Cleveland Health Sciences
Library/CASE Interlibrary Loan

ILLiad TN: 143224 *143224*

Location: ALLEN
Call #:
ISSN: 0026-6620

Journal Title: Missouri medicine

Volume: 90 Issue: 11
Month/Year: 1993
Pages: 711-3

Article Author: Wright AJ

Article Title: Testosterone pellet implant therapy for lichen scl

Imprint:

Received: 1/27/2010 12:53:45 PM

28505682

Borrower: OHUDAC
Lending String:
Patron: Glaser, Rebecca - TN; 179567

Need By: N/A
Regular
ARIEL
Charge
Maxcost: $15.00
Shipping Address:
Fordham Health Sciences Library, ILL
Wright State University
3640 Colonel Glenn Hwy
Dayton Ohio 45435-0001

Fax: 1.937.775-2232
Ariel: 130.108.121.58
Odyssey:
Email: fill@www.libraries.wright.edu
Phone: 937-775-4110
Notes:
GMR-RL. Please dont fax or Ariel (we wil

Testosterone Pellet Implant Therapy for Lichen Sclerosus

Andy J. Wright, MD

This material may be protected by copyright law (Title 17 U.S. Code).

Lichen sclerosus is a benign chronic skin disease predominantly affecting the vulva in post-menopausal women. Various methods of therapy have been recommended for this stubborn and uncomfortable condition. The article describes a new method of therapy for patients suffering from this disorder, utilizing subcutaneously-implanted testosterone pellets to obtain extended remission of symptoms.

Lichen sclerosus (LS) (formerly lichen sclerosus et atrophicus) is a benign chronic condition affecting the epidermis and dermis of the skin. This disease is most commonly seen in women, usually presenting immediately pre- or post-menopausally; but is also seen in prepubertal children and, to some extent, in men. It is most commonly seen in the vulvar and perianal areas, but can be seen anywhere on the body with the most common extragenital sites being on the trunk and limbs.[1]

Genital LS shows symptoms of pruritus and burning, which are usually the presenting complaint. The typical lesion appears as atrophic white papules which coalesce to form placques of "cigarette paper" atrophy.[2] Telangiectasias and subdermal induration are characteristic. Hyperkeratosis of sweat and sebaceous gland orifices are seen on extravulvar sites,[2] the most frequent of which are the flexor surfaces of the wrist and the upper areas of the trunk.

Histologic examination of affected tissue shows variable degrees of thinning of the squamous epithelium with progressive loss of the rete ridges. The dermis has a characteristic acellular homogenous appearance and chronic inflammatory cells are found in a layer just below this homogenous zone. Hyperkeratosis or parakeratosis may be present or absent.[3]

The terminology has changed over the years since this entity was first reported in 1929 under the name kraurosis vulvae. In 1969 Gardner proposed the concept of vulvar dystrophy, which could be divided into hypertrophic dystrophy, characterized by acanthosis and hyperkeratosis; atrophic dystrophy, characterized by thinned epithelium, homogenous dermis, and deep lymphocytic infiltrate; and mixed dystrophy containing foci of both types.[1] The term hypertrophic dystrophy was related to the conditions otherwise known as benign epithelial hyperplasia and lichen simplex chronicus, whereas atrophic dystrophy was synonymous with lichen sclerosus et atrophicus.[3] Most recently the name has been shortened to lichen sclerosus.[4]

The cause of LS has not been demonstrated; however, it is undoubtedly multifactorial. There have been reports suggesting genetic predisposition to the disease; but, in general, statistical significance has been difficult to show. The concept of an association of LS with autoimmune diseases has also been investigated.[2,5] A loss of hyaluronic acid coupled with increased urinary excretion of hyaluronic acid and disappearance of elastic fibers in patients with LS have suggested that an elastase-type protease produced in human vulvar fibroblast may be responsible for many of the physical findings.[1,2] Friedrich and Kabra demonstrated that women with LS had serum levels of dihydrotestosterone well below normal values for their age, whether they were pre- or post-menopausal. Also, their free testosterone levels were elevated, suggesting a block in the conversion of testosterone to dihydrotestosterone. When these patients were treated with topical testosterone, their dihydrotestosterone rose to levels exceeding normal. The enzymatic mechanisms responsible for these findings have yet to be elucidated.[1] The relationship of vulvar dystrophies and LS, in particular, to vulvar carcinomas has been studied by many. The conclusions of such studies have varied widely. The preponderance of literature seems to suggest that the actual incidence of carcinoma developing in association with LS is in the range of 4% or lower. Conversely, LS is often found as an associated lesion in patients with invasive vulvar carcinoma.[1]

