

What wart?

Anogenital warts:

a pictorial guide to diagnosis and management

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Introduction

Genital warts are little more than a cosmetic nuisance – right? Medically speaking that's true, but you try telling someone who has just been given the diagnosis or has found some lumps and bumps, and looked up an internet site and realised they have this infection. The emotional and psychological implications of the diagnosis are often one of the most difficult things to deal with. Patients need a lot of help and considerable time and guidance in dealing with the condition and managing the therapies. The vast majority of genital warts are managed in GUM / Sexual Health clinics. Possibly up to 20% are managed in interested general practices. The location is irrelevant. It is expertise, time and sympathy that are the important factors for the patient.

The current UK estimate of genital warts is probably around 100,000 new cases per year (including general practice) and when one realises that only 1% of patients who actually get infected with the virus produce genital warts we can see that genital HPV infection is almost ubiquitous. Over 90% of clinically obvious genital warts are caused by HPV types 6 & 11. There is a vaccine available (Gardasil) that contains HPV types 6 & 11, as well as 16 & 18, and most developed countries have chosen this vaccine for the national programme in contrast to the UK who chose Cervarix which only contains types 16 & 18. This missed opportunity will ensure that genital warts continue to be a significant burden on the NHS and a large proportion of the workload of GUM clinics for the foreseeable future¹.

This book has clinical images of warts in all shapes and sizes, and how I think they are best managed. The BASHH National Guidelines are a good source of evidence and expert opinion. However, with the multitude of treatments available, competence, personal experience and patient preference often dictate which modality is used. The initial section on 'normal variations in the genital area' is very useful for clinic staff to be able to reassure patients who are convinced they have genital warts, but what they have is just a common normal variant.

I use many of these pictures on my clinic computer during consultations and hope you find them just as useful in your clinic or practice. The normal variations are reassuring and some patients with extensive/difficult warts may benefit from being shown images of patients as bad or worse, in whom we still achieve total clearance.

Treatment

Most treatment aims to remove the bulk of the wart tissue. It is postulated that damaging the wart-infected area draws the infection to the attention of the immune system which recognises the virus as foreign and mounts the appropriate response. Until immune recognition occurs, there is a risk of recurrence, and even new wart development. Previously, treatments were time consuming and required numerous clinic visits. Fortunately, there are therapies available (podophyllotoxin and imiquimod) that patients can apply in the comfort of their own home. There is a wide range of treatment available and

therapy should be tailored to the individual patient taking a number of factors into consideration, including the number and distribution of warts present, the morphology of the lesions and the patient's preference for management. Therefore, each individual patient poses a unique clinical problem, so it is neither possible nor sensible to be prescriptive about treatments.

In general, small fleshy warts on moist skin can be treated with Podophyllotoxin home therapy. If there are one or two large warts initial cryotherapy or Trichloroacetic acid (TCAA) can be used. Larger areas of infection and where warts are also on dry keratinised skin Podophyllotoxin will not work. In these cases imiquimod is required, with or without initial cryotherapy or TCAA, but treatments should not be mixed in the same session. Recurrent disease is best treated with imiquimod; with additional destructive therapy on separate occasions, guided by patient preference.

Section I: Normal variations in genital area.

Many young people only see their own genitalia. It is therefore almost impossible for young men and women to know if recent changes, new developments, colour variation and lumpy bumpy bits are, in fact, a normal variant or something they should rush to their clinic with. Indeed, in a few cases, even experienced doctors and nurses can be uncertain whether pearly penile papules or vestibular papillae are really that or early genital warts.

It is, however, a satisfying consultation to be able to totally reassure some patients that the 'lesions' they are looking at are just a normal variation or else a harmless anomaly of no significance. It is even more reassuring if they can be shown a picture, from an atlas such as this, that is identical to their condition.

Pearly penile papules

Most penises have some and some penises have a lot.

(Figure 1) These seem to develop more prominently during teenage years and can be alarming to young men.

They are completely normal glands. They will never go away and they should not be treated, even if some patients think they look ugly and are demanding something must be done.



Figure 1: normal glands on the corona glandis often called pearly penile papules

Parafrenular glands

These are normal glands that are scattered on either side of the frenulum. Often there are just three or four lined up symmetrically. However, more often there is a scattering of glands that can look suspiciously like genital warts to the inexperienced eye (Figure 2).

