EASILY MISSED

Syphilitic condylomata lata mimicking anogenital warts

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, professor of primary care, Department of Primary Care Health Sciences, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at practice@bmj.com.

A 41 year old man who has sex with men visited our dermatology outpatient clinic with a three month history of non-painful anal papules. He reported protected anal contact with multiple (anonymous) male partners.

Physical examination showed perianal flesh coloured papules with a verrucous surface (fig 1). One papule showed partial ulceration. Our differential diagnosis was between human papillomavirus (HPV) associated genital warts and condylomata lata, a cutaneous manifestation seen in secondary syphilis. On histopathological examination of a lesional biopsy, immunostaining for *Treponema pallidum* showed a dense plasma-cellular infiltrate and numerous spirochetes. An HPV specific nucleic acid amplification test did not detect viral DNA in the biopsy. The diagnosis was confirmed by serological testing with a *T pallidum* specific enzyme immunoassay and the Venereal Disease Research Laboratory (VDRL) test; HIV-1 and HIV-2 serology were both negative. He was given intramuscular injections of 2.4×10^6 IU benzathine benzylpenicillin, and the lesions had disappeared completely at a follow-up visit.

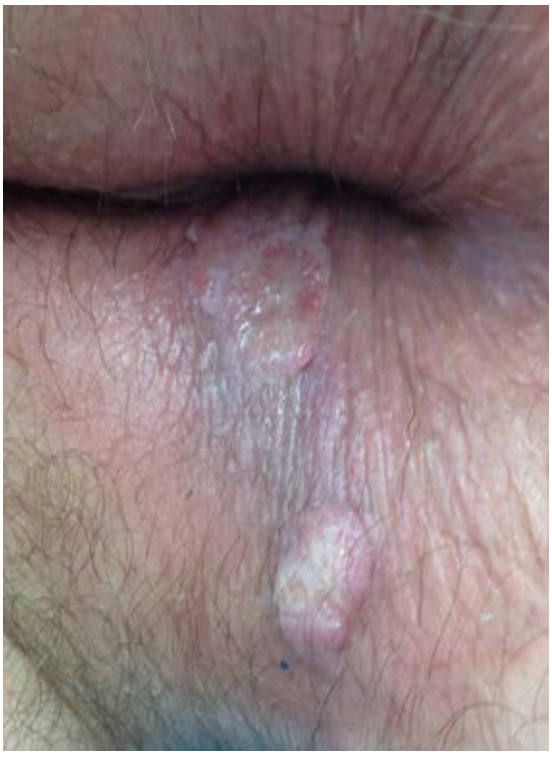

Fig 1 | Condylomata lata in a man with secondary stage syphilis characterised by verrucous hyperkeratotic perianal papules. The condylomata latum on top shows partial ulceration

What are condylomata lata?

These are one of the cutaneous signs of secondary syphilis. They reside in skin folds, such as those seen in the inguinal, perianal, and perivaginal regions and appear as flat papules with a moist, cauliflower-like or velvety surface. Moreover, they contain numerous spirochetes and are highly infectious (fig 2A).[1] They can mimic anogenital warts (condylomata acuminata), which are associated with HPV infection, and are characterised by verrucous or papilliform, pink or skin coloured papules (fig 2B).[2]

How common are they?

Between 2012 and 2013 the overall incidence of infectious syphilis in England increased by 9%—3249 cases were reported.[3] In genitourinary medicine clinics, syphilis is mainly seen in men who have sex with men, with 81% (2393/2970) of cases in men being in this group.

Why are they missed?

Because of the painless nature of condylomata lata patients can easily miss these lesions, especially if they are located at an internal site such as the anus, vagina, or mouth. Moreover, they can easily be mistaken by doctors for another dermatological condition such as anogenital warts (fig 2B), bowenoid papulosis, HPV induced anal intraepithelial neoplasia, or skin tags.[4]

Why does this matter?

