

Desquamative inflammatory vaginitis. A review

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Abstract

Desquamative inflammatory vaginitis is an uncommon cause of an intractable vaginitis often accompanied by serious dyspareunia, which can occur at any stage of reproductive life and after the menopause. The cytological changes are identical with those seen in atrophic vaginitis yet the disorder often occurs in the presence of apparently normal ovarian function. Vaginal synechiae and stenosis develop in an appreciable number of patients. Treatment is unsatisfactory though there is some response to either local or systemic steroid therapy. The literature is reviewed and the association of some cases with lichen planus of the mouth and genitals discussed. Its causation and natural history remain largely unknown and there is as yet, insufficient evidence to regard it as a single entity. It is likely that the incidence of the disorder is underestimated.

Introduction

This disorder of unknown aetiology is the occasional cause of a persistent vaginitis. It was probably first described by Scheffey *et al*¹ in a single patient under the title of "exudative vaginitis". Subsequently Gray and Brewer² and Gardner³ both published short series of patients and the latter author defined its clinical, and cytological characteristics and gave it the name of "desquamative inflammatory vaginitis" (DIV) by which it is now generally known. However, other authors have been less exact in defining the condition and this has inevitably led to some confusion. Furthermore, the observation that vaginitis may be associated with *Lichen planus* (LP), has given rise to the hypothesis that DIV may be part of a syndrome in which LP involves the oral cavity and the genitalia.

The first section of this review examines in detail the available literature concerning DIV with special emphasis on the diagnostic criteria employed and the clinical findings. The last section attempts to integrate this material in order to clarify as far as possible the epidemiology, clinical course, pathological findings, diagnostic criteria and potential for treatment.

Review of the literature

Scheffey *et al*¹ are generally credited with the description of the first case though Franken and Rotter⁴ described a premenarchal girl aged 12 years whose illness had some of the characteristics of DIV. Their patient complained of a profuse persistent watery discharge and her vagina was found to have "a reddened, velvety surface with many minute vesicles being present". The discharge, from which no pathogens were grown in culture, was found to contain "fibrin, lymphocytes and squamous cell debris". Vaginal biopsy revealed that "epithelial cells showed hydrops with pyknotic nuclei". Histiocytes were increased and there was a depletion of granulocytes. There was a rapid response to treatment with local oestrogens and she remained well over a 4 year period of observation. The patient's age, the lack of polymorphonuclear cells in the vaginal secretions and the rapid and apparently complete response to oestrogen therapy however marks this case out as being very different from the other reported examples of DIV.

Scheffey's patient was 50 years old and complained of a copious vaginal discharge for 14 months. The vulva was described as "showing secondary inflammation" whilst the vagina was inflamed and covered with a white membrane. The vaginal walls were "hard and rigid". The vaginal secretions contained many leucocytes and parabasal cells. Culture produced a mixture of bacteroides, streptococci, *E coli*, *Neisseria catarrhalis*, haemolytic streptococci and yeasts. Vaginal biopsy showed "loss of the surface epithelium and diffuse inflammation".

Gray and Barnes² described six cases all occurring during "menstrual life". In all, the vaginae were described as "thin and reddened" and the vaginal discharge was purulent containing many basal cells. Cultures of the discharge produced *Trichomonas vaginalis* in two patients, whilst β haemolytic streptococci and yeasts were found in some of the others. The response to a variety of forms of treatment (which did not include steroids) was poor, improvement being noted in only two and the condition was described as "an obstinate infection".

Gardner³ described eight patients and included the observation that these were seen in a series of 3000 patients with vaginitis seen over a 15 year period. Though the ages of his patients were not given, they were described as having "high oestrogen levels and normal ovarian function" though it is not clear how this was judged. All complained of vaginal discharge which was described as being moderate to copious in

amount and bloodstained in some though malodour was not a feature. He noted that the vaginal inflammation could be patchy and often affected the upper one third especially the opposed surfaces of the posterior fornix and the ectocervix. Some of the affected zones were described as "fiery red serpiginous areas many of which showed shallow ulceration". The vaginal walls often showed ecchymotic bleeding points, and were often covered with a grayish membrane which peeled off to reveal the inflamed surface. Examination of the discharge showed pus cells, basal and parabasal vaginal epithelial cells as well as small numbers of intermediate and superficial cells. Lactobacilli were "essentially lacking" and relatively few microorganisms were present. The vaginal pH ranged from 5 to 6.8. Vaginal cultures showed streptococci to be present in seven, *Staphylococcus aureus*, *S epidermis* and *E coli* being isolated on single occasions. These microorganisms were considered by him to play a secondary or opportunistic role in the condition and the response to antibacterial agents was uniformly poor. Histologically thinning of the vaginal epithelium with ulceration was observed in addition to acute and chronic inflammatory changes in both mucosal and submucosal tissue. Some epithelial cells showed vacuolation and stromal haemorrhages were common. With or without treatment the course of the illness was protracted whilst ulcerated lesions were slow to heal whatever treatment was employed. Local oestrogens were found to be ineffective though there was some improvement noted in four of five patients who were treated with intravaginal corticosteroids. Two of the patients developed a mild degree of stenosis of the vaginal vault.