In darker coloured skin they can be even more dramatic (Figure 3). The glands are usually small and smooth in comparison to warts which have a rough surface.

When both are present as in figure 4, it is very important to point these out to the patient because during home treatment some patients will treat these glands thinking they are warts.

The glands, of course, will not respond to the home therapy (podophyllotoxin or imiquimod) and the patient will become disillusioned with the treatment.



Figures 2 and 3: Parafrenular glands



Figure 4:
parafrenular glands with
wart on the frenulum

Fordyce spots

These glands are scattered in clusters along the reflex prepuce, the shaft of the penis and in the vestibular area of the vulva. In some patients, these patches of glands can be extensive and can be quite dramatic, especially when the skin is stretched (Figure 5).

Figure 6 shows penile skin with many of these small glands and there is a wart for comparison.

In some patients there can be sheets of it as in figure 6, in others there are just a few small patches, as in figure 7.

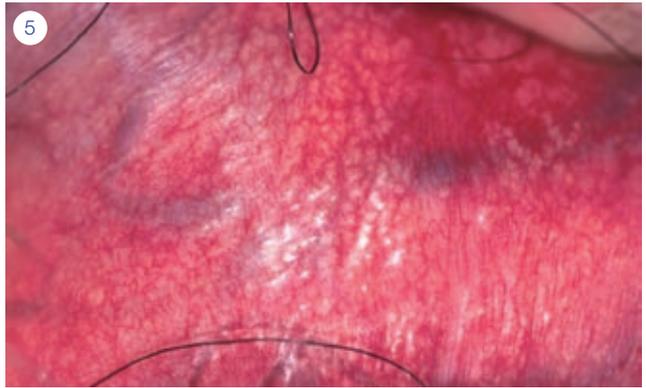


Figure 5: Fordyce spots in a male

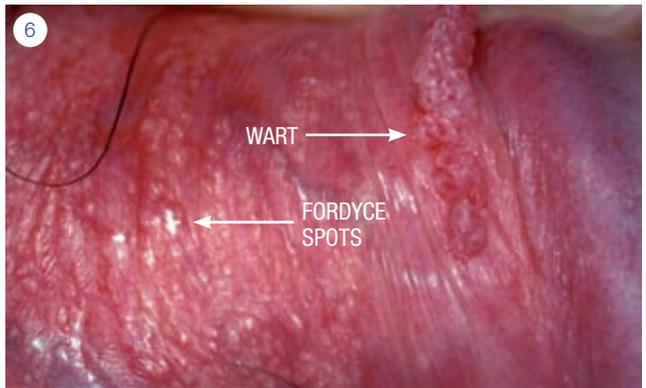


Figure 6:

Fordyce spots alongside a wart

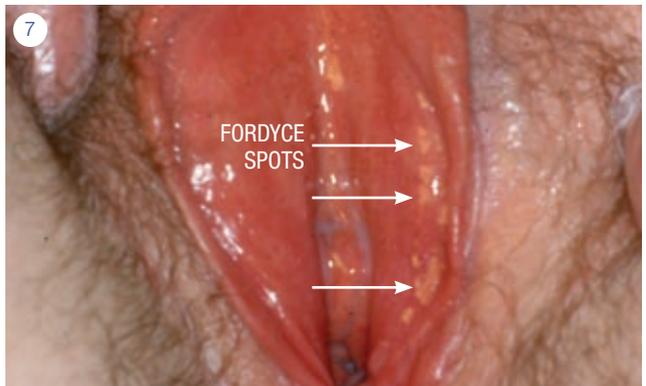


Figure 7:

small patches of Fordyce spots

Vestibular papillae

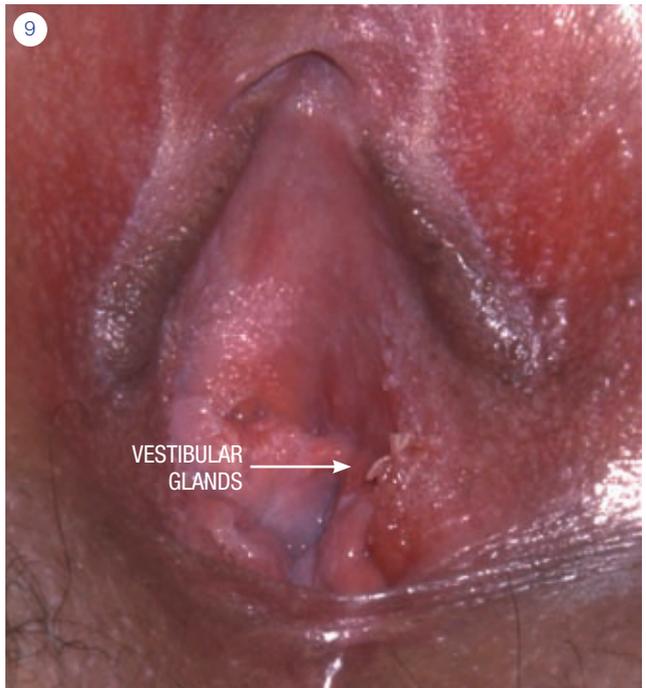
These small frond-like glands (Figure 8) can be quite confusing if they are extensive. In some patients it may be almost impossible to tell whether they are early genital warts or vestibular papillae (Figure 9).

Unlike warts, vestibular papillae are usually located in a symmetrical fashion. However, if uncertain, it's best just to wait a month or two and review.



Figure 8: vestibular papillae

Figure 9:
close-up of vestibular glands



Sebaceous cysts

These are very common in the genital area. They can be alarming. They can grow quite fast, and many patients want surgical excision of these for cosmetic reasons. In some cases, however, they can be relatively discreet, painless and even unnoticed, as in figure 10. When they are on the scrotum they can be very prominent and most men want something done (Figure 11). These, however, are quite harmless, can be left alone, other than for cosmetic reasons.



Figure 10:
sebaceous cyst female



Figure 11:
sebaceous cyst close-up view male

Lymphocele

This is a cordlike swelling that develops behind the coronal sulcus. It is a lymph channel that has become solidified. The cordlike swelling can be smooth (Figure 12) or develop knobbly lumps and cause concern over cancer (Figure 13). This can happen spontaneously or it can happen after vigorous sex or masturbation. It can be painful, so anti-inflammatory medication may be necessary i.e. Ibuprofen 400mg three times daily with food. The cordlike swelling gradually disappears and is of no consequence. Patients must be reassured that it is not a clot.



Figure 12:
lymphocele with
smooth surface



Figure 13:
lymphocele with rough
solidified surface

Conclusion

Fear and embarrassment over perceived genital anomalies is relatively common. Reassurance, delivered with authority and confidence and occasionally backed up by images such as these, is all that is needed.

Section 2: Superficially similar conditions

The following cases illustrate typical examples of conditions that have superficial similarities to warts but which have different origins.

Molluscum contagiosum

This viral infection produces multiple lesions which can be mistaken for genital warts. However, they usually occur in clusters and have a central punctation. They enucleate quite easily when scraped with a suitably broken wooden swab. Here, in figure 14, one has been removed leaving a small bleeding point, cryotherapy is also effective.

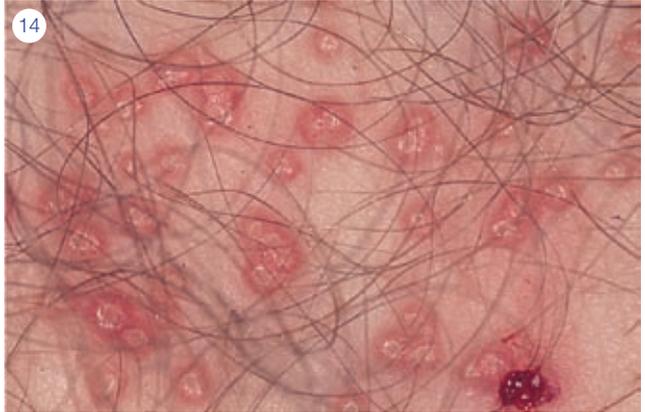


Figure 14: Molluscum contagiosum

Section 3: Malignant lesions and when to biopsy

This is all down to experience. If warts are being managed in general practice, anything that is not a completely obvious wart should be referred to sexual health. Pigmented areas, flat warts, older age group, immunosuppression and heavy smoking are all features that tilt us in sexual health towards biopsy.

Flat warts or Bowen's disease

These are often a particular problem and the attitude should be 'when in doubt, biopsy'. Bowen's disease is a pre-malignant condition that should be recognised clinically, and a biopsy done. In this case, in figure 15 on the following page, biopsy showed Bowen's disease.

