

A Case of Misdiagnosed Cervical Syphilis

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Abstract

Syphilis is a chronic, systemic sexually transmitted disease caused by *Treponema pallidum*. This article reports a case of cervical syphilis with ulcerative cervical swelling and multiple lymphadenopathy. The 33-year-old female patient was diagnosed with "irregular vaginal bleeding". Gynecological examination, imaging and pathology all pointed to cervical cancer or cervical lymphoma. Specialist physical examination: Gynecological examination: vaginal patency, cauliflower-like swelling of the cervix, size 5.4*4.8 CM, ulcerated surface, easy to bleed when touched. Laboratory examination showed that the titer of nonspecific serum test for syphilis was 1:32, and the test for syphilis-specific antibody was positive. Further physical examination showed that multiple clustered reddish-brown papules were found on the +shoulders and back. The diagnosis was cervical syphilis. After 3

weeks of treatment with benzathine penicillin, the cervical swelling and swollen lymph nodes subsided. This case suggests that cervical syphilis with systemic reactive lymph node hyperplasia can be easily misdiagnosed as cervical cancer or cervical lymphoma. It highlights the importance of careful observation of typical symptoms and multidisciplinary collaboration, as well as the necessity of excluding other diseases during the diagnosis process.

Keywords: Cervical syphilis; Diagnosis; Cervical cancer; Cervical lymphoma

Introduction

Syphilis is a chronic systemic sexually transmitted disease caused by *Treponema pallidum* that can cause damage to multiple systems and organs in the human body [1]. *Treponema pallidum* can cause infection at any contact site on the human

body. About 25% of patients with untreated primary syphilis will develop systemic lesions, namely secondary and tertiary syphilis [2]. Secondary syphilis often presents with systemic symptoms, such as syphilitic rash, chancre, multiple sclerotic lymphadenitis, flat warts, ocular syphilis, and visceral syphilis [3]. Cervical syphilis refers to syphilis lesions located in the cervix, which is rarely reported in my country. Its main manifestations are cervical tumors, vaginal bleeding, increased secretions, etc., and the trunk and limbs may be combined with maculopapular rash, herpes and other skin changes. Vaginal examination, gynecological ultrasound and magnetic resonance imaging are all suspected of cervical cancer. Syphilis serological tests and Treponema pallidum antibody immunohistochemical staining can confirm the diagnosis [4]. The author reports a case of cervical syphilis with systemic reactive lymph node hyperplasia in order to improve the diagnosis and treatment of patients with cervical syphilis by clinical physicians.

Case Presentation

Chief complaint, current medical history and physical examination

The patient is a 33-year-old female. She was admitted for "irregular vaginal bleeding for 1 month". The patient had vaginal bleeding without obvious cause since October 2023. It was initially bloodshot and then bright red blood. The amount was small and she was not treated. She was healthy in the past, had no history of chronic diseases, and had a history of

unclean sexual contact. Physical examination: body temperature 36.6°C, pulse 87 times/min, respiration 20 times/min, blood pressure 110/80 mmHg (1 mmHg=0.133 kPa). She was conscious, with multiple clustered reddish-brown papules on the shoulders and back, some of which had surface exudate, accompanied by itching, no pain, and enlarged lymph nodes could be touched in the neck and bilateral groins. They were tough, with clear borders and good mobility. The breath sounds of both lungs were clear, and no obvious dry or wet rales were heard. The heart rate was 87 beats/min, and the heart rhythm was regular and without murmurs. The abdomen is flat and soft, with no obvious tenderness in the whole abdomen, the liver and spleen are not palpable under the ribs, and there is no edema in both lower limbs. Specialist examination (gynecological examination): The vulva is normally developed, the vagina is unobstructed, dark red blood can be seen in the vagina, the vaginal wall folds exist and there is no contracture, there are no nodules in the vaginal wall, the anterior vaginal fornix is shortened, and a cauliflower-like mass can be seen at the cervical opening (Figure 1), which is about 5 cm*5 cm in size and has a brittle texture. There is active bleeding at the cervical opening and the mass, and there is no cervical pain. The uterus is anterior, enlarged as if it is 4 months pregnant, medium in texture, with normal mobility, no tenderness, no masses are palpable in the bilateral adnexal areas, and no tenderness. Triple diagnosis: No shortening or nodules are palpable in the bilateral aortosacral ligaments.



