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Case Report

Clinical and pathologic diagnosis and different diagnosis of syphilis cervical lymphadenitis

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Abstract: Purpose: To study the clinical pathologic characteristics and differential diagnosis of syphilitic cervical lymphadenitis, and to improve the rate of its diagnosis and treatment. Methods: Retrospectively analyzed the clinical history, Trepone pallidum-ELISA (TP-ELISA), rapid plasma regain test (RPR) and routine pathological examination of the patient diagnosed as syphilis lymphadenitis. And review related literatures. Results: The main clinical presentation was multiple palpable cervical lymph nodes. The multiple nodes were hard, fixed, and the major diameter of the larger one was 2 cm. The main pathological changes included: the capsule was significantly thickened; reactive hyperplasia of lymphoid follicular with sky star phenomenon; occlusive endovasculitis; perivascular inflammation; the proliferation of epithelioid histiocytes can form granulomas with few multinucleated giant cells; few necrosis. TP-ELISA and RPR were positive. Conclusions: The pathological changes of syphilitic lymphadenitis have a variety of performance with relatively specific and suggestive alterations which requires a combination of clinical history and laboratory test before the diagnosis, and the clinicians can reduce misdiagnosis and missed diagnosis of the disease by increasing vigilance of it.

Keywords: Syphilis, lymphadenitis, pathologic, clinical, diagnosis

Introduction

Syphilis is a chronic, systemic sexually transmitted disease caused by spirochaete bacterium Trepone pallidum [1]. The transmission and prevalence of syphilis has been a serious public health problem worldwide including China [1, 2]. The continued increase in reported syphilis cases is obvious in recent years, and syphilis will be incurable with the progress of the disease, so the early diagnosis is particularly important. After invading, genital chancre as the classic lesion of primary syphilis is a single, painless, indurated ulcer with a clean base, which accompanied by nearby lymph nodes painless enlargement (mainly for inguinal lymph nodes). With the improvement of detection technology and health consciousness of the sub-health population (including the core group of sexually transmitted diseases, population with homosexual, bisexual or orogenital activity), the clinical manifestations of syphilis were enriched in a certain extent, and extragenital chancre and cervical lymphadenitis can be detected in less than 2% of patient [3, 4]. Syphilis lacks typical clinical presentation, and misdiagnosis is not uncommon.

This case was mainly manifested as the right cervical lymphadenitis and local swelling of pharyngeal recess. The clinical history was retrospectively analyzed and the relevant literature is reviewed.

Materials and methods

Case report: A 45-year-old man presented to Anyang Tumor Hospital, Anyang, China, in February 2015 with a non-tender mass in the right neck that had been progressively enlarging for a month. Physical examination revealed an egg sized mass of the right neck. The mass was hard, fixed with a 7 cm long diameter. Patients denied any adverse personal history. The patient was treated with antibiotics for a

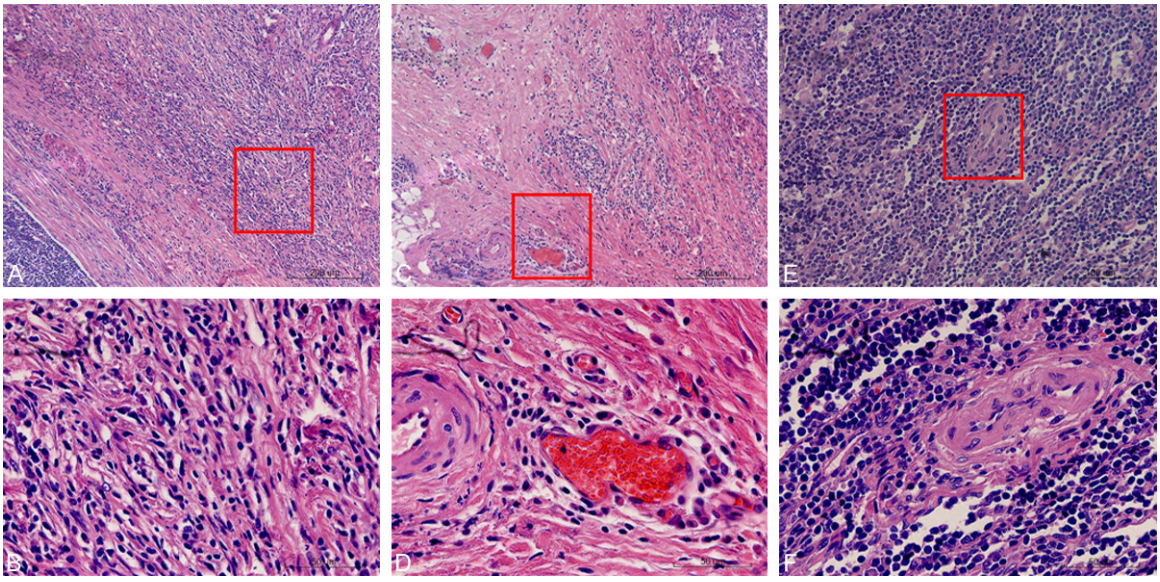

Figure 1. Characteristic morphological findings. (A) The capsule was significantly thickened (×100). (B) Infiltration of chronic inflammatory cells chiefly plasma cells in the capsule (×400). (C) Perivascular inflammation (×100). (D) Plasma cells around the vessel (×400). (E) Swelling endothelial cells (×200). (F) Occlusive endovasculitis (×400). Note: (B, D, F) respectively corresponding to (A, C, E).

