

Lichen Sclerosus in Monozygotic Twins: A Familial LS

Caoimhe Máire Róis Fahy^{1*}, James Fitzgibbon² and Michelle Murphy¹

¹Department of Dermatology, South Infirmary – Victoria University Hospital, Cork, Ireland

²Department of Pathology, Cork University Hospital, Cork, Ireland

*Corresponding author: Caoimhe M.R. Fahy, Department of Dermatology, South Infirmary – Victoria University Hospital, Cork, Ireland, Tel: 0035318032676; E-mail: cafahy@tcd.ie

Received date: June 24, 2014, Accepted date: February 16, 2015, Published date: February 23, 2015

Copyright: © 2015 Caoimhe Fahy et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Lichen sclerosus (LS) is a chronic inflammatory skin disorder. Although aetiology remains unclear and is likely to be multi-factorial, a genetic association has been suggested. We report of the development of lichen sclerosus in monozygotic adult twins.

Case study

A 29 year old female was referred with a 5 year history of steroid responsive vulvar pruritus. Although it was intermittent, without dyspareunia, flares were disabling to the extent that she was unable to sit comfortably. It was noted in her family history, that her twin sister also suffered from vulvar pruritus. Clinical examination of the patient demonstrated loss of architecture, sclerotic changes on the labia majora and burrowing of the clitoris. Histopathological analysis of a skin biopsy showed hyperkeratosis, epidermal atrophy and over-hyalinised connective tissue in the underlying dermis. There was a mixed chronic inflammatory cell infiltrate below the hyalinised dermis and basal cell hydropic degeneration at the basement membrane zone. These features are consistent with the diagnosis of lichen sclerosus (Figure 1), although her age was not typical for this diagnosis. There was a good clinical response to appropriate use and duration of clobetasol ointment. An appointment for review of the patient's sister was offered and accepted.

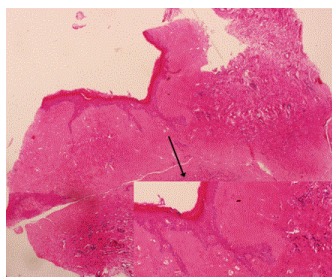


Figure 1: Histopathology of a biopsy of affected vulval skin, stained with haematoxylin and eosin, showing hyperkeratosis, epidermal atrophy and over-hyalinised connective tissue in the underlying dermis. There is a mixed chronic inflammatory cell infiltrate below the hyalinised dermis and basal cell hydropic degeneration present at the basement membrane zone.

Her twin sister attended some months later and gave a history of vulval irritation for some years. Like her sister, there was no history of atopy, psoriasis or thyroid disease. Although she never experienced dyspareunia and had no extra-genital rash, there was clitoral fusion,

some loss of architecture and sclerosis on the labia majora with evidence of raw areas on the labia minora. There was also perineal sclerosis and perianal erythema. Overall, the clinical impression was also that of lichen sclerosus, not as severe as her sister's but treatment gave a rapid response, similar to her twin.

Discussion

Lichen sclerosus is characterised by white sclerotic plaques which are most commonly found in the anogenital region [1]. There is a bimodal peak in incidence of LS in females, in the pre-menarchial age group and the post-menopausal period [2]. It is thought that the wide range of prevalence estimates is due to under-reporting because of lack of diagnosis and patients not reporting symptoms for diagnosis secondary to fear or embarrassment [2]. An increasing number of studies and case series discuss various associations with lichen sclerosus. A significant association between LS and HLA antigens was reported by Marren et al. where it was shown that 78% of patients studied had HLA class 2 DQ7, DQ8, or DQ9 antigens [3]. Powell et al. showed a stronger association of HLA DQ7 with early onset LS [4]. This study discussed that HLA DQ8 is seen in increasing frequency in adult females affected with LS. Other types of HLA genotype seem to have protective effects with regards to vulvar LS [1]. HLA-DRB1*0301/04 and DRB1*0301/04/DQB1*0201/02/03 have been demonstrated in a study on 187 patients attending vulvar clinics to be associated with decreased incidence of LS in controls and increased numbers of DRB1*12 and the haplotype DRB1*12/DQB1*0301/04/09/010 in vulvar LS patients [1].

There are varying associations of autoimmunity with LS. Studies have shown that up to 34% of patients, have increased incidence of autoimmune disease, up to 41% have autoantibodies and between 21-36% have a family history of autoimmune disease compared to controls [2,5]. Taking this and the data linking HLA Class 2 antigens with LS a genetic aetiology is very likely. Familial LS is rare and is evidenced by case reports and case series of patients, both children and adults. The largest study group assessed by Sherman et al. discussed the findings of 1052 patients with LS [1]. One hundred and twenty one patients (12%) had a positive family history of the disease [1]. Meyrick Thomas et al. reported the first monozygotic twins to develop LS with occurred for them within 6 months of each other at 4 years old [6]. Since this report, other cases have been reported as documented in Table 1 [1,4,6-8]. Familial LS had only been described in 37 families up until the observational cohort study on women attending the Oxford paediatric vulvar clinic with a diagnosis of LS [1,4,6,9]. The diagnosis of LS has been reported in 3 pairs of female siblings who were monozygotic twins aged 2-16 years [4,6]. Monozygotic male twins aged 9, were diagnosed with balanitis xerotica obliterans, following circumcision, secondary to progressive phimosis [9]. The observational