Figure 1. Gynecological examination revealed a cervical cauliflower-like mass

Imaging, laboratory tests and diagnosis and treatment process

PET/CT examination showed: 1. Irregular soft tissue mass of cervix, about 48 mm×25 mm×41 mm in size, SUVmax about 17.3, unclear boundary with rectum, cervical cancer is considered; 2. Multiple small/enlarged lymph nodes in the neck (left II-V area, right II-III group), mediastinum, left internal mammary area, liver portal area, retroperitoneum, bilateral iliac vessels, presacral and

bilateral groin, SUVmax about 19.5, metastasis is considered; 3. Splenomegaly (**Figure 2A and B**). MR enhancement of lower abdomen showed cervical mass, continuous low signal band of cervical matrix, clear cervical os structure, relatively uniform enhancement; multiple slightly larger/enlarged lymph nodes beside abdominal aorta, bilateral iliac vessels, presacral; splenomegaly, lymphoma is considered comprehensively (**Figure 2C**).

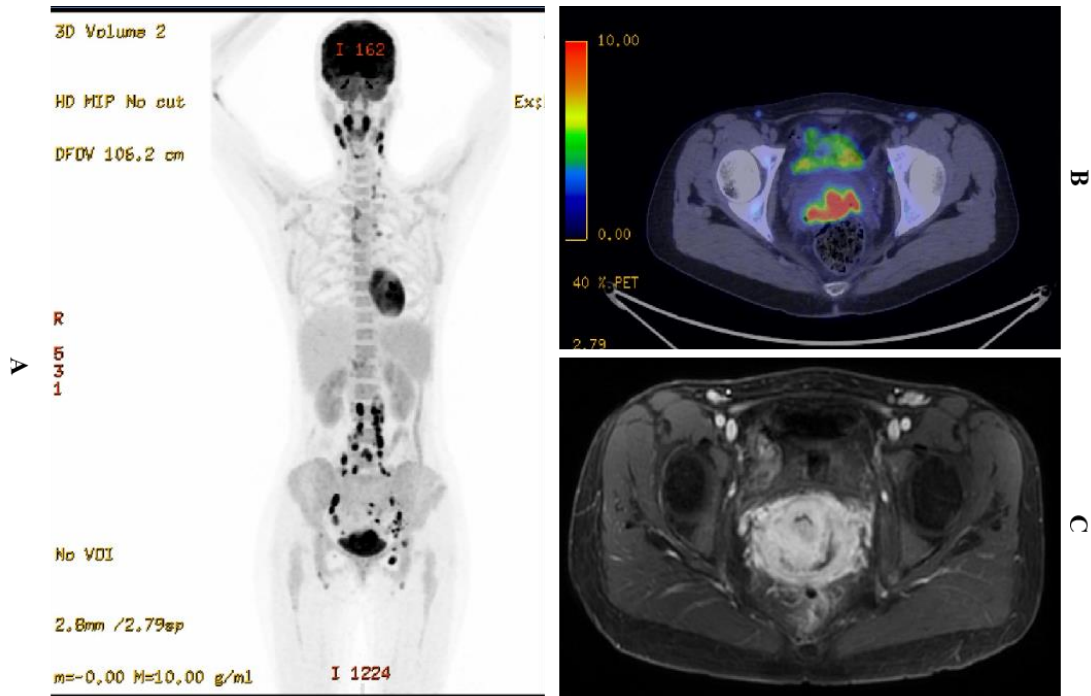


Figure 2. PET/CT showed significantly increased radioactive uptake in multiple enlarged lymph nodes and cervical masses throughout the body (A); PET/CT showed the range of high radioactive uptake in the cervix (B); MR T2WI: diffuse thickening of the cervical mucosa, which was significantly enhanced after enhancement, the low signal band of the cervical stroma was continuous, and the structure of the cervical os was clear (C).

Laboratory examination: blood routine, urine routine, liver and kidney function tests were normal. The titer of the toluidine red syphilis serological titer test was 1:32, and the *Treponema pallidum* antibody was positive. The cervical tissue pathology showed mild squamous epithelial hyperplasia, focal tissue hyperplasia under the epithelium, and more large-nucleated translucent lymphocytes, as well as granulation tissue (Figure 3A-C). The swollen lymph nodes were positive for *Treponema pallidum* antibody immunohistochemical staining (Figure 4), HIV antibody test was negative, no bacteria and fungi were detected in the secretion culture, and the human papilloma gene test of cervical tissue was negative,

and the diagnosis was secondary cervical syphilis. Benzathine penicillin 2.4 million IU was given intramuscularly on both sides, once a week, for 3 consecutive weeks. The swollen lymph nodes were significantly reduced in the second week of treatment, and the rash on the trunk and limbs became lighter in color and partially disappeared after the third week. The cervical tumor basically disappeared, and the biopsy pathology suggested cervicitis (Figure 3D), TRUST titer test: 1:2. It is considered that the treatment of syphilis is effective and the diagnosis of cervical syphilis is clear. The patient is still being followed up as of the date of submission.

