Case Report
Primary natural killer/T cell lymphoma of the cervix: Case report and clinicopathological analysis

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ARTICLE INFO

Article history:
Accepted 26 June 2013

Keywords:
nasal type NK/T cell lymphoma uterine cervix

ABSTRACT

Objective: To present pathological and molecular characterizations of a rare case that was diagnosed as nasal-type natural killer (NK)/T cell lymphoma primarily arising in the cervix.

Case report: An Asian woman was admitted to hospital with a hysteromyoma, and laparotomy was performed. A large tumor of the uterus was found, which was limited to the cervix. Pathological examination showed NK/T cell lymphoma, which was supported by histological and immunohistochemical studies and was confirmed by evidence of Epstein–Barr virus infection. Less commonly, this case concerned a cytotoxic T cell phenotype, as molecular studies showed evidence of a clonal T cell receptor γ chain gene rearrangement. Microscopically, prominent and extensive necrosis was the distinctive feature of this case, which reminded us of considering it as a tumor.

Conclusion: Primary NK/T lymphoma of the cervix is rare. Our experience in this case provided variable information on both pathological and molecular studies. This case may be of value in the differential diagnosis of lymphoid lesions and other small cell tumors of the cervix.

Introduction

Extranodal natural killer (NK)/T cell lymphoma is a heterogeneous group of uncommon hematological malignancies with distinct clinicopathological features, which usually occurs in the nasal or nasopharyngeal region and is occasionally seen in the upper aerodigestive tract, skin, testis and soft tissue [1]. Primary NK/T cell lymphoma of the female genital tract is rare, with < 10 cases reported in the English-language literature. Most series have reported involvement of the uterus, vagina, ovaries, or the entire gynecological tract as a systemic NK-cell lymphoma. Primary NK/T cell lymphoma of the cervix was reported only as a case report by Mhawech et al in 2000 [2–4]. To the best of our knowledge, this is the second case of primary NK/T cell lymphoma originating in the cervix and the first proven to be a cytotoxic T cell phenotype.

Such tumors are confusing to clinicians and pathologists because of their unusual location and noncharacteristic symptoms, as well as the limited information available. Prognosis may be good compared to other gynecological malignancies if the tumors are diagnosed at an earlier stage, which provides a diagnostic challenge for pathologists. Here, we report the case of a nasal-type NK/T cell lymphoma arising in the cervix and summarize the clinical and pathological features of the tumor.

Case Report

A 54-year-old woman was admitted to the hospital complaining of difficulty in micturition. She denied hematuria, odynuria, and other unusual symptoms. Her complaints did not improve after treatment with anti-inflammatory drugs. Physical examination revealed a hard, irregular uterus and a relaxed vagina without well-defined masses. Ultrasonography showed a multiple myoma in the cervix and cervical cysts. A complete blood count revealed the following: hemoglobin, 94.0 g/L; white blood cell count, 3.2 × 10^9/L, with a differential count of 65% segmented neutrophils, 27% lymphocytes, 2.5% monocytes, 0% basophils, and 0.5% eosinophils.

Total abdominal hysterectomy and unilateral salpingo-oophorectomy were performed. The specimen was sent to the Department of Pathology for pathological—anatomical analysis.

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Grossly, the specimen consisted of a uterus, cervix, and unilateral adnexa. The uterus measured 10 cm × 6 cm × 4 cm. The cervix contained a soft, irregularly outlined, pinkish-grey tumor located primarily outside the cervical canal with a maximum diameter of 4 cm. An intramural, white 1.5-cm leiomyoma was present. The endometrium and left ovary and fallopian tube were grossly unremarkable.

Histologically, the whole wall of the cervix was infiltrated by neoplastic cells, but the squamous epithelium and endocervical glands were not infiltrated or destroyed (Fig. 1A). There was a diffuse dense lymphoid infiltrate, with prominent coagulative necrosis and apoptotic bodies. An angiocentric and angiodestructive growth pattern was frequently present (Fig. 1B). Higher magnification showed that neoplastic lymphoid cells invaded and destroyed the blood vessel walls of the cervical stroma, and lymphoid cells were atypical, medium-sized with irregular nuclear contours and scanty cytoplasm (Fig. 1C).