Lynch⁵ presented a patient who had LP of the buccal and gingival mucosa in association with what is described as a chronic "idiopathic" vaginitis. She had complained of an odourless pink vaginal discharge with dyspareunia for nearly 7 years. Various treatments were of no avail. Examination of the vagina showed bright red patches of friable mucosa. Cultures and smears were negative for "infectious organisms". Scrapings from the lesions showed only parabasal cells and the vulval biopsy specimen revealed nonspecific inflammation. On the basis of these findings he considered the vaginitis resembled that described by Gardner and went on to suggest that DIV might be a vaginal manifestation of LP. This was followed in 1982 by the first of several reports also suggesting that some cases of DIV may have a link with LP.

Pelisse *et al*⁶ described the cases of four patients whose illness they considered represented a new syndrome to which they gave the name "vulvo-vaginal-gingival plurimucosal erosive lichen planus". All four had erosive vulval and gingival LP along with a desquamative vaginitis. Vaginal

adhesions were present in two. In three patients oral LP lesions preceded genital involvement. They did not state the criteria on which the diagnosis of DIV was made. Vulval biopsy was said to be typical of LP in three and suggestive in a fourth. LP was proven histologically in one vaginal biopsy.

Hewitt *et al*⁷ reanalysed these patients along with a further 15. Their patients ages ranged from the 20s to the 70s. The main symptoms complained of were vaginal pain, soreness and dyspareunia. Vulvo-vaginal and gingival LP developed simultaneously in about one third whilst in another one third vulvo-vaginal lesions were the first to appear. The remainder commenced their illness with gingival lesions. Once again the criteria adopted for the diagnosis of DIV are not given. Vaginitis was diagnosed in all except one patient. The vaginitis was variously described as "erosive" in 11, as "erythematous" or "diffuse" in five, as "haemorrhagic" in one and merely as "vaginitis" in one patient. No account is given of the cytology of the vaginal secretions. Vaginal biopsy was performed in seven patients and in four the findings were typical of LP. The condition of the vagina in these biopsy positive patients was described as "erosive" vaginitis in two and as "haemorrhagic" and "diffuse" vaginitis in the remainder. The other three vaginal biopsies showed non specific inflammation. Seven patients developed vaginal adhesions. The authors recommended that the development of LP at any of the mucosal sites mentioned should lead to an examination of the others and any suspect lesions biopsied. They suggested that the new syndrome may cause certain examples of DIV.

Edwards and Freidrich⁸ reported five cases of DIV and found clinical and histological evidence of erosive and/or non erosive LP at genital or oral sites and, on the basis of these findings, concluded that LP was a "principal cause" of DIV. The age range of their patients was from 38 to 68 years and the duration of their illness was from under 1 year to 9 years. In three vulval soreness, burning and itching were the main complaint. In the remaining two patients vaginal discharge was predominant although they also had a degree of vulval soreness, pain or pruritus. An important feature of this series was that in all patients the vaginal secretions were examined and all showed inflammatory cells, some parabasal cells and a paucity of mature squamous cells. The pH was 7 in three patients and not recorded in the remainder. Vaginal biopsy was performed in one patient and showed the epithelium was largely absent, being replaced with a thin fibrin layer. There was a dense inflammatory infiltrate in the stroma. Three of the patients had clinical and histological evidence of LP in the mouth and two had both oral and genital LP. In addition, vaginal adhesions were present in three patients. All were treated with

antibiotics, most received oestrogens and some were also treated with dapsons and/or griseofulvin. One received isotretinoin. The response was universally poor, though all showed some improvement after intravaginal corticosteroids and/or short courses of oral steroids.

Soper *et al*⁹ reported three patients aged in their 50s who presented with vulval itching and burning, the original diagnosis having been atrophic vulvovaginitis which had failed to respond to oestrogen therapy. The state of the vagina was described as erythematous in one and as atrophic with a stenosed apex in another. The third patient had a markedly atrophic vulva and vagina with stenosis and an erythematous mucosa. Examination showed LP of the mouth whilst biopsy of the vestibular area revealed histological evidence of the disease in all three. They also reported a 63 year old patient who 7 months after developing cutaneous LP, began to complain of vulval pruritus and ulceration. Biopsy of the ulcerated area of the vestibule showed histological changes of LP. No account was given of the cytological character of vaginal secretions. Only one patient showed any response to steroid therapy whilst retinoids used in 2 were of no avail. All had also received a number of antibiotics without effect.