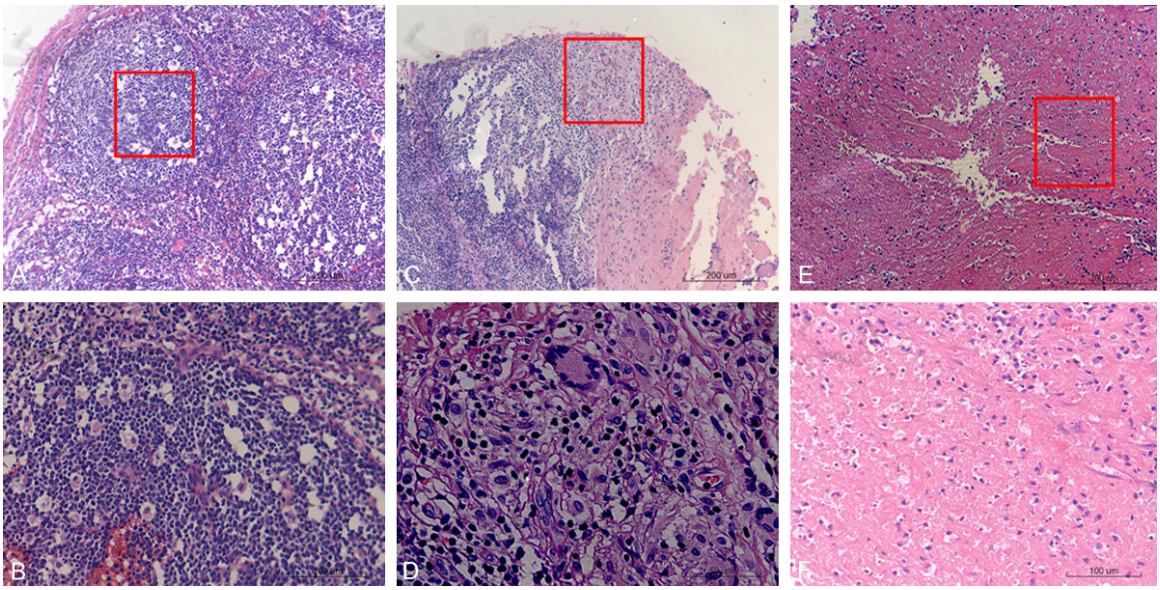

Figure 2. Auxiliary morphological findings. (A) Hyperplasia of lymphoid follicular (×100). (B) Sky star phenomenon (×200). (C) The proliferation of epithelioid histiocytes (×100). (D) Multinucleated giant cells (×400). (K) Non- caseating necrosis (×100). (E) Trace of vessels and plasma cells in the edge of the necrosis (×200). Note: (B, D, F) respectively corresponding to (A, C, E).

short period postoperatively and was then discharged. When followed up after 5 months, he was in good health with no recurrence or discomfort. His father had died from carcinoma of gastric cardia. Samples were collected from surgical cases in Anyang Tumor Hospital and fixed in 10% neutral formalin, then dehydrated. Sections of the excised neck mass were embedded in paraffin and stained with haematoxylin and eosin and immunohistochemistry. Pathological examination was done under light microscopy, and TP-ELISA and RPR were detected.

Results

Nasopharyngeal endoscopy

The right pharynx fossa of nasopharyngnx was local bombe with slight blood congestion and smooth surface, and the left pharynx fossae was lobular and local hyperplasia with smooth surface. Color Doppler ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) scans of the neck showed multiple palpable cervical lymph nodes.

Pathological changes

Macroscopically, multiple palpable cervical lymph nodes with thickened capsule and ill-defined contour were located in the upper of right neck, measuring 7 cm×3 cm×1.5 cm, gray or grayish yellow in section. Microscopically, the cervical lymphatic node with mild structural disorder showed occlusive endovasculitis with thickened capsule and perivascular inflammation (**Figure 1**). The thickened capsule mainly presented as hyperplasia of capsule accompanied by fibrosis with swelling vessels and infiltration of chronic inflammatory cells chiefly plasma cells, few histocytes and eosinophils also can be seen; the folliculi lymphaticus densely and unevenly distributed in the cortex and medulla with various sizes and star sky phenomenon; the proliferative vasculars with different lumen size in the paracortical area and medulla were narrow or round, and endothelial cell proliferated in the vessels with a few of which were occlusive; perivascular inflammation; a small amount of necrosis and few multinucleated giant cells can be seen in and around the hyperplasia epithelioid histiocytes, and trace of vessels and plasma cells can be seen in the edge of the necrosis (**Figure 2**).