Bowen's disease

This patient had a circumcision performed by a plastic surgeon with an excellent result.



Figure 15:
flat warts or Bowen's disease?



Figure 16:
Bowen's disease post-circumcision

Vulval Intraepithelial Neoplasia (VIN)

Although there are some wart-like lumps present in figure 17, on the vulva there are obvious pigmentation changes and excoriation, and biopsies from several sites here showed VIN 2-3.

Figure 17:
VIN 2-3



Section 4: Case studies

The following cases illustrate typical examples of anogenital warts and discuss treatments that are likely to bring about the fastest clearance with the least disruption to the patient's lifestyle.

Preputial warts

In this common presentation, all of the warts are of the soft, fleshy type on moist skin and would absorb topical preparations readily. Home therapy with podophyllotoxin or imiquimod would be an ideal initial therapy in this case. (Figure 18)



Figure 18:
preputial warts

Long-standing preputial warts

These have been present for some time owing to the patient's embarrassment about attending the clinic. (Figure 19). There would be several options to consider here: one might be to de-bulk the area initially with cryotherapy before prescribing home therapy such as podophyllotoxin or imiquimod. Alternatively just go straight for podophyllotoxin or imiquimod and clear any stubborn warts with cryotherapy.



Figure 19:
long-standing preputial warts

Scattered warts on the dry skin area of the penis

These keratinised warts would not usually respond well to podophyllotoxin and as there are only a few small warts, destructive therapy on the first visit might lead to a complete resolution. In this case, the patient was treated with 90% TCAA applied using a double-ended cotton bud. (Figure 20). Any TCAA that trickles onto the skin should be mopped up immediately, although with practice, the liquid can be restricted neatly to the wart area, as in figure 21. In persistent/recurrent cases imiquimod is indicated.



Figure 20: applying TCAA with a double-ended cotton bud, any inadvertent trickle can be dried up with the dry end instantly.

Figure 21: TCAA 'frosting' occurs rapidly after application.





Penile shaft warts

These are often dry and keratinised and do not respond well to podophyllotoxin. The preferred options might be TCAA or imiquimod 5% cream.

However, if the warts are small in number, as in this case, a single application of TCAA will suffice provided there are no recurrences. The picture shows the scabbing and crusting caused by TCAA five days post application.

Figure 22: penile shaft warts

Extensive penile warts

These are mainly on dry keratinised skin. In this case there are far too many for TCAA or cryotherapy, which might indeed cause some stricturing. Imiquimod was the first choice in this case and the warts resolved within weeks. Prior to imiquimod such cases often required circumcision.



Figure 23:
extensive penile warts



Vulval warts

Scattered, soft, fleshy warts in the vestibular area are a common presentation of vulval warts. They often respond to home therapy with either podophyllotoxin or imiquimod.

Figure 24:
vulval warts

Single large genital warts

Such cases are usually best treated with cryotherapy and one or two visits are usually sufficient.

Scissors excision is an option. Hyfrication or electrocautery are used by some but there is concern about inhaling plumes of viral DNA.



Figure 25:
single large genital warts

Urethral warts

Cryotherapy is the usual method of treatment and if this is extensive, patients have to be warned to keep the opposing surfaces separate or they may adhere, leading to meatal stricture.



Figure 26:
urethral wart before treatment



Figure 27:
urethral wart undergoing cryotherapy treatment



Peri-anal warts

Treatment of warts in the peri-anal area is often difficult as the patient cannot see how therapies are going. Also, cryotherapy and TCAA, and other destructive methods in this area can lead to pain and difficult hygiene.

As there is often a mixture of keratinised and non-keratinised warts, the options are for possible initial de-bulking with cryotherapy of the more peripheral larger warts. This can be followed at a later stage by imiquimod. Indeed, this home therapy could be tried as first-line treatment, depending on the patient's preference.

Figure 28:
peri-anal warts

Peri-anal and anal warts

Many patients with genital warts also have anal or peri-anal warts. (Figure 29). Anal sex is not a prerequisite for infection, the virus can track round in sweat etc. Some patients are very embarrassed and delay seeking treatment, hoping they will go away. This can result in some patients presenting with very large and difficult to treat warts. (Figure 33 and figure 34 anal warts only).