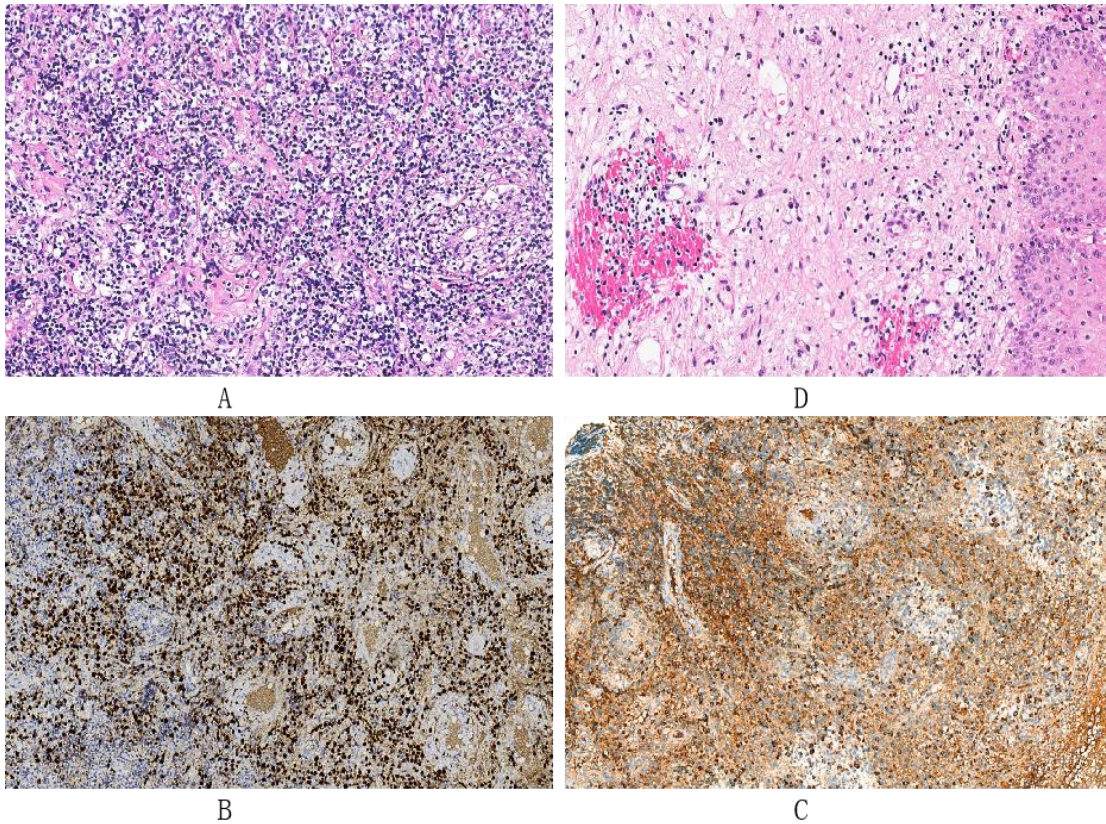


Figure 3. HE staining of cervical biopsy tissue before treatment, with a large number of single lymphocyte infiltration (A); immunohistochemistry showed that a large number of cells were labeled by MUM1 and KAPPA (B-C); HE staining of cervical biopsy tissue after treatment, with clear epithelial structure, lymphocytes, plasma cells, eosinophils, neutrophils and other cell morphologies in the stroma, and mixed background (D). (A-D, X200)

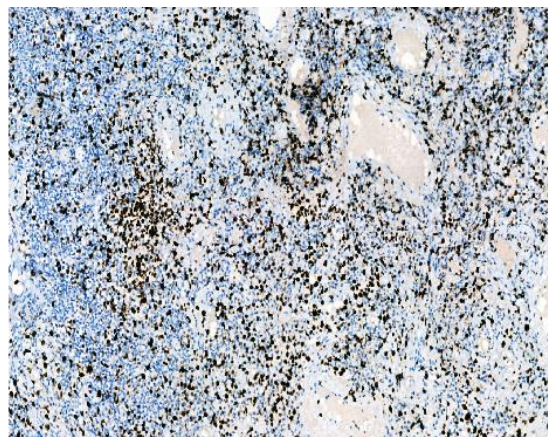


Figure 4. Immunohistochemistry positive for *Treponema pallidum* antibody ($\times 200$)