Misdiagnosis delays adequate treatment and results in ongoing transmission to sex partners. Syphilis is treated completely differently from genital warts. If untreated, syphilis can have irreversible consequences, including neurosyphilis (such as syphilitic meningitis and cerebrovascular disease) and cardiovascular disease (such as aortic valve destruction).

How are they diagnosed?

Clinical

Condylomata lata are characteristic of secondary syphilis. By contrast, the primary stage of syphilis is characterised by a small painless, indurated ulcer, typically with rolled edges, which is accompanied by regional lymphadenopathy. Secondary syphilis can present with a variety of symptoms, most often a maculopapular rash, but also

THE BOTTOM LINE

- Condylomata lata are a cutaneous manifestation of secondary syphilis and can be misdiagnosed as genital warts
- Prompt diagnosis and treatment with intramuscular benzathine benzylpenicillin are needed to prevent serious neurological complications (such as syphilitic meningitis and cerebrovascular disease), cardiac complications (such as aortic valve destruction), and ongoing transmission
- Initial diagnostic tests includes an anti-treponemal serological assay and an anticardiolipin test
- Once condylomata lata are suspected, refer promptly to a specialist centre such as a sexual health clinic or to a (dermato-)venereologist for further investigations (including sexually transmitted infection screen), treatment, contact tracing, and follow-up

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- Posterior shoulder dislocations (*BMJ* 2015;350:h75)
- Lung cancer (*BMJ* 2014;349:g6560)
- Nasal septal haematoma (*BMJ* 2014;349:g6075)
- Pancreatic cancer (*BMJ* 2014;349:g6385)
- Perthes' disease (*BMJ* 2014;349:g5584)

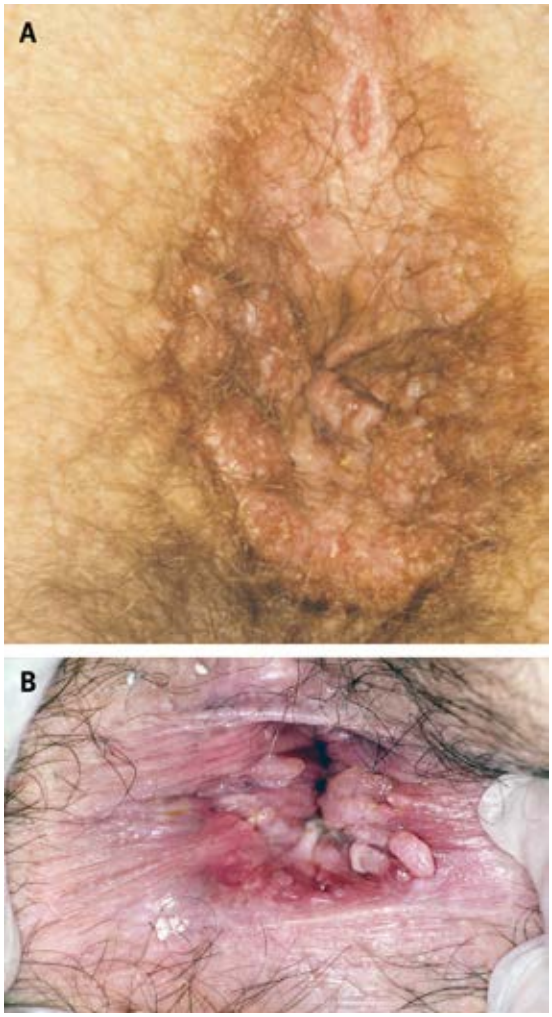

Fig 2 | (A) Perianal condylomata lata with a typical verrucous aspect. (B) Perianal and intra-anal genital warts characterised by verrucous papules

alopecia, leucoplakic or erythematous lesions on oral mucous membranes, and perianal or perivaginal condylomata lata.

