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A dopamine agonist successfully treats a case of chronic lichen sclerosus

Case Report

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Abstract

The dermatological inflammatory disorder known as lichen sclerosus (LS) frequently involves the vulva. The most common therapy are very potent glucocorticoids e.g., clobetasol, although recently laser therapy has been evaluated with some success. However, in general, the standard therapies have not been overly impressive with their results. Dopamine agonists, e.g., dextroamphetamine sulfate (DS), have been very successful in ameliorating pelvic pain, vulvovaginitis, and different types of dermatological conditions that were refractory to standard therapy. A case is presented of a patient with dysmenorrhea and vulvar LS.

The LS worsened progressing to painful fissures despite treatment with three different types of potent topical glucocorticoids. Her dysmenorrhea and LS went into total remission after a short time of treatment with DS. The remission has lasted 1.5 years while remaining on DS therapy. The hypothesized mechanism of action of DS is to release more dopamine. This biogenic amine probably corrects these inflammatory defects by the effect of dopamine on decreasing cellular permeability thus precluding the abrogation of the mucosal barrier thus preventing infiltration of unwanted irritants into various tissues causing inflammation by cellular immune cells, including, but not limited to, the vulvar region.

Introduction

Lichen sclerosus (LS) is a common chronic inflammatory condition with a prevalence that may be found in 1-2% of all women [1]. In the early stages, erythema is found which is typically shiny and is present in the vulva, perineum, and anus [2]. Persistent inflammation leads to a porcelain-like thickening of the dermis. This can lead to the development of painful fissures. The chronically inflamed dermis also may tend to hemorrhage [2]. The highest prevalence is at the prepubertal and post-menopausal time periods. Especially for post-menopausal patients, the development of adhesions and possibly vulvar carcinoma can result from long-term LS [2].

The recommendation for treatment has been published in the 2023 EuroGui Derm guideline of the European Dermatology Forum [3]. For early stages, the recommendation is to apply potent topical glucocorticoids e.g., clobetasol 0.05% once daily for 3 months then reduced to using it at a less frequent interval or on an individual basis that keeps the LS from returning [3]. There is evidence that the use of topical glucocorticoids to treat LS may decrease the risk of vulvar carcinoma [4].

Another therapy that has been recommended for LS is the use of topical calcineurin inhibitors [3]. There may also be a role for phototherapy [3]. For very severe cases oral methotrexate has been recommended [3]. Similarly, for severe cases an oral retinol named acitretin has been used [3]. Acetretin is generally used for treatment of refractory psoriasis, but because of significant side effects, it is generally used as a last resort. There is no evidence that topical estrogen, progesterone, or testosterone provides significant benefits for LS [3].

A state-of-the-art review was published by Mortensen et al in 2022, reviewing the beneficial use of LASER for various gynecological issues including lichen sclerosus [5]. They reviewed 11 studies evaluating the effect of vulvar LASER on LS. One randomized control trial of 40 women treated with CO2-LASER or Sham LASER found no significant difference in histopathological changes 8 weeks after the last session [6]. Another RCT compared clobetasol to fractionated carbon dioxide laser and found a significant improvement In the laser treated group vs ultra potent topical glucocorticoids [7] two studies found improved clinical symptoms following CO2 laser treatment in patients who were not showing improvement with clobetasol therapy 3-12 months after initiating Co2 laser treatment [8,9]. Another clinical study found that adding laser therapy with topical glucocorticoids was more effective than glucocorticoids alone [10].

There are other studies finding clinical benefits with laser the use of Er: YAG symptoms in patients who did not respond to clobetasol [11]. We present a case of LS who was resistant to clobetasol and other glucocorticoid topical agents who had a marked long-term improvement of her LS following treatment with the off-label use of the dopamine agonist dextroamphetamine sulfate (DS).

Case Report

A 32-year-old woman sought a second opinion concerning possible treatment of LS which had been present continually for 2.5 years. It was described as pruritic and painful. What prompted the visit was an intensification of the pain partly because of the fissures in the area between the posterior fourchette and the anus. She had been previously treated with clobetasol propionate 0.05% ointment and cream, triamcinolone acetonide 0.5% and augmented betamethasone dipropionate ointment 0.05%. Not only did these topical glucocorticoids fail to improve the pain and discomfort, but they all increased the pain. Thus, she stopped them after about 6 months of therapy. Though she had dysmenorrhea since her early teens, the duration and the degree of pain intensified also at age 30 and was getting progressively worse.