At one time vulvectomy was the treatment of choice for LS both to relieve symptoms and to prevent the development of carcinoma. When it was realized that the risk of carcinoma was not as great as originally believed, treatment became more conservative. Corticosteroids have been used in this condition and are often a benefit topically to relieve symptoms. Unfortunately, the use of the stronger fluoridated steroids does not cause resolution of the lesions and may lead to even greater epidermal atrophy than would generally be present with the disease itself.[1] Topical testosterone has been strongly recommended by gynecologic authorities for some time for genital lichen sclerosus. Friedrich stated after review that the literature suggested a 93% response rate to testosterone.[3] This is generally prescribed as testosterone propionate 2% in Vaseline or similar vehicle. This treatment tends to reverse labial architectural changes, relieves pruritus, and restores most of the histologic abnormalities caused by the disease. The drawbacks to testosterone therapy have included the fact that it is not commercially available and must be compounded by a pharmacist. Some patients find that many applications a day are necessary in order to get satisfactory relief. Further, a number of patients will report swelling of the site and burning or irritation when testosterone is originally applied. If this frequent reaction is expected by the patient, it can be tolerated and usually subsides with time. However, a number of patients will interpret this as an allergic reaction and refuse to use the preparation any further. Treatment may need to be administered for up to 6 to 8 weeks before the maximum response occurs. A recent study reports sustained long-term control of resistant cases of LS after 12 weeks of super-potent topical corticosteroid treatment (Clobetasol), followed by p.r.n. treatment with steroids. Contact sensitization to the agent seems to be the main drawback to the therapy.[6]

In my experience the most common presentation of lichen sclerosus is the post-menopausal patient who is having vulvitis. Ordinarily this patient will have been treated in the past for a "yeast infection" or other vaginal infection more than once with no appreciable relief. Often symptoms have been present a number of years. These patients may no longer offer the complaint of vulvar itching, having concluded that physicians cannot help them. Patients who show hallmarks of the disease must, therefore, be asked whether they are having symptoms. Physical appearance of the lesions is not sufficient for making a diagnosis of lichen sclerosus. A tissue diagnosis should always be obtained by vulvar biopsy. Other clinical entities, such as squamous cell carcinoma in situ, squamous cell hyperplasia (hyperplastic dystrophy), Paget's disease and lichen planus may present with similar history and physical findings.[4] Once the diagnosis has been confirmed, treatment can be administered.

My residency training had led me to utilize topical testosterone propionate ointment for all cases of lichen sclerosus. Then, several years into my practice, a patient of mine brought me information about a form of treatment she found superior to what I was doing. While visiting Colorado Springs, Colorado, she had an opportunity to be seen by Dr. Jack Ford. He implanted a testosterone pellet for her and the patient got complete relief of her symptoms for seven months. On her return to my city, she was very insistent that I contact Dr. Ford and learn the details of the treatment method.

In talking to Dr. Ford, he related that he had, for some time, been treating patients receiving post-menopausal hormone replacement with estrogen and testosterone pellet implants. He had noted empirically that patients who had LS improved when they received this particular type of hormone replacement and reasoned that the testosterone component likely brought about the improvement. At that point, he deliberately began to select patients with lichen sclerosus to receive treatment with testosterone pellets and found that this was effective and well tolerated.[7]

I was persuaded to obtain the materials to do the testosterone pellet implant for this particular patient, and first did so in 1987. This patient continued to receive good relief of her symptoms and to prefer this method of treatment above all others. Having gotten good results in this patient, the therapy was offered to others and, as a result, I have accumulated a small base of patients receiving this therapy over the past six years.

PATIENT SELECTION

All patients had biopsy-proven LS prior to being offered this therapy. Patients were initially offered a choice of conventional testosterone ointment or implant, and some patients on oral post-menopausal hormone replacement were also offered the addition of an oral androgen to their estrogen supplement. Some patients received a pellet as their primary therapy, and some came to it after becoming dissatisfied with other methods of treatment.