Investigations

A clinical suspicion of syphilis is initially confirmed by serology, using an anti-treponemal serological assay (for example, the *T pallidum* enzyme immunoassay, which is usually reported as positive or negative or as a semi quantitative index; or the *T pallidum* haemagglutination assay (TPHA)) and an anticardiolipin test (such as the VDRL test, reported as titre). In primary syphilis, serological tests can be falsely negative in the window phase, so serology may need to be re-evaluated after several weeks; the TPHA and VDRL tests have 70.4% and 74.9% sensitivity, respectively. In secondary syphilis serological testing is highly sensitive—98.6% and 97.4% for TPHA and VDRL tests, respectively[5]; VDRL also usually shows a high titre (>1:16).

In specialist clinics, dark field microscopy may be used to diagnose ulcerative primary stage lesions and condylomata lata, by visualising *T pallidum* in lesional exudate. This is a cheap and quick diagnostic method but requires a specialised microscope and expertise.

To differentiate syphilitic condylomata from HPV induced manifestations, such as genital warts or bowenoid papulosis, a biopsy is needed for histopathological examination. A dense plasma cell infiltrate and numerous spirochetes visualised by immunostaining confirm condylomata lata. Numerous nucleic acid amplification tests to detect *T pallidum* have been developed in house but are not available routinely. These tests are highly specific and sensitive in the diagnosis of primary syphilis, irrespective of the serological window phase.[6]

How are they managed?

It is advisable to refer patients suspected of having syphilis to a specialised setting, such as a sexual health or infectious diseases clinic, or to a (dermato-)venereologist, where additional investigations and treatment are readily available and contact tracing and follow-up can be offered.

The primary, secondary, and early latent stages of syphilis can easily be treated with a single intramuscular 2.4×10^6 IU dose of benzathine benzylpenicillin. Patients diagnosed as having syphilis should always undergo tests for other sexually transmitted diseases, including HIV and hepatitis B serology, and nucleic acid amplification testing of urine, vaginal, anorectal or pharyngeal swabs (depending on the patient's sexual practices) for chlamydia and gonorrhoea. Furthermore, partner notification is needed to prevent transmission, although this may be a problem when sexual contacts are anonymous.[7] Men who have sex with men who often have new or casual partners are advised to be screened for sexually transmitted infections and HIV every three months.[3]

CPD/CME

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10-MINUTE CONSULTATION

Foot drop

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This is part of a series of occasional articles on common problems in primary care. *The BMJ* welcomes contributions from GPs.

A 42 year old healthy female yoga instructor consults with frequent stumbling and numbness of the upper side of her left foot. She has no pain or other symptoms.

What you should cover

Foot drop (weakness of the dorsiflexion muscles in the foot) is common, causes difficulty in walking, and greatly increases risk of falling. Spontaneous unilateral foot drop usually has a peripheral cause. The lesion can be in the L5 nerve root, sciatic nerve, common peroneal nerve, deep peroneal nerve, or superficial peroneal nerve (figure). The extent of the sensory or motor deficit depends on the location (or level), severity, and duration of the injury or compression.[1]