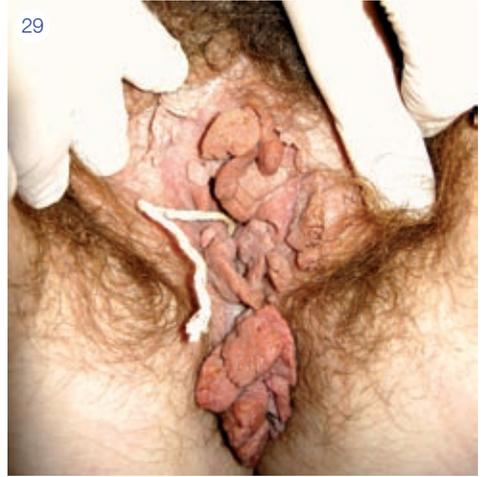


Figure 29:
vulval and anal
warts in a 19
year old



Figure 30:
needle diathermy with smoke
extractor at start of process



Figure 31:
needle diathermy with smoke
extractor near end of process



Figure 32:
3 weeks post-op

This 19 year old's teenage years had been blighted by chronic recurrent genital warts. She had even had surgery but they recurred. When I first saw her (Figure 29) I encouraged her to use imiquimod for 2 months whilst I organised surgery. Delicate needle diathermy removed or destroyed all lesions.

At 7 weeks post-op there were two small anal margin recurrences which cleared on 2 weeks of imiquimod. She remains clear, 9 months later.

Often the infection is more widespread and includes keratinised warts. Initial debulking preceded and/or followed by imiquimod is best².

Figures 35, 36 and 37 show carpet warts, is proctoscopy necessary in these cases?

Some patients will be concerned that they have felt 'lesions' inside also and they will need to be reassured one way or the other. However, there are almost always enough warts available for treatment externally to be going on with and one would hope that immune clearance would eventually clear any internal warts also.³



Figure 33:
anal warts only



Figure 34:
extensive perianal warts

HIV positive homosexual men have a higher incidence of anal cancer from infection with HPV16 and 18 and may require

detailed examination and a lower threshold for sending for biopsy of anal or perianal lesions.



Figure 35:
carpet warts, pre-treatment



Figure 36:
close-up view



Figure 37:
after 2 months' imiquimod

Vaginal warts

Usually, vaginal warts occur with vulval warts. It is possible that by eliminating the vulval warts an immune response is created leading to spontaneous clearance of the vaginal warts. However, vaginal warts can be treated at the same time, if necessary, using either TCAA or careful application of cryotherapy.



Figure 38:
vaginal warts

Cervical warts

Cervical warts are uncommon. Previously it was thought necessary to refer these patients for colposcopy, as there is often some degree of dyskaryosis associated with these lesions. However, many are caused by types 6 & 11, and the current guidelines from the British Association for Sexual Health & HIV (BASHH)⁴ do not recommend automatic referral for colposcopy. The genital wart guidelines on the BASHH website say:

“In keeping with the NHS cervical screening programme we would not recommend colposcopy in women with genital warts, including those with cervical lesions, unless there was diagnostic uncertainty or clinical concern.”

I would therefore treat the wart on the cervix (figure 39) with cryotherapy and use imiquimod for any external lesions.

Despite availability of good data, opinion varies widely on the best age to commence cervical cytology. In England it is 25, whereas in Scotland and Wales it is 20. In Finland it's 30, Australia it's 18 and in the



Figure 39:
cervical warts

United States it's any age after commencement of sexual activity.

Cervical screening under the age of 20 unearths an enormous amount of HPV infection that was destined for spontaneous regression and has never been shown to be an effective use of national resources.⁵



Figures 40/41:
warts in pregnancy

Cryotherapy

When using cryotherapy, a carbon dioxide ‘gun’ can give an accurate deep freeze.

It is essential to freeze tissue below the wart and not just the wart itself so that necrosis occurs deep to the wart tissue.

There is no substitute for experience in judging the length of the time required.

Warts in pregnancy

These can be alarming in terms of both size and the speed of growth. Podophyllotoxin is potentially teratogenic. The risk of transmission to the baby is small at 1 in 400. If infected the baby could develop laryngeal papilloma. Any intervention, i.e. caesarian section, has not been shown to be effective in preventing transmission, so probably best not to mention it – unless the woman initiates the discussion.

