CASE REPORT

Syphilis: an unusual manifestation?

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SUMMARY

Syphilis is a widely investigated infectious venereal disease with varied presentations frequently mimicking other diseases. It progresses in distinct, well-characterised stages: early (primary and secondary), latent, and late (tertiary), each stage having its own unique presentations. However, there has been increasing evidence of atypical presentations. We describe one such presentation of early syphilis in its secondary stage. A man in his late 20s presented with a rash (which is typical of the secondary stage) and with bone pain with multiple lytic lesions (which is rare in the secondary stage but more typical of the tertiary stage). The patient was successfully treated for secondary syphilis. On the basis of our case, and on analysis of other case reports and research of early-stage syphilitic bone involvement, we conclude that the true incidence of bone involvement in early-stage syphilis may be higher than has been previously appreciated, and thus may be under-recognised and underdiagnosed.

BACKGROUND

Syphilis is an infectious venereal disease caused by the spirochete *Treponema pallidum* entering the blood stream, through which it can spread to all organs. Consequently, the disease presentation can be extremely varied and can mimic that of many other diseases. Thus, syphilis has rightfully earned its classical designation as one of 'the great imitators', reflecting a wide variety of symptoms and presentations, which can cause difficulties in diagnosis. However, once diagnosed, it can now be cheaply and easily treated, avoiding its well-known, long-term devastating complications.

The disease is divided into early, latent and late stages. The early stage is divided into a primary stage, usually marked by chancre development, and a secondary stage, marked by varied systemic manifestations. These commonly include a rash of the trunk and extremities, involving the palms and soles, the oculo, alopecia and other systemic symptoms; arthralgias and periostitis are less commonly observed.

In the latent phase, which can last for many years, the symptoms disappear, and the disease is detectable only by serological tests. However, this is a chronic progressive stage with ongoing inflammation leading to the tertiary (late) stage, characterised by several severe complications. Neurosyphilis results from spirochetal invasion of the central nervous system causing meningitis, meningovascular neurosyphilis and parenchymatous neurosyphilis. Cardiovascular syphilis is characterised by the involvement of large arteries including the aorta, while gummatous syphilis is marked

by nodular granulomatous lesions (gummas), which can affect the bones and skin throughout the body. While syphilitic musculoskeletal involvement is relatively well described in tertiary syphilis (ie, gummatous involvement), bone lesions have been considered highly unusual in the secondary stage, other than osteitis, osteomyelitis and osteoperiostitis, which have been described in this context.¹⁻⁶ In addition to tertiary syphilis, skeletal manifestations are more frequent in congenital syphilis. In pregnant women who have syphilis, after 14 weeks, spirochetes may cross the placental barrier vertically and infect the fetus. Congenital syphilis commonly involves the skeletal system and usually affects the tubular bones (mostly in the upper arm, eg, humerus) in a symmetrical diffuse involvement. We report a case of secondary syphilis presenting with multiple lytic bone lesions and weight loss in a male HIV-negative patient in his late 20s.

CASE PRESENTATION

A man in his late 20s was admitted to hospital due to weight loss and bone pain of 2 months duration. The pain started at the anterior aspect of the left shin and subsequently involved additional locations including the upper forehead, the left shoulder joint and the left lower ribs. He described a weight loss of 6 kg over this period. In addition, he reported a diffuse rash involving the torso, hands and feet, without genital, anal, perianal or oral involvement, and with no ulceration.

The patient was a schoolteacher. He was unmarried and denied unprotected sexual intercourse but reported multiple partners.

On physical examination, the patient was afebrile and appeared in generally good condition. Bony protrusions, with soft tissue swelling and tenderness were demonstrated in multiple sites: left shin, shoulder, chest and frontal area of the skull. The skin showed a rash on the lateral side of the trunk containing dull pink macules with sharp borders. Red nodules with clear demarcation were observed on the genitalia and on the soles of the feet. No other pathological findings were observed on physical examination.