Immunohistochemical staining

CD21 shows Follicular dendritic cells (FDC) network; CD20, CD79a, CD10, Bcl-6 were positively expressed mainly in follicular especially in the germinal center; Bcl-2, CD3, CD5 were positively expressed mainly in interfollicular region; Ki-67 was highly expressed in germinal center. Laboratory test: TP-ELISA and RPR were positive.

Discussion

Both congenital syphilis and acquired syphilis may involve lymph nodes. In the early stage of acquired syphilis, also named primary syphilis which had a strong infective power, mainly manifested as hard chancre and inguinal lymphadenitis, but it was easily treated and controlled. In some patients who were symptomless with deep inguinal lymph nodes, syphilis can not be detected in the early stage, especially in obese individuals [1]. With the development of science and technology and social diversity, the diversification of clinical manifestations of syphilis were promoted, and in some cases, extragenital chancres can occur infrequently, which can be seen in the fingers, border of the tongue, anus, mouth, lip, pharynx and tonsil mucosal, and in rare cases, neck lymphadenopathy can be the only presentation [3, 4, 6]. Extragenital chancres have little or no basal induration with edges rising above the surrounding surface, and pain is a prominent manifestation in extragenital lesions [3-5, 7]. And for the lack of sufficient vigilance and understanding of syphilis, it was usually misdiagnosed.

The patient here denied adverse sexual activity and complained for neck mass in the right side, which made it difficult to diagnose. After the initial diagnosis of our hospital, patient went to the higher level hospital for consultation and got correct diagnosis and follow-up treatment in time, and also avoided the progress and spread of the disease.

The pathological changes of the lymph nodes were the main basis for diagnosis, and the diagnosis should be combined with clinical manifestations and laboratory tests. The diagnosis of syphilis can be confirmed if the silver staining of spirochaetes is positive, but the lymph nodes are always negative, which may be related to the antigen expressing on the site of infection, but not on the presenting organs and immune organs [4, 8].

Cervical mass can be caused by many diseases, which have been summarized in the mnemonic 'KITTENS' (K, congenital anomalies; I, infectious/inflammatory; T, trauma; T, toxic; E, endocrine; N, neoplasms; S systemic disease) [9]. 80% of non thyroidal neck masses were tumor, and 80% of the tumor is malignant [10]. Combining with the cervical lymph node enlargement, slightly thickening nasopharyngeal mucosa and the history of carcinoma in the family, clinical diagnosis of nasopharyngeal carcinoma was made. Therefore diagnosis and

differential diagnosis of syphilis is very important in pathological examination. After exclusion of nasopharyngeal carcinoma (NPC) based on pathological examination, the pathological features of syphilis can be confused with the following diseases: (1) Reactive hyperplasia Especially those with significantly hyperplasia follicular, but occlusive endovasculitis, perivascular inflammation and plasma cell infiltration and thickened capsule is rare or not exist. (2) Granulomatous lymphadenitis, such as tuberculosis, sarcoidosis, cat scratch disease, massive necrosis (coagulative necrosis or fibrinoid necrosis with larger area), epithelioid cell hyperplasia (for sarcoidosis, the proliferation of epithelial like cells was well-defined and multituberculate) and multinucleated cells can be observed. Sometimes swelling vessels or infiltration of plasma cells can occur, but those diseases always have normal or mildly thickened capsule, fewer follicles, accompanied by relevant clinical history and laboratory test (acid fast stain, vascular angiotensin converting enzyme examination). (3) Follicular lymphoma Marked hyperplasia of follicular, but in the immunohistochemical staining, Bcl-2 expression was positive in the germinal center whose polarity disappeared.

In short, occlusion vasculitis, perivascular inflammation, plasma cell infiltration and fibrous thickened capsule are relative characteristic findings in syphilis lymphadenitis; whereas necrosis, granulomatous, follicular hyperplasia and germinal center star sky phenomenon is auxiliary diagnosis index. After the exclusion of lymphoma, other specific or non specific lymph node hyperplasia, if the patients or their sexual partner have adverse sexual activities, syphilis lymphadenitis should be considered as different diagnosis. And specific serological test should be done. It can be further detected the DNA of the syphilis when needed. The diagnosis of syphilis lymphadenitis should be made on the basis of clinical manifestations, serological test and pathological examination, and reduce misdiagnosis and missed diagnosis for timely treatment and prevent disease from progressing and spreading.

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Disclosure of conflict of interest

None.

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