Pelisse¹⁰ described 19 patients, eight of whom had experienced one or more episodes of post coital bleeding. She also noted that all but one had had significant vulval pain. Vaginal biopsies carried out on four patients showed the characteristic histological changes of LP. Vulval biopsies were performed on 16 patients (20 specimens). Thirteen specimens showed "unequivocal" LP. (It is not clear however how many patients this figure represents.) Immunofluorescent studies on tissue from six patients failed to demonstrate significant deposition of immune reactants. A variety of therapies were used including etretinate, dapsons, griseofulvin and local steroids. None of these treatments were universally successful. High dose oral steroids, used in 10 patients were found to be moderately useful, but only if continued for at least 3 weeks. Relapse ensued when the dose was reduced below 10 mg daily.

Ridley¹¹ in a study of chronic erosive vulval disease reported 22 patients with vulval or vaginal LP, the diagnosis being made by a combination of histological findings and/or the presence of typical lesions of LP at other sites such as the mouth or skin. Some of them presented with vulval soreness and vaginal discharge though no details of the cytology of the discharge are given. Most had a history of 4 or more years duration, several having symptoms for 15 or more years. Their ages ranged from 24–72 years. In addition to vulvitis, 14 patients had vaginitis variously described as haemorrhagic or erosive. Vaginal stenosis and/or adhesions were present in six patients (only one of these being aged over 50 years).

Vulval biopsy was performed in 14 patients and vaginal biopsy in eight (21 patients). Histological changes of LP were found in seven of the former and in two of the latter. She also emphasised the practical difficulties often met with in the clinical and the histological diagnosis of LP affecting mucous membranes.

Conclusions

Age at onset

Although the ages of all the reported patients are not given, the illness can clearly develop both before and after the menopause. (If Franken's case is included then it may on occasion begin before the menarche.) The cases which develop after or around the menopause will have to be distinguished from atrophic vaginitis by the lack of response to oestrogens.

Incidence

All authors agree that DIV is uncommon. Gardner¹² wrote after the publication of his paper that "communications received indicate that the condition occurs more often than previously suspected". It may be that a number of cases developing at or after the menopause may not be recognised; failure of atrophic vaginitis to respond well to oestrogens seems to be a far from rare experience.

Aetiology

1. A defect in the supply of oestrogens or their metabolism

DIV differs from atrophic vaginitis in its failure to respond to oestrogen therapy, and in its tendency to patchy vaginal involvement. As it can occur in premenopausal patients with apparently normal ovarian function it is unlikely to be due to hormone deficiency. There remains the theoretical possibility that there could be some local defect of metabolism in the vaginal epithelium which prevents maturation though this seems to be very unlikely.

2. Infection

This remains a possible explanation though the few microbiological studies carried out so far have produced no likely candidate, most of the isolates being regarded as opportunist invaders. (A similar cytological picture to that in DIV can be seen in some cases of trichomonas infestation and anaerobic infections though these respond rapidly to therapy.)³ Furthermore, treatment with a wide range of antimicrobial preparations has achieved little apart from a slight and usually temporary improvement in some individuals. Viral infection cannot yet be excluded.

3. Association with LP

From the observations of Pellise,^{6,10} Hewitt *et al*,⁷ Edwards and Freidreich,⁸ Lynch,⁵ and Ridley¹¹ it seems clear that some cases of DIV may be due to LP,

mostly of the uncommon erosive variety. Unfortunately Edwards and Freidrich's report is the only one of those associating DIV with LP to give a description of the cytological changes in the vaginal secretions, information which is essential for the diagnosis of DIV (as defined by Gardner³) as the vaginal findings alone are both variable and somewhat non specific. The oral and genital lesions of LP found in their patients however, exactly match those described by the other authors reviewed here.

Vulvo-vaginal lesions of LP are perhaps unlikely to have gone unnoticed in the other series though oral lesions could easily have escaped attention. In addition the few vaginal biopsies carried out showed no evidence of LP though the histological appearances of mucous membrane lesions can be atypical. Thus there seem to be patients with DIV which is not obviously associated with clinical LP.

Furthermore, in the group reported to have DIV in association with LP, the chief symptom reported has been vulval soreness, pain and dyspareunia rather than discharge which is prominent in those not associated with LP.

Vestibular lesions and the development of vaginal synechiae seem to be common in the LP group whilst in the cases described by Gardner, the majority of changes were seen in the upper third of the vagina.

At the moment therefore we cannot be sure what part LP plays, beyond noting that it is closely associated with DIV in some patients. In some patients their illness has been observed to begin with oral LP before genital lesions and symptoms of DIV develop. Perhaps sometimes DIV may develop first with lesions of LP appearing much later.