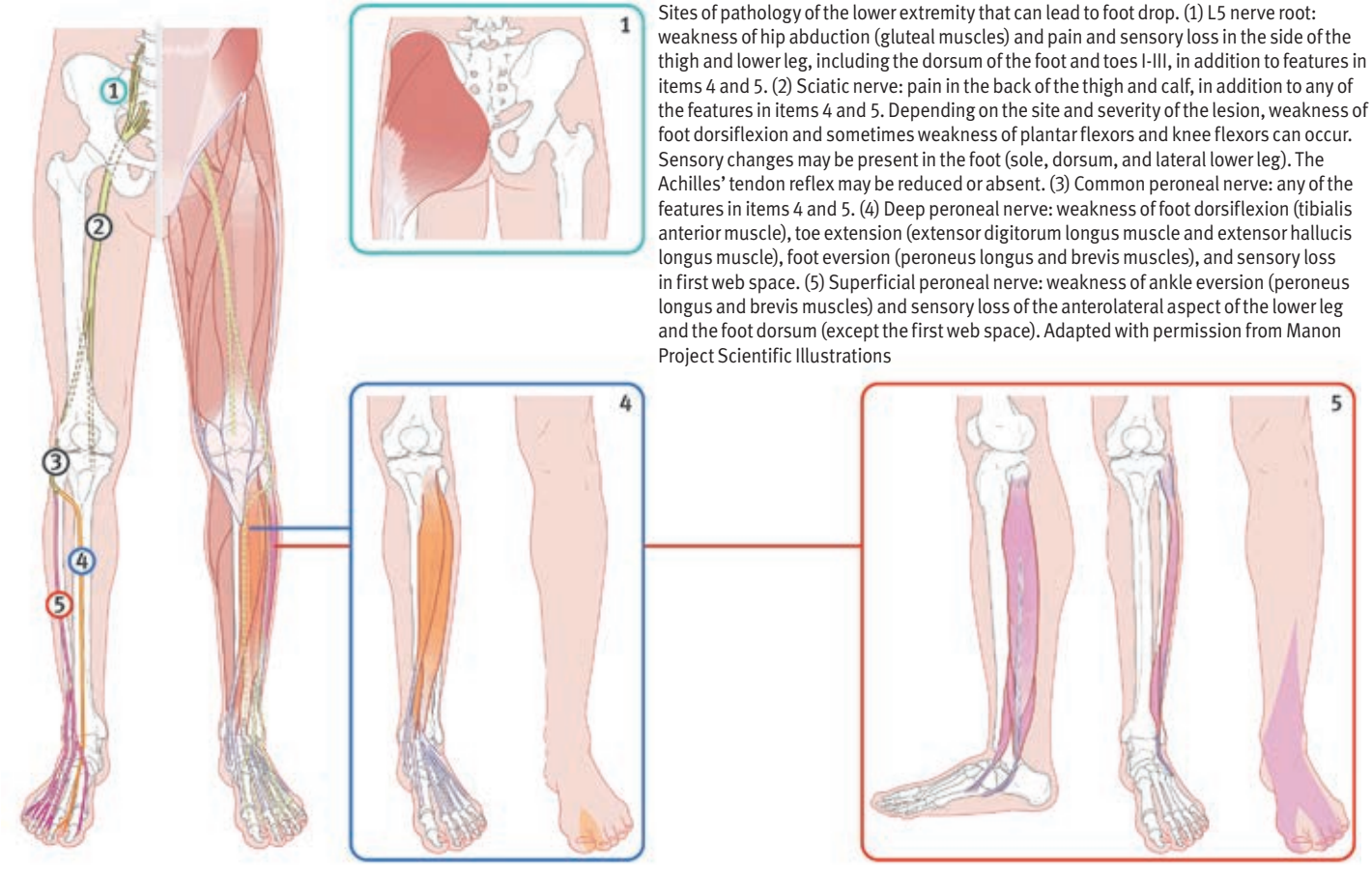
The most common cause of spontaneous foot drop is peroneal neuropathy, often as a result of compression at the neck of the fibula at knee level, where the common peroneal nerve is covered only by skin and subcutaneous tissue. Less often, foot drop is caused by L5 radiculopathy or polyneuropathy and much less often by sciatic neuropathies, lumbar plexopathies, mononeuritis multiplex, or myopathies. Central causes (such as cerebral ischaemia), anterior horn cell diseases, cauda equina compression, and muscle dystrophy are rare and usually produce other symptoms.[2]

THE BOTTOM LINE

- Consider isolated peroneal neuropathy as the most likely cause of foot drop in patients with weakness of foot dorsiflexion and eversion; sensory loss of the anterolateral aspect of the lower leg and the foot dorsum; normal reflexes; no pain swelling, or erythema of the leg; and no other neurological features
- Offer conservative treatment in unilateral foot drop caused by isolated peroneal neuropathy, but refer patients with acute bilateral foot drop, one sided foot drop with fasciculations, or more widespread neuropathy to a neurologist

Medical history

Because external pressure is the most common cause of peroneal neuropathy, ask about habitual leg crossing, habitual or prolonged squatting or kneeling (may be work related), confinement to bed, use of leg brace or recent plaster cast below the knee, use of leg positioning or leg supports during recent surgery, or other causes of compression at the fibular neck.