METHODS AND MATERIALS

Patients were implanted with a single 75 mg. testosterone pellet available from Bartor Pharmaceutical Company in Rye, New York. Implants were done in the inguinal skin. A small skin wheal of 1% Xylocaine with Epinephrine was used and a small incision was then made allowing entry of the trocar. The pellets were displaced about 3 cm. laterally from the incision in hopes of reducing the chance the pellet would work its way back up to the skin closure. Initially the incisions were closed with a single chromic suture; but, at this time, I

close the incision with steristrips. The site of implantation is varied to the other side of the trunk each time the patient has an implant. Of a total of 36 implant procedures done, one pellet worked its way back up into the skin incision, resulting in a foreign body reaction with patient removal of the pellet. There were no other complications of insertion of pellets. The pellet insertion sites were not detectable on subsequent examination.

I recently surveyed 15 patients who had received this therapy between 1987 and 1992. Of those patients identified, all had medical records available for review. In addition, 12 of the 15 patients returned a survey form commenting on their experience with the implants. Of 15 patients treated, 87% (13) responded noticeably to the treatment with 33% (5) reporting complete relief and 27% (4) reporting substantial relief of symptoms. Two patients received significant relief of symptoms with the first implant, but did not experience the same degree of relief with subsequent implants. Of those 12 patients responding to the survey, 83% experienced relief of symptoms. Of these responders, 20% experienced relief within one week of the implant, 60% had responded by two weeks, and 40% took greater than two weeks to respond.

An index of patient satisfaction with the treatment method might ultimately be the number of patients returning to request a repeat of the implant. Of those 15 patients treated at the time of the report, 9 patients had multiple implants done, 2 patients had their implant less than six months prior to the study, and 1 patient had not experienced recurrence of symptoms as of 17 months after the first implant. One patient had decided, after the first implant, that she preferred other methods of therapy, although she did respond to the implant. The other 2 patients (20%) were the 2 patients who did not obtain any response to the initial implant. Of the 15 patients, 5 became regular users of the implants, coming in to have their implants repeated once they began to experience symptoms again. These patients, between them, had a total of 29 implants done during the study interval with an average interval between implants of 6.4 months.

Patients responding to the survey had a past history of other previous types of treatments. Of those patients answering the survey, 42% had been treated with testosterone ointment, 8% had had testosterone as a tablet or injection, 25% had been previously treated with female hormones, 17% with antibiotics or antifungals, 25% with specific dermatologic preparations such as corticosteroids, and 42% with other or unidentifiable topical treatment.

Patients were asked for their comments about what they liked about the implant therapy. Comments included being impressed with the degree of relief obtained, the fact that many patients did not require any additional therapy between implants, and that the implants were "convenient" as opposed to "messy" topical preparations. No patients reported any side effects attributable to the use of the implants.

In summary, subcutaneously implanted testosterone pellets represent an alternative to therapy of lichen sclerosus with other methods. Many patients experience substantial relief and patients tend to prefer the method because it avoids the inconvenience and messiness of multiple daily applications of topical preparation. It's been my experience that, in patients who are very symptomatic and show significant inflammation, it's necessary to also administer topical corticosteroids at first to help relieve inflammation in order to obtain a response. Also, patients who have been habitually treating themselves with multiple topical preparations may have caused as much irritation by their overtreatment as the disease itself causes and these patients are more difficult to relieve of symptoms.

REFERENCES

1. Tremain Robert, Miller Robert: *Int J of Derm* 1:10-16.
2. Rook Arthur, Ebling, FJG, Burton, JL: *Textbook of Dermatology*, 34th Ed, Blackwell Scientific Publications, Oxford/Yearbook Medical Publication, Chicago. 221-2225, 1986.
3. Friedrich Eduard G: *Vulvar Disease*. W D Sanders Co., Philadelphia. 115-130, 1976.
4. Laube Douglas W: Proceedings of ACOG District 7 Annual Meeting, St. Louis, MO. September 26, 1992.
5. Ridley CM: *British Med J* 295:1295-1296, November 21, 1987.
6. Dalziel Katherine L, Wojnarowska Fenella: Long term control of vulval lichen sclerosus after treatment with a potent topical steroid cream. *J Reprod Med* 38:25-27, 1993.
7. Ford J. Personal communication.

The Author

Dr. Wright is in private practice in Springfield, Missouri with the Smith-Glynn-Callaway Clinic. He also serves on the Obstetrics/Gynecology staffs of the Lester E. Cox Medical Center and the St. John's Regional Health Center.

For reprints contact:

Dr. Andy Wright
Smith-Glynn-Callaway Clinic
3231 S. National Ave.
Springfield, MO 65807-7396