone or in conjunction with corticosteroids have produced some success though limited by the side effects and high relapse rate[23]. Capsaicin has been shown to cause regrowth of hair with result comparative to the use of clobetasol 0.05%[23].

Biologics like etanercept, etaluzimab, adalimumab and infliximab, topical calcineurim inhibitors like tacrolimus and pimecrolimus; and prostaglandin analogues like latanoprosts have failed to show hair growth in AA[23, 29]. Photo therapies like excimer lasers, infrared irradiation are useful in the treatment of AA while photodynamic therapy has not been found useful[22]. Treatment options in children in children include anthralin, topical sensitizers, ultra potent corticosteroids under occlusion and 5% minoxidil[3].

Patients with AA need a lot of psychosocial support. The need to use antidepressants as supportive therapy needs to be substantiated by large randomized controlled studies[23]. Differential diagnose of AA includes trichotillomania, T. capitis, traction alopecia and telogen effluvium. A genetic disorder of the hair, atrichia with papular lesions has been described as a differential of recalcitrant AU in childhood; presenting with normal hair at birth, shedding and lack of hair regrowth[30].

In conclusion, we have presented two female siblings with extensive AA and AT with poor prognostic factors. The patients presented would have been ideal for genetic study of alopecia areata. Studies to determine the efficacy of therapeutic options and genetics of alopecia areata will be necessary in Nigeria.

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AGE GROUPS (YEARS)	NUMBER OF MALES	NUMBER OF FEMALES	TOTAL NUMBER OF PATIENTS (%)
0 - 10	8	22	30 (18.6)
11 - 20	11	12	23 (13.8)
21 - 30	23	29	52 (32.3)
31 - 40	14	23	37 (22.0)
41 - 50	3	7	10 (6.2)
51 - 60	1	3	4 (2.5)
61 - 70	2	3	5 (3.1)
	62	99	161 (100%)

Table 1: Age Distribution of Patients with Alopecia Areata

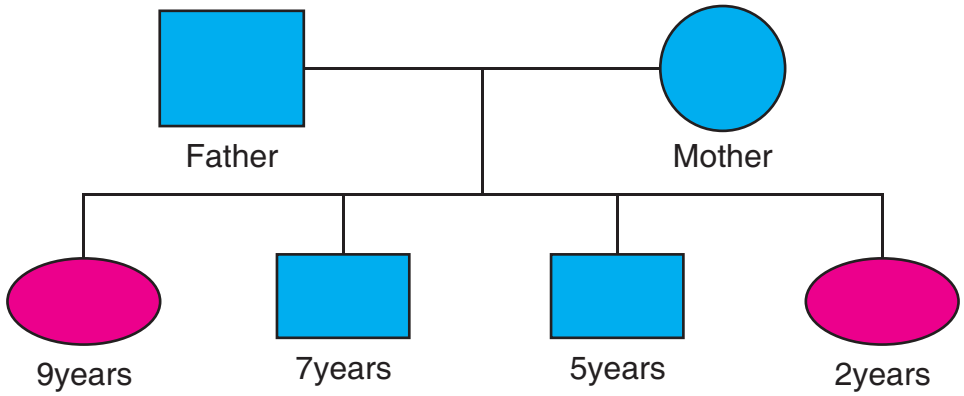

Figure 1: Pedigree of Patients Presented (Affected female patients in red oval shape)

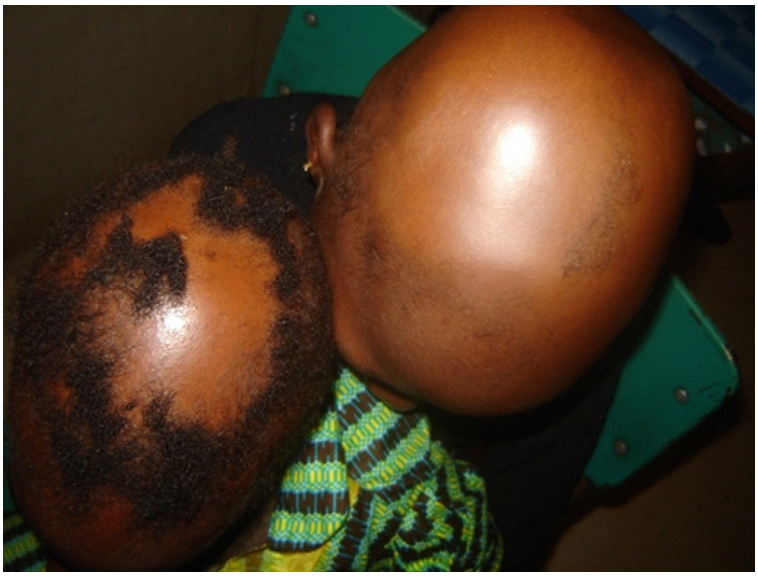

Figure 2: Alopecia Areata in Female Siblings

Figure 3: Alopecia totalis in the Older Sibbling