The effect of imiquimod during pregnancy is unknown. One option is to do nothing and reassure the woman that these warts often spontaneously resolve within 6–8 weeks post-delivery, at which point any remaining wart tissue can then be treated. If the patient wishes, treatment can be carried out during the pregnancy with either TCAA or cryotherapy.



Figure 42:
performing cryotherapy

Case study: Podophyllotoxin

Initial presentation

This patient presented with a small cluster of warts on the coronal sulcus.



Figure 43: initial presentation



After 7 days

Seven days after presentation and a three day course of Podophyllotoxin cream, the wart is whitened and disintegrating. There is also some painless inflammation in the surrounding area.

Figure 44: after 7 days



After 14 days

The skin is completely back to normal and the wart has been cleared. Some patients get inflammation, but once the treatment is stopped this resolves completely.

Figure 45: after 14 days

Section 5: imiquimod case studies.

Case study number 1.

Imiquimod Cream 5% (Aldara™) activates the body's immune response to clear genital warts. This mode of action can quickly lead to extreme erythema which, if not explained to the patient beforehand, can lead to cessation of treatment. Experience shows that the greater the erythema the more successful the outcome, although it is not a pre-requisite for imiquimod to be effective. The erythema is usually painless and can be managed by simple washing and salt baths. Many clinics use physical (ablative) therapies, as some patients psychologically like to see some of the larger warts being de-bulked.



Figure 46:
Initial presentation



Figure 47:
Early treatment response

Initial presentation

24 year old female with extensive genital warts, of 2-months' duration. (Figure 46). The largest wart areas were treated with cryotherapy on the first visit.

Early treatment response

Patient applied imiquimod cream in her own home 3 times per week. She returned to the clinic with severe vulval erythema, and with extensive warts still present. (Figures 47 and 48). The erythema indicates the area where HPV may be present.

The patient was advised to take a treatment break of 2–3 weeks and then gradually re-start. The patient started re-applying the imiquimod Cream 6 weeks later.

Successful treatment outcome

4 weeks after finishing the course the patient was reviewed, the warts had completely cleared and there was no further erythema (Figures 49, 50). Some patients and clinics get alarmed at the erythema, which can even look like a herpes infection if the reaction is intense. However it is not usually painful. It is not an allergic reaction and imiquimod can be safely resumed if necessary, when the inflammation has settled.



Figure 48:
Early
treatment
response



Figure 49:
4 weeks after
finishing course
of imiquimod



Figure 50:
4 weeks after
finishing course
of imiquimod

Case study number 2.

19 year old girl did not want any initial cryotherapy or TCAA, just wanted home treatment.

Figures 51, 52 and 53 show pre-treatment, after 5 weeks and at 3 months.

Only mild asymptomatic erythema developed and resolved on stopping treatment.

There were no recurrences.



Figure 51:
pre-treatment



Figure 52:
Imiquimod
treatment at
5 weeks



Figure 53:
Imiquimod
treatment at
3 months

Case study number 3.

Case 3 is a 35 year old male with warts on the glans penis and the prepuce. Within 3 weeks of imiquimod the warts have gone. There was slight erythema and swelling which resolved over the following week.

Some uncircumcised patients get slight oedema and tightening of the foreskin during treatment. If this is a concern the man should be told to make sure the foreskin is not left retracted for any length of time or a paraphimosis can develop.

Note the slight constriction of foreskin in figure 55. This constriction resolved within days of stopping treatment.



Figure 54:
before imiquimod treatment



Figure 55:
Imiquimod
treatment at
3 weeks

Case study number 4.

An 18 year old had been too embarrassed to attend and his warts became extensive. I tried cryotherapy on first visit but he found it excruciatingly painful.

Within 4 weeks of imiquimod treatment there was dramatic reduction (Figure 57).

Some oedema and tightness of the foreskin did develop but at 3 months all was clear.



Figure 56:
extensive glans and foreskin warts



Figure 57:
after 1 month of imiquimod



Figure 58:
slight oedema of foreskin with excoriation of glans penis



Figure 59:
all clear at 3 months

Case study number 5.

37 year old man presented with a white wart patch (Figure 60). Biopsy showed wart virus infection only. He was treated with imiquimod. The wart cleared but he developed florid lichen sclerosus needing circumcision (Figure 61).

In hindsight there were features of early LS there with slight adherence already of the prepuce. There is increasing evidence that imiquimod can exacerbate auto-immune conditions of the skin and should not be used in patients with eczema, psoriasis, lichen sclerosus, lichen planus etc.