4. Chemical inflammation

Short lived episodes of vaginitis which have a cytological picture similar to that seen in DIV have been reported following the use of overstrong chemical vaginal douches,^{12,13} though they resolve as soon as the offending solution is withdrawn and are unlikely therefore to play any part in such a persistent and unresponsive disorder as DIV.

Course

The natural history of DIV is not known but from the published observations there can be no doubt that in most patients it persists for long periods with only minimal remission and that it is refractory to most forms of treatment except steroids. (The senior author however has observed spontaneous remission to take place in two patients which persisted for 20 months and over 2 years before they were lost to observation.)

Symptoms and signs

The most commonly reported symptom has been that of an intractable, purulent vaginal discharge

which has often persisted for years and is sometimes associated with a degree of vulval soreness, burning and dyspareunia. In those patients in whom the condition is associated with LP at oral and/or genital sites, there seems to be a tendency for vulval soreness, burning, pain and dyspareunia to be more prominent symptoms.

The physical findings are of a vaginitis which is frequently patchy in distribution and which has a marked tendency to affect the upper one third of the vagina most severely in some patients. The mucous membrane appears reddened and thin, and the affected areas often have a serpiginous configuration. Some are covered with a grayish membrane which is easily removed to leave a raw looking surface. Bleeding points, ecchymoses and superficial ulceration are often found. Vaginal adhesions and even stenosis may develop in an appreciable number especially of those associated with LP.

In those cases associated with LP, typical prominent lesions of LP are often present on the vulva, the gingival margins and elsewhere in the mouth. Proven lesions in the vagina, though reported, seem to be relatively uncommon.

The vaginal discharge which is often copious may be blood stained though malodour is surprisingly uncommon. The pH tends to vary between 5.5 and 7.

Pathological findings

The characteristic cytological feature is the presence in the vaginal secretions of many polymorphonuclear leucocytes, basal and parabasal cells and a paucity of mature squamous cells. Lactobacilli are scanty and there tend to be few microorganisms. Red blood cells may also be present. (The microbiological findings have shown the presence of organisms best regarded as secondary invaders which appear to play no part in the disorder.)

Similarly the histological changes where vaginal biopsies have been carried out have been unhelpful merely showing areas of ulceration and acute and chronic inflammation. Where LP was present the typical changes of this dermatosis were usually noted, namely dermal infiltration with a dense narrow band of lymphocytes immediately below the epidermis whilst in places the basal layer showed liquefaction necrosis and the escape of melanin to the dermis. Necrotic keratinocytes were seen in the upper dermis or epidermis. Some of the epidermal cells showed loss of structure when stained with eosin ("colloid bodies"). Acanthosis and hyperkeratosis were often seen when skin was involved though on mucous membranes a thin epithelium with parakeratosis or alternating parakeratosis and hyperkeratosis was more usual.

Diagnosis

In premenopausal patients this is usually easy and

can be made on the typical findings of a persistent vaginitis associated with an atrophic vaginal cytology. In peri- and post menopausal patients the diagnosis depends on the physical findings associated with a failure to respond to oestrogens. In those cases associated with LP, a biopsy of any suspect lesions will ensure correct diagnosis. A search of the mucous membranes and skin for such lesions should be a part of the investigation of all patients with DIV.

A desquamative type of vaginitis can occur in association with pemphigus vulgaris and cicatricial pemphigoid, and lesions may initially be confined to the genitalia. Biopsy and immunofluorescent stains will usually enable these conditions to be diagnosed with confidence.

Lichen sclerosus can cause extensive genital lesions with labial/clitoral atrophy and adhesions though the vagina is not affected. This picture may sometimes closely resemble LP and even the histological findings may not always be distinctive. Transient forms of vaginitis with a desquamative cytological picture associated with chemical douches, and sometimes infection, never pose a practical problem of diagnosis. Similarly, the desquamative vaginitis which can be seen in non staphylococcal toxic epidermal necrolysis and the Steven's Johnson syndrome is clearly related to the acute disease process.

Treatment

Treatment with oestrogens and antimicrobials are largely ineffective. In cases associated with LP improvement has followed the use of short courses of oral prednisone or other steroids and the drug has been applied to vaginal lesions in a variety of

preparations ranging from tablets to creams. Even after steroid treatment, relapse appears to be common and relief only temporary. (Rectal preparations of steroids that can be used for vaginal therapy include: hydrocortisone suppositories, 25 mg hydrocortisone or hydrocortisone acetate [BNF] "Ultraproct" flucortolone pivalate 630 mg, flucortolone hexanate 610 mg [Schering]. "Predsol" 5 mg prednisolone [Glaxo].)

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