Discussion

Cervical syphilis is relatively rare in clinical practice, and its symptoms may be similar to those of cervical cancer or other gynecological diseases, making diagnosis challenging. In this case, the patient presented with abnormal vaginal bleeding, and a mass was found in the cervix during physical examination. Gynecological ultrasound, pelvic CT, and MRI are often used in clinical diagnosis to indicate the location of the lesion, benign or malignant, and the extent of involvement. The ultrasound manifestations of cervical syphilis are low-echo masses and rich blood flow signals, similar to the ultrasound manifestations of clinical stages II-III of cervical cancer. In this case, physical examination revealed cervical cauliflower-like masses, multiple enlarged lymph nodes throughout the body, and tumors invading the vaginal vault and cervical fibromuscular layer. PET/CT suggested "cervical cancer with multiple lymph node metastasis (stage IVB)", and MRI suggested "considering cervical lymphoma". Therefore, imaging examinations are limited in the differential diagnosis of cervical syphilis from cervical cancer and cervical lymphoma [5]. Cervical cancer is divided into endophytic and exophytic types. Endophytic type is characterized by cervical enlargement, which may even involve the uterine body. The uterus is abnormally barrel-shaped, often manifested by lower abdominal pain, and/or irregular vaginal bleeding. Exophytic type is characterized by cervical enlargement, which often invades the vagina, anterior bladder wall and other parts, with contact bleeding or irregular vaginal bleeding as the main manifestations. Pathology is the gold standard for the diagnosis of cervical cancer [6], so it is easy to exclude cervical cancer through pathological examination. Female

reproductive system lymphoma is rare clinically. The incidence of primary cervical non-Hodgkin's lymphoma is less than 0.12%, and is mainly diffuse large B-cell type [7,8]. The clinical manifestations are similar to those of common cervical tumors, such as irregular vaginal bleeding or discharge. A few cases may be asymptomatic. Gynecological physical examination and imaging examinations have the characteristics of malignant tumors [9], and are easily misdiagnosed as cervical cancer. In this case, the patient had a cervical tumor accompanied by multiple lymphadenopathy and splenomegaly. Physical examination and imaging studies were difficult to identify lymphoma. Previous literature [8] reported that it is more common in middle-aged and elderly women. It is difficult to make a correct diagnosis based on the HE morphology under light microscopy alone. It requires multiple immunohistochemical examinations and the diagnostic criteria for primary malignant lymphoma of the female reproductive system proposed by Vang R et al. [10] for diagnosis [11].

During the active stage of secondary syphilis, the pathological manifestations of the lesions are mainly vascular swelling, chronic inflammatory cell infiltration, mainly plasma cells, with a small number of tissue cells and eosinophils; lymphoid follicles are densely and unevenly distributed in the cortex and medulla, with different sizes, and a star-shaped sky phenomenon; hyperplastic blood vessels of different lumen sizes in the paracortical area and medulla are narrow or round, with endothelial cell proliferation in the blood vessels and a few blood vessels occluded; perivascular inflammation; a small amount of necrosis and a small number of multinucleated giant

cells can be seen in and around the hyperplastic epithelial tissue cells, and blood vessels and plasma cells can be seen at the edge of the necrosis [12]. The patient was initially suspected of having cervical cancer or lymphoma. KI67 was highly expressed in the germinal center of the enlarged lymph nodes, and a large number of CD20-labeled B cells were helpful for the pathological diagnosis of lymphoma, which made the diagnosis of syphilis more difficult. However, she was eventually diagnosed with syphilis through immunohistochemistry and pathological examination. In the pathological examination, a large number of plasma cells (MUM1/KAPPA markers) were found in the initial cervical biopsy pathology HE and IHC, which is a pathological sign of active syphilis. After penicillin anti-syphilis treatment [13], the cervical biopsy was performed again, and the lymphocytes were significantly reduced. Various cell forms such as plasma cells and eosinophils appeared in the background. At this time, serology showed that the syphilis load was significantly reduced, which further confirmed the diagnosis of cervical syphilis. In addition to histopathology and syphilis serological tests, immunohistochemical staining of *Treponema pallidum* antibodies and a large number of *Treponema pallidum* were found in the cervical ulcer [14], providing the most direct evidence.

The patient was a young and middle-aged woman with an active sex life, who was at high risk for sexually transmitted diseases. Due to the lack of timely treatment, she rapidly developed multiple rashes on the trunk, multiple lymphadenopathy throughout the body, and large cervical masses. In order to make a clear diagnosis, in addition to histopathology and syphilis serological tests, immunohistochemical staining of *Treponema pallidum* antibodies was performed. The final

diagnosis was secondary cervical syphilis. After penicillin treatment, the cervical mass completely subsided, the lymph nodes shrank, and the rash basically disappeared, suggesting that the patient should receive standardized treatment in a timely manner after being diagnosed with syphilis. This case emphasizes that when faced with atypical symptoms, doctors need to remain vigilant and conduct comprehensive examinations to rule out other possible diseases to avoid misdiagnosis and waste of medical resources. In addition, the collaboration of a multidisciplinary team is essential for the diagnosis and treatment of complex cases.

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