Laboratory tests were unexceptional, including normal complete blood count, biochemistry, coagulation profile, immunological profile and thyroid markers, and negative serology for HIV, HBV and HCV. The only notable finding was an elevated C reactive protein of 30.

The four strongest differential diagnoses were (1) metastatic bone disease with paraneoplastic rash, (2) lymphoma, (3) syphilis and (4) primary bone disease. Other infectious, rheumatological and metabolic diseases appeared less likely in the light

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of the history and physical examinations. Serological markers for syphilis, venereal disease research laboratory (VDRL) and *T. pallidum* haemagglutination assay (TPHA) were taken. Pending these results, lytic bony metastases were considered the most probable diagnosis.

While a differential diagnosis of syphilis was initially entertained, a number of factors made this possibility appear less likely. The patient was too young for tertiary syphilis, and the rash was not typical of that presentation. Although the patient had a rash which could have been compatible with secondary syphilis, he did not report chancre or a history of syphilis in the past, or risk factors for syphilis such as HIV positivity or male sex with male (MSM) partners. In addition, as noted above, bone involvement is considered unusual in secondary syphilis. There is evidence of atypical presentations of chancre, such as multiple chancres and/or extragenital sites, for instance on the lips, mouth, fingers and buttocks. Nevertheless, in our case, the red nodules on the genitalia did not have the morphological appearance typical of a chancre. In addition, the rash distribution on the lateral aspect of the trunk, in combination with the bone manifestations mentioned above, makes an atypical presentation of primary syphilis unlikely.

Keeping the above in mind, additional investigations were carried out. Bone scintigraphy exhibited an uptake in the left proximal tibia, left 11th rib and right parietal bone. Total body CT, including CT of the head, cervix, shoulder, chest, abdomen and thigh, revealed a 9×6×18 mm, sharp bordered lytic bone lesion in the anteriolateral aspect of the left proximal tibia, with periosteal reaction and no penetration (figure 1).

Another lytic lesion with periosteal reaction was demonstrated at the left acromioclavicular joint (figure 2).

In addition, there was a lucent irregular 10×19 mm lytic lesion involving the left 11th rib, with a pathological fracture and peripheral enhancement (figure 3).

An additional sclerotic lytic lesion was observed adjacent to the left sacroiliac joint (figure 4).

No significant lymphadenopathy was observed, but small lymph nodes were demonstrated in the retroperitoneum. Mild splenomegaly (14 cm) was also demonstrated.

Figure 1 CT scan of the left proximal tibia shows a subcortical lytic lesion with a small soft tissue component. An aggressive-appearing periosteal reaction surrounds the lesion.

Figure 2 Oblique reconstruction of a left clavicle CT shows a lytic lesion at the distal clavicle, with a small sclerotic nodule within.

At this stage, after revision of the findings on CT, the primary diagnosis suggested by the bone radiologist was Langerhans cell histiocytosis (LCH); other possibilities compatible with the appearance of the bone lesions, which were considered less likely, included lymphoma and other bone metastasis.

As the results of the CT examination became available, additional imaging modalities were being contemplated (eg, positron emission tomography CT); at this stage, however, results of seriological tests for syphilis were received. These showed a positive VDRL test at a titre of 1:32 and a positive TPHA.

In reanamnesis, the patient had not taken antibiotic treatment prior to hospitalisation, which could have changed the course of the disease to lead to an unusual manifestation as in this case.

Skin biopsy results became available several days later and showed mild superficial perivascular dermatitis with scattered plasma cells. According to the pathological report, 'the findings are not definitely diagnostic but may represent secondary syphilis'.

TREATMENT

On the basis of the clinical presentation and the serological results, a diagnosis of syphilis was confirmed and treatment with penicillin was started according to the Center for Disease Control (CDC) guidelines and the stage of the disease. During this treatment, the patient suffered a classical Jarish-Herxheimer reaction, which was dealt with by administration of fluids.

