Non-caseous Granulation Lymphadenitis in the Neck as an Initial Manifestation of Prostate Carcinoma

Satomi Asai, Shuhei Komiya, Masanori Yasuda, Kenji Okami, Shinichi Yamamoto, GuiLan Jin, Hiromichi Matsushita, Hideshi Miyakita and Hayato Miyachi

Abstract

We encountered a 54-year-old Japanese man who presented with painless swellings on his bilateral neck. Although ultrasonographic findings suggested metastatic lymphadenopathy, histological examination of the mass revealed non-caseous granulation lymphadenitis. He was subsequently diagnosed as having prostate carcinoma with metastasis to the multiple bones. The present case suggested that prostate carcinoma could cause cervical lymphadenopathy due to non-caseous granulation as an initial manifestation, and could be a sign for an impending clinical expression of metastasis to an area draining to the lymph nodes.

Key words: ultrasonography, metastasis, inflammation, granulation, prostate carcinoma

Introduction

With recent advancement in ultrasound technology, ultrasonography has been widely used in the diagnosis of neck masses including differentiation between benign and malignant lymphadenopathy (1-3). Ultrasonographical findings of lymph node metastasis in the neck are featured by a thickness/longitude>0.5, heterogeneous and/or coarse internal echo, and deviation or disappearance of the hilum echo (2-4). However, these features have been also reported in a few cases with benign diseases such as tuberculous lymphadenitis and sarcoidosis (2, 3, 5).

We encountered a patient who presented with painless masses in the bilateral neck and was ultrasonographically suspected as having lymph node metastasis, but histologically diagnosed as non-caseous granulation lymphadenitis. He was subsequently diagnosed as having prostate carcinoma with metastasis to the multiple bones. Here, we describe the presumptive association of non-caseous granulation lymphadenitis in the neck with prostate carcinoma and its diagnostic implication in the ultrasonographic examination.

Case Report

A 54-year-old Japanese man, who noticed painless swellings on his bilateral neck and nuchal pain, was seen at Tokai University Hospital. At physical examination, thumb-sized, hard and immovable masses were palpable in the bilateral neck, which were not associated with skin changes. Oral and nasopharyngeal examinations were normal. There were no other abnormal findings including prostate at rectal examination. Laboratory examination revealed mild leukocytosis (WBC 11,000/μL: neutrophil 83%, lymphocytes 10%, monocytes 4% and eosinophils 3%) and elevated serum levels of C-reactive protein (7.25 mg/dL: normal range <0.3 mg/dL) and alkaline phosphatase (445 IU/L: normal range 100-310 IU/L). Serum levels of tumor markers including CEA, CA19-9, AFP and SCC were in the normal range. That of PSA was slightly elevated (10.7 ng/mL: normal range>4.0 ng/mL) and that of IL-2R was markedly high (2,560 U/mL: normal range 220-530 U/mL). There were no other abnormalities in laboratory tests including angiotensin-converting enzyme (14.1 IU/L: normal range 8.3-21.4 IU/L).

Ultrasonographic examination for the bilateral cervical
masses revealed various-sized, round, multiple lymphadenopathy. The largest one with a size of 25×24×18 mm in the right lateral neck had an irregular boundary with basically hypoechoic and heterogeneous internal echo (Fig. 1-a). Surrounding it, there were rather small and oval swollen lymph nodes with hypoechoic internal echo (Fig. 1-b). Doppler mode sonography of the second largest lymph node showed abundant flow signals running from the center to the periphery (Fig. 1-c). The ultrasonogram of the abdomen revealed multiple para-aortic swollen lymph nodes (Fig. 2-a). They were basically round and hypoechoic with increased internal echogenicity, suggesting metastatic lymphadenopathy. There were no abnormalities in abdominal and urogenital organs including prostate (Fig. 2-b).

The chest X-ray was normal. The fiberscopic examination of the upper gastrointestinal tract and colon showed no abnormalities. Taken together, the neck masses were suspected as metastatic lymphadenopathy of unknown primary origin with metastatic abdominal lymphadenopathy. Bone scintigraphy for a general image with Tc-99m MDP intravenous infusion revealed hot accumulations with the radioisotope defect image in the sternum, the cervical vertebrae, the bilateral ribs and clavicles, suggesting metastasis to the multiple bones (Fig. 3).