Sites of pathology of the lower extremity that can lead to foot drop. (1) L5 nerve root: weakness of hip abduction (gluteal muscles) and pain and sensory loss in the side of the thigh and lower leg, including the dorsum of the foot and toes I-III, in addition to features in items 4 and 5. (2) Sciatic nerve: pain in the back of the thigh and calf, in addition to any of the features in items 4 and 5. Depending on the site and severity of the lesion, weakness of foot dorsiflexion and sometimes weakness of plantar flexors and knee flexors can occur. Sensory changes may be present in the foot (sole, dorsum, and lateral lower leg). The Achilles' tendon reflex may be reduced or absent. (3) Common peroneal nerve: any of the features in items 4 and 5. (4) Deep peroneal nerve: weakness of foot dorsiflexion (tibialis anterior muscle), toe extension (extensor digitorum longus muscle and extensor hallucis longus muscle), foot eversion (peroneus longus and brevis muscles), and sensory loss in first web space. (5) Superficial peroneal nerve: weakness of ankle eversion (peroneus longus and brevis muscles) and sensory loss of the anterolateral aspect of the lower leg and the foot dorsum (except the first web space). Adapted with permission from Manon Project Scientific Illustrations

PATIENT INFORMATION

NHS Choices. Foot drop. www.nhs.uk/conditions/foot-drop/Pages/Introduction.aspx

Mayo Clinic. Foot drop. Lifestyle and home remedies. www.mayoclinic.org/diseases-conditions/foot-drop/basics/lifestyle-home-remedies/con-20032918

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- High INR on warfarin (*BMJ* 2015;350:h1282)
- Teenagers with back pain (*BMJ* 2015;350:h1275)
- Pain at the base of the thumb (*BMJ* 2015;350:h182)
- The drooling child (*BMJ* 2015;350:h38)
- Gastro-oesophageal reflux disease in children: NICE guidance (*BMJ* 2015;350:g7703)

Ask about other precipitating factors for peroneal mononeuropathy: recent weight loss ("slimmer's palsy"), overstretched peroneal nerve (owing to ankle strain or prolonged leg stretching), and masses in the popliteal space (for example, Baker's cysts). Check medical history for other causes of neuropathy or mononeuritis multiplex (although these are less likely if symptoms are sudden or isolated), such as diabetes, alcohol misuse, vitamin B_{12} deficiency, or chemotherapy.

Exclude direct injury as a result of acute trauma (such as fibula neck fracture) or surgery. Hip arthroplasty can injure the sciatic nerve, mimicking a peroneal neuropathy. Foot drop is usually seen immediately after injury, but it appear after several days.

Ask about other weakness or sensory problems of the leg(s), lower back, or arms. If foot drop is painless and not accompanied by other neurological symptoms, it is almost always caused by peroneal mononeuropathy. Painful foot drop may suggest L5 radiculopathy, trauma, lumbar plexopathy, or mononeuritis multiplex.

What you should do

Physical examination

Observe the patient's gait. A high stepping gait (to prevent the foot from dragging) is a sign of severe weakness of the dorsiflexion muscles. Examine the patient while he or she is walking on the heels and toes. Peroneal neuropathy will cause difficulty walking on the heel of the affected leg.

Inspect the legs. Look for swelling and erythema, which may be present after trauma and may suggest compartment syndrome. Look for fasciculations in legs and arms, which can suggest a more extensive neurological problem (such as motor neurone disease).