OUTCOME AND FOLLOW-UP

Within 24 h of treatment initiation, complete resolution of the rash was observed and the bone pain had virtually vanished.

Figure 3 A lytic, slightly expansile lesion in the 11th left rib.

Figure 4 Pelvic CT demonstrates a mixed lytic and sclerotic lesion at the left ileum near the sacroiliac joint.

Four weeks later, the patient reported that he had returned to his normal working life, and had experienced no repetition of his previous medical symptoms. A follow-up physical examination showed a return to his normal weight, with no evidence of rash and no skeletal tenderness.

DISCUSSION

Bone lesions such as osteitis, osteomyelitis and osteoperiostitis have been considered rare in secondary syphilis. When they do occur at this stage (as in our case), the mechanism of injury is considered to involve spirochetal invasion of periosteal vascular beds, leading to inflammation and granulation tissue formation. The extension of this inflammation into the haversian canals causes osteitis and osteomyelitis, most commonly in the tibia and skull,⁵ as in the case of our patient, in which there were multiple lytic and sclerotic lesions including the tibia, clavicle, 11th rib and pelvis.

On the basis of the following points, early stage syphilitic bone involvement may be an under-recognised (and underdiagnosed) manifestation of this protean disease.

First, the most comprehensive study on bone-destructive involvement in early syphilis, which has been widely quoted since its publication in 1942,⁷ was carried out by Reynolds and Wasserman at Johns Hopkins Hospital between the years of 1919 and 1940. This study reported only 15 cases (0.15%) of bone-destructive lesions out of a total of 10 000 cases of early syphilis, laying down the platform for the conception that bone lesions are extremely rare in early-stage syphilis (primary and secondary). However, a 1952 study by Thompson and Preston⁸ reported that 9% (7 of 80) of patients with secondary syphilis had cranial lesions. Although this study included only 80 patients, the vast difference in percentages (0.15% vs 9%) nevertheless needs to be explained.

One explanation could be that until the 1932 report of Nitchew,⁹ there had been no recorded X-ray observations of patients, suggesting that cases of early bone-involvement syphilis may not have been identified. Obviously, even the introduction of X-ray examinations could not compare with the vast array of imaging modalities subsequently developed (CT, MRI, bone scans etc), which undoubtedly acted to increase the diagnostic

yield and the likelihood of detecting previously unrecognised bony involvement. Thus, despite the overall decline in the incidence of syphilis during the past decades, there have been more frequent reports regarding skeletal involvement in early syphilis.^{1–6 10–12} This may imply that the true incidence of bone involvement in early-stage syphilis may be higher than had previously been appreciated. More specific investigation of the true incidence of such involvement, implementing state-of-the-art imaging modalities, is thus called for.

In conclusion, we present a case of extensive lytic bone lesions as part of the presenting symptoms of syphilis. While this presentation, including its appearance on imaging, is not usually considered a typical part of the clinical spectrum of early syphilitic infection, dogma on this point may be dated and indeed outdated. Even in the 21st century, syphilis continues to be a great imitator, and a high index of suspicion must be kept for this classical (and highly treatable) diagnosis in the appropriate clinical set-up.

Learning points

- Syphilis is an infectious venereal disease caused by the spirochete *Treponema pallidum* entering the bloodstream, through which it can spread to all organs. Hence the disease has varied presentations frequently mimicking other diseases. When making a differential diagnosis, syphilis should be considered.
- Syphilis is a treatable disease. One can prevent devastating consequences by treating it.
- Bone involvement in secondary syphilis appears to be much more common than is thought to be the case, but more investigations should be carried out.

Contributors SB and JA wrote the manuscript. JA and GJ participated in the patient management and diagnosis and reviewed the manuscript. GF reviewed the rentgenological findings.

Competing interests None.

Patient consent Obtained.

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