Figure 60: unusual white patch raised concern that this might not be a wart



Figure 61: adhesions, excoriation and erythema after 3 weeks of imiquimod

Case study number 6.

This 34 year old man had penile warts. After months of other therapies he tried imiquimod three times a week and noted an improvement. He decided to apply imiquimod three times daily to speed up the process. After one week the penis became very inflamed (Figure 62).

It was not as painful as it looked and simple hygiene with salt baths was enough for complete resolution in ten days (Figure 63).

It is important to reassure patients that even severe inflammation will resolve without sequelae. It is best to resist the temptation to prescribe a steroid cream to suppress the response as this might undo the otherwise beneficial immune process.



Figure 62:
severe inflammation after excessive use of imiquimod



Figure 63:
complete resolution with
simple hygiene

Aldara™ (imiquimod) Cream prescribing information

Presentation: Aldara cream contains 5mg imiquimod per 100mg of cream.

Indications: For the topical treatment of external genital and perianal warts (condylomata acuminata) in adult patients.

Action: Imiquimod is an immune response modifier.

Dosage: Apply 3 times per week on non-consecutive days prior to sleep. Rub in a thin layer of cream on the clean wart area until the cream vanishes and leave for 6 to 10 hours. Then remove with mild soap and water. Each single-use sachet covers a wart area of 20 cm². Uncircumcised males treating warts under the foreskin should retract the foreskin and wash the area daily. Imiquimod cream treatment should continue until there is clearance of visible genital or perianal warts or for a maximum of 16 weeks per episode of warts.

Contraindications: Patients with known hypersensitivity to imiquimod or any of the excipients.

Precautions: Avoid contact with the eyes, lips and nostrils.

Imiquimod cream therapy is not recommended until the skin has healed after any previous drug or surgical treatment. It should be used with caution in patients with autoimmune conditions, organ transplant recipients or reduced haematologic reserve. Based on current knowledge, treating urethral, intra-vaginal, cervical, rectal or intra-anal warts is not recommended. Imiquimod cream therapy should not be initiated in tissues where open sores or wounds exist until after the area has healed. Imiquimod cream has the potential to exacerbate inflammatory conditions of the skin. Use of an occlusive dressing is not recommended during imiquimod therapy. Repeat treatment with imiquimod cream is not recommended in immunocompromised individuals. Imiquimod cream should be washed from the skin before sexual activity. It may weaken condoms and diaphragms, therefore concurrent use is not recommended.

Interactions: Use with caution in patients receiving immunosuppressants.

Pregnancy and lactation: No clinical data on exposed pregnancies is available. Exercise caution when prescribing to pregnant women. No advice can be given on use in lactating mothers.

Undesirable effects: Local skin reactions including erythema, erosion, excoriation, flaking and oedema were common in controlled clinical trials with imiquimod cream. Application site pruritus and pain were very common. Most skin reactions were mild to moderate in severity and resolved within 2 weeks of treatment discontinuation. Systemic side effects such as headache and influenza-like symptoms have been commonly observed in clinical trials. Infection at the treatment site has also been commonly reported.

Reports have been received of localised hypopigmentation and hyperpigmentation following imiquimod cream use. This may be permanent in some patients.

Reductions in blood cell counts have been seen in clinical trials although these are not considered to be clinically significant in patients with normal haematologic reserve. Rare reports of exacerbation of autoimmune disease and remote site dermatologic drug reactions, including erythema multiforme, have been received. Postmarketing reports of suspected alopecia during treatment of EGW have been received. There have been postmarketing reports of elevated liver enzymes.

Prescribers should consult the Summary of Product Characteristics for a complete listing of side-effects.

Special precautions for storage: Do not store above 25°C.

Basic price (UK): Carton of 12 sachets £51.32.

Legal category: POM.

Marketing authorisation number: EU/1/98/080/001.

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk.
Adverse events should also be reported to Meda Pharmaceuticals on 0845 460 0000.

Further information available from: Meda Pharmaceuticals Ltd, Skyway House, Parsonage Road, Takeley, Bishops Stortford, CM22 6PU. Tel: 0845 4600000. Fax: 0845 4600002. Aldara is a trademark of Meda AB.

Date of preparation of prescribing information: January 2009. JB2046

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Photography: All photographs were taken by Dr O'Mahony