Check for reduced pain (pin prick) sensation and light touch in the (lower) legs and feet. Sensory abnormalities only in the first web space suggest a deep peroneal nerve lesion, whereas those only in the anterolateral aspect of the lower leg and the foot dorsum suggest a superficial peroneal nerve lesion (figure).

Assess strength of:

- Foot dorsiflexion and eversion (peroneal nerve)
- Foot plantar flexion and inversion (tibial nerve)
- Hip abduction (superior gluteal nerve, L5 nerve root).

Weakness of hip abduction may differentiate lumbar L5 radiculopathy from peroneal neuropathy (no weakness), with a positive predictive value of 95% and negative predictive value of 90%.[3]

Check knee and Achilles' tendon reflexes and plantar response, because hyper-reflexia and Babinski's sign indicate an upper, rather than lower, motor neurone lesion.

Palpate the course of the common peroneal nerve for local tenderness and Tinel's sign (lightly tap over the nerve at the fibular head; tingling or "pins and needles" in the nerve distribution indicates a lesion here). Check the popliteal space for masses and refer for imaging if necessary.

In isolated peroneal mononeuropathy, only foot dorsiflexion or eversion (or both) will be weak; reflexes will be normal; and there will be no leg pain, swelling, or erythema. Consider electromyography or nerve conduction studies to confirm this working diagnosis.

Advice and treatment

Refer immediately to a neurologist if foot drop is acute and bilateral, or within one week if unilateral foot drop is accompanied by fasciculations or widespread neuropathy. Refer urgently to a surgeon if compartment syndrome is suspected.

If local nerve compression at the knee is the cause, explain that this can cause weakness of the muscles that lift the foot and toes, and thus foot drop or a "floppy foot." Advise the patient to avoid leg crossing, squatting, and kneeling. Symptoms caused by these activities usually resolve in two to three months.

Recommend flat shoes that support the ankles to prevent ankle sprain. Depending on the severity of foot drop and the patient's condition, consider an ankle foot orthosis to support the foot while walking and to reduce risk of falling.

Consider physiotherapy for specific muscle training if weakness is severe.

Ask the patient to return for review in two months and refer to a neurologist if the foot drop has not improved.

ANSWERS TO ENDGAMES, p 43 For long answers go to the Education channel on thebmj.com

ANATOMY QUIZ

Axial T1 weighted magnetic resonance image through the upper thorax in a 20 year old woman

A: Trachea
B: Aortic arch
C: Medial right clavicle
D: Left pectoralis minor muscle
E: Left pectoralis major muscle
Chest wall anomally is Poland Syndrome

STATISTICAL QUESTION

Measuring the benefit of treatment: number needed to treat

Statement *b* best describes the NNT.

CASE REVIEW A 77 year old man with asthma and renal impairment

1 In view of the history of asthma and nasal polyposis, eosinophilia, and severe renal impairment, the likely diagnosis is eosinophilic granulomatosis with polyangiitis (EGPA formerly Churg-Strauss syndrome) with renal involvement.
2 EGPA is a multisystem disorder and assessment for neurological, gastrointestinal, and cardiac involvement is required. An autoimmune screen, including anti-neutrophil cytoplasmic antibodies (ANCA), is indicated. Diagnosis requires renal biopsy. Histology showed crescentic glomerulonephritis, segmental necrosis, and interstitial inflammation with an eosinophilic infiltrate, characteristic of EGPA renal disease.
3 EGPA typically responds well to steroids but more severe cases may require cyclophosphamide. Steroid sparing agents such as azathioprine and methotrexate can be used to maintain remission. Small scale studies suggest a role for the novel agents, rituximab and mepolizumab, in the management of refractory disease.
4 Overall prognosis in EGPA is favourable, with remission in 90% of patients, and five year survival exceeding 90%.