Though we had never tried dopamine agonists for LS, we have had great success with dysmenorrhea with this treatment. We hoped it could also help the LS. After 1 week of taking 9.4mg dextroamphetamine sulfate (DS) upon arising and at noon (using 15mg of amphetamine salts twice daily), she noticed an improvement in the LS. The dosage gradually increased to 18.8mg DS twice (upon arising and noon) and within one week of this increased dosage, the fissures closed and she had 100% relief of vulvar pain. Furthermore, her dysmenorrhea was also eradicated. This relief has lasted over 1.5 years.

Discussion

Though this is the first case report of very effectively treating LS of the vulva with DS, it is not the first case of the treatment of vulvar disorders with DS. A 5-year-old girl suffering for two years with severe vulvovaginitis had the problem completely eradicated by the treatment with the dopamine agonist DS [12]. Dopamine agonists have also been reported to correct other disorders of the dermis that were refractory to standard therapy including chronic urticaria, eczema, palmoplantar eczema, bullous pemphigoid and cutaneous discoid lupus erythematosus [13-20].

The concept of using dopamine agonists for treating a plethora of medical conditions is based on studies on the mechanism allowing successful implantation of the fetus [21]. The hypothesis based on experimental studies is that it is essential that progesterone blocks dopamine to allow infiltration of inflammatory elements across the mucosal barrier to stimulate an increase in the presence of cellular immune cells needed to remodel thick walled uterine arteries to form thin-walled spiral arteries by autoimmune stripping off of the thick walls of some of the uterine arteries [21,22]. Dopamine functions to diminish cellular permeability, and there is evidence that progesterone blocks dopamine allowing infiltration of inflammatory substances into pelvic tissues. The increase in natural killer cells, macrophages, and cytotoxic thymic (t) cells that ensue must then be suppressed to prevent rejection of the fetal semi-allograft [23].

The basis of the concept of the benefit of the dopaminergic therapy is that the release of extra dopamine by sympathetic nerve fibers can correct the rent in the mucosal barrier, leading to the prevention of the inflammatory condition in the first place. In contrast, glucocorticoids and other immunosuppressants work by blocking the downstream pathways leading to the final step of inflammation, which is the infiltration of cellular immune cells, which, in turn, cause the symptoms. However, immunosuppressants leave the patient more prone to serious infections and also more prone for the development of cancer related to generalized immune suppression.

Since the secretion of P may further increase cellular permeability, some conditions, both pelvic and extra pelvic, may only manifest at certain times of the menstrual cycle [24-28]. On the other hand, sometimes the permeability defect in a given organ system is so severe that the problem is constant and not related to hormonal events [29,30]. Even males are also prone to this disorder that we call the increased cellular permeability syndrome, and also show marked improvement of their symptoms after taking dopaminergic drugs [31-35].

Another potential advantage of using a dopamine agonist as opposed to topical ultra potent glucocorticoids or laser is that frequently patients present concomitantly with debilities related to other organ systems. Thus, the treatment with DS or other dopamine agonists also eradicates these other symptoms. For example, the aforementioned pediatric patient with the vulvovaginitis also had severe attention deficit hyperactivity disorder, marked weight gain related to orthostatic edema, and marked fatigue [12]. These other symptoms, besides the vulvovaginitis, responded quite well to DS.

Dopamine agonists also work well for dyspareunia [25,36]. One woman in her early 30's sought an opinion to treat a very painful blistery type of rash on her face that only started a week before her menses and stopped with the onset of her bleeding. She also mentioned that because of severe dyspareunia she has never been able to insert a tampon or have sexual intercourse despite pelvic floor physical therapy and anti-neuropathy drugs. The dyspareunia occurred all month in addition to the premenstrual facial rash. They both were completely eradicated following treatment with DS in a very short period of time [37].

She illustrates the fact that the permeability defect was so severe in the vulvar tissues (she only had mild dysmenorrhea) so that the dyspareunia was present all the time but, the defect in permeability involving the dermis of her face was not sufficient until the extra increase in permeability that occurred after P secretion allowed infiltration of irritants thus causing the facial rash only in the pre-menstrual time [38]. Sometimes the use of DS corrects a problem that is likely to improve but also helps a problem that surprisingly dissipates after DS therapy. A male sought a therapy to provide relief of his constant backaches with DS. We were not surprised that his backaches markedly improved with DS [38, 39].

However, it was surprising that his treatment refractory nightmare disorder of 30-year duration that occurred after witnessing the death of many of his fellow soldiers in a jeep accident also completely dissipated [40]. As mentioned, the pediatric aged girl with vulvovaginitis also had marked improvement of her severe attention deficit hyperactivity syndrome, unexplained significant weight gain, and marked fatigue was also following DS therapy [41-45].

Thus, LS can be added, to the very long list of treatment refractory conditions that respond very well to, in general, much safer and better tolerated dopamine agonist therapy.

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