An open biopsy specimen of the neck mass was histopathologically composed of granulation tissue: inflammatory cellular areas were surrounded by fibrotic tissue. There was infiltration of many mononuclear inflammatory cells such as histiocytes, lymphocytes and plasma cells. No metastatic disease was detected (Fig. 4-a, b). Microbiological examinations were negative for mycobacterium, fungus and other bacterial infections. Because the serum level of PSA was slightly elevated, needle biopsy of prostate was performed and histological examination of the biopsy specimen revealed well-differentiated adenocarcinoma (Fig. 4-c).

With androgen deprivation treatment (ADT, bicalutamide 80 mg per day) for 4 weeks, there was remission of the symptoms including the cervical lymphadenopathy, systemic pain and fever. The swellings of cervical lymph node were reduced in size from 25×24 mm to 15×15 mm (the largest one), and some small ones surrounding it as well as the swollen abdominal lymph nodes disappeared, as assessed by
The general image of the bone scintigraphy: anterior (left) and posterior (right) views. Hot accumulations with the radio-isotope defect image were found in the sternum, the cervical vertebrae, the bilateral ribs and clavicles.

Histological findings of the cervical lymphadenopathy and the prostate (Hematoxylin and Eosin staining). a: Low magnification view of an open biopsy specimen of the cervical lymphadenopathy showed cellular and fibrotic granulation tissue. b: High magnification view of the granulation tissue showed infiltration and aggregation of many mononuclear inflammatory cells such as histiocytes, lymphocytes, and plasma cells. Some histiocytes were syncytial and possessed plump cytoplasm. No evidence of metastatic malignancies was noted. c: A needle biopsy specimen of the prostate showed adenocarcinoma cells which were compactly arranged in a tubular manner, categorized as Gleason’s score 3+3.

ultrasonography. There was also normalization of the serum level of PSA (0.2 ng/mL) after ADT.

Discussion

Exploration of metastases in patients with carcinoma is important to determine the treatment and to know the prognosis. Cervical lymph node metastases are seen in carcinoma of nasopharynx, oral cavity and upper gastrointestinal tracts, but are rare in patients with carcinoma of colon or genitourinary organ (5-8). We encountered a patient who presented with painless masses in the bilateral neck and ultrasonographically was suspected as having metastatic lymphadenopathy, but histologically diagnosed as non-caseous granulation lymphadenitis.

In responding to the instillation of ADT for prostatic carcinoma, swellings of cervical and abdominal lymph nodes regressed with concomitant normalization of the serum level of PSA. This clinical course would support that these lymph node swellings could have been caused as a part of systemic lymphadenopathy with causative association with the prostatic carcinoma. Non-caseous granulation or granulomatous lymphadenitis histologically consists of mononuclear inflammatory cells including histiocytes, lymphocytes and plasma cells surrounded by fibrotic tissue. It has been reported in various types of carcinoma such as supraglottic, gastric and breast carcinoma (9-12). These lesions can occur in lymph nodes draining an area housing a malignant tumor through an immune reaction to antigenic factors derived from the tumor cells. This phenomenon is also found in non-regional tissues and complicates the diagnostic process. In the present case, the cervical non-caseous granulation
lymphadenitis was an initial manifestation of the prostate carcinoma. Appearance of it was followed by the detection of metastasis of carcinoma to the cervical spine.

Although the prostate in our case was ultrasonographically normal and elevation of the serum level of PSA was mild, prostate carcinoma was diagnosed in an advanced state with distant metastases. Transabdominal ultrasound of the lower abdomen has difficulty in diagnosing prostate carcinoma in an early stage, unless transrectal images were not obtained. However, prostate carcinoma is prone to metastasize to distant areas such as para-aortic lymph nodes or bones at any stage. Our case suggested that prostate carcinoma could cause cervical lymphadenopathy due to non-caseous granulation even when the prostate was ultrasonographically normal, and which could be a sign for an impending clinical expression of metastasis to an area draining to the lymph nodes.

In conclusion, when ultrasonographic appearance of cervical lymphadenopathy is characteristic to metastases, non-caseous granulation lymphadenitis associated with carcinoma is also to be considered as a differential diagnosis and primary organ or neighboring metastatic lesions should be investigated. As a primary origin, prostate carcinoma is also to be excluded even if the transabdominal ultrasound appearance of the prostate is normal.

References


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