cohort reported by Powell and Wojnarowska were from 95 families and 12% of women had a positive family history of probable LS [4]. Familial LS has been shown to have increased susceptibility of progression to malignancy [1]. Genetic factors have a role to play in antioxidant enzymes. The study by Sander et al. highlighted that oxidative DNA damage is found to occur in lesions of LS [7]. Dermal sclerosis and inflammation has been demonstrated to contain oxidative protein damage [7]. Perhaps the role of genetically associated antioxidant enzymes may be associated with the increased susceptibility to vulvar cancer in familial LS. While some studies highlighted a relationship between autoimmune disease and LS, this association was not confirmed by the Oxford study [10]. This may suggest that a genetic predisposition to autoimmune disease is not associated with familial LS [10].

Study	Number of Cases	Diagnosis of LS	Age of onset (years)
Meyrick Thomas & Kennedy (1986) [6]	1	Genital	4
Powell et al. (2001) [4]	2	Genital	Childhood
Sherman et al. (2010) [1]	2	Genital	Unknown
Doulaveri et al. (2013) [8]	1	Genital	34
Lis-Swiety et al. (2014) [7]	1	Extragenital	10
		Genital	19

Table 1: Associations of autoimmunity with LS

Atopy has also been associated with LS. Becker et al. illustrated in a study of 350 boys that there existed a comorbidity of significance of LS and atopic dermatitis in boys with genital LS [8]. While the aetiology of the atopic diathesis is multifactorial, it is well established that there are strong genetic influences on the aetiology of the various atopic disorders such as atopic dermatitis, allergic rhinitis and asthma [11]. Mutations in genes associated with the skin barrier and immunological cytokines may be linked to LS and atopy which also needs further investigation.

Conclusion

We report the development of LS in twins. This is in line with literature supporting the hypothesis that genetic factors play a role in the aetiology of LS. The diagnosis of LS in pre-menopausal women may be under recognised and it is important to consider and recognise LS in female patients of all age groups. This report also explores that with appropriate treatment, both of these patients had a rapid resolution of their symptoms and signs, suggesting that pre-menopausal women may respond faster and better than those that are

post - menopausal. This report highlights the importance of history taking when reviewing patients and asking about other family members affected with the same symptoms and signs. In this case, the sister of the initial patient would not have had prompt diagnosis and treatment.

Contribution to Authorship

Caoimhe Máire Róis Fahy acquired and extracted the data and drafted and revised the article. James Fitzgibbon made a substantial contribution to analysis and interpretation of data. Michelle Murphy made substantial contribution to conception and design of the article and revision of the article for important intellectual content.

Consent

Patient consent was obtained for publication.

References

1. Sherman V, McPherson T, Baldo M, Salim A, Gao XH, et al. (2010) The high rate of familial lichen sclerosis suggests a genetic contribution: an observational cohort study. *Journal of the European Academy of Dermatology and Venerology: JEADV*. 24: 1031-1034.
2. Tasker GL, Wojnarowska F (2003) Lichen sclerosis. *Clin Exp Dermatol* 28: 128-133.
3. Marren P, Yell J, Charnock FM, Bunce M, Welsh K, et al. (1995) The association between lichen sclerosis and antigens of the HLA system. *Br J Dermatol* 132: 197-203.
4. Powell J, Wojnarowska F (2001) Childhood vulvar lichen sclerosis: an increasingly common problem. *J Am Acad Dermatol* 44: 803-806.
5. Cooper SM, Ali I, Baldo M, Wojnarowska F (2008) The association of lichen sclerosis and erosive lichen planus of the vulva with autoimmune disease: a case-control study. *Arch Dermatol* 144: 1432-1435.
6. Meyrick Thomas RH, Kennedy CT (1986) The development of lichen sclerosis et atrophicus in monozygotic twin girls. *Br J Dermatol* 114: 377-379.
7. Lis-Swiety A, Mierzwinska K, Wodok-Wieczorek K, Widuchowska M, Brzezinska-Wcislo L (2014) Co-existence of lichen sclerosis and localized scleroderma in female monozygotic twins. *Journal of pediatric and adolescent gynecology*. 27: 133-136.
8. Doulaveri G, Armira K, Kouris A, Karypidis D, Potouridou I (2013) Genital vulvar lichen sclerosis in monozygotic twin women: a case report and review of the literature. *Case Rep Dermatol* 5: 321-325.
9. Fallick ML, Faller G, Klauber GT (1997) Balanitis xerotica obliterans in monozygotic twins. *Br J Urol* 79: 810.
10. Sander CS, Ali I, Dean D, Thiele JJ, Wojnarowska F (2004) Oxidative stress is implicated in the pathogenesis of lichen sclerosis. *Br J Dermatol* 151: 627-635.
11. Irvine AD, McLean WH, Leung DY (2011) Filaggrin mutations associated with skin and allergic diseases. *N Engl J Med* 365: 1315-1327.