Immunohistochemically, the neoplastic lymphoid cells expressed T-cell– and NK-cell-associated antigens such as CD3 (Fig. 2A), CD43, CD56 (Fig. 2B), granzyme-B and T–cell-restricted intracellular antigen–1 (TIA–1) (Fig. 2C), but were negative for CD20, CD79a, CD38 and CD138. Proliferative activity was assessed by intracellular antigen-1(TIA-1) (Fig. 2C), but were negative for CD20, growth pattern was frequently present (Fig. 1B). Higher magnification showed that neoplastic lymphoid cells invaded and destroyed the blood vessel walls of the cervical stroma, and lymphoid cells were atypical, medium-sized with irregular nuclear contours and scanty cytoplasm (Fig. 1C).

The histological, immunohistochemical, and molecular studies were interpreted as a nasal-type NK/T cell lymphoma arising in the cervix. The endometrium and unilateral adnexa were not involved.

Two months after the operation, the patient presented with high fever, painful urination, dysuria, and hematuria. Renal failure followed, and the family members of the patient refused further treatment.

Discussion

Female genital tract lymphomas are uncommon. In a substantial review performed by the Pathology of Lymphoma Collaborative Group (China), female genital tract non-Hodgkin’s lymphoma accounted for ~0.31% of all lymphomas in China. With regard to histological subtype, most cases previously reported concerned the B-cell type [5–7]. Furthermore, some cases had secondary involvement. For lymphoma to be considered confined to the cervix, it should meet the criteria such as those previously put forward by Fox and More [8]. The present case completely met these criteria and we believe that it is an example of primary cervical origin. To the best of our knowledge, only one case of nasal-type NK cell lymphoma arising in the cervix has been reported [4]. However, unlike the first case mentioned above, the neoplasm presenting in the present case was EBV positive and had evidence of T cell receptor γ chain gene rearrangement, which revealed it to be a cytotoxic T cell phenotype.

The most common symptoms of lymphoma in the cervix are abnormal vaginal bleeding, cervicouterine enlargement, and fixed uterine cervix on pelvic examination, which may be palpated [6,7]. Urinary obstruction as reported in the present case is uncommon. The presenting symptoms are not characteristic of cervical lymphoma, because they occur in many diseases, so obtaining the correct diagnosis may be time consuming.

Histologically, NK/T cell lymphomas of the cervix are characterized by vascular invasion and coagulative necrosis, similar to other extranodal nasal-type NK/T cell lymphomas. The neoplastic lymphoid cells must coexpress NK cell markers, such as CD56, CD57 and T-cell-associated antigens such as CD2, CD3, CD5, and CD7. Neoplastic T cells may lack one or more T cell receptors, and choosing a complete T cell receptor complex may be required. NK/T cell lymphomas also express cytotoxic molecules such as TIA-1, perforin and granzyme-B.

The differential diagnosis for this disease includes chronic cervicitis, carcinoma and other hematopoietic lesions. NK/T cell lymphoma may be especially difficult to distinguish from florid benign immune proliferation, which often has a mixed, polymorphous cell population including plasma cells, neutrophils, and lymphocytes, and the lymphocytes may have atypia that closely mimics lymphoma. Malignant lymphoma has a monomorphic

![Fig. 1.](image) (A) The whole wall of the cervix was infiltrated by neoplastic cells. Note that scattered tubular glands were not destroyed in the lower right (H&E, 40×). (B) Neoplastic cells with an angiocentric growth pattern and coagulative necrosis (H&E, 100×). (C) Medium-sized lymphoid cells invading and destroying the wall of an artery (H&E, 400×). H&E = hematoxylin and eosin.
appearance, often with cellular necrosis or sclerosis, and immunostaining is necessary. Molecular gene rearrangement is helpful in some cases [9]. Prominent necrosis in the present case reminded us to consider it as a tumor. Additionally, ulceration is more frequent in benign processes than in lymphoma. Some other tumors of hematopoietic and lymphoid origin must be included in the differential diagnosis, such as peripheral T cell lymphoma. Unspecified, the tumor cells can closely mimic NK/T cell lymphoma but may be negative for EBV and cytotoxic molecules. Granulocytic sarcoma should also be excluded, the neoplastic cells with granulocytic or eosinophilic myelocytes express MPO and CD117 but are negative for lymphoid markers. Small cell carcinoma of the cervix can microscopically resemble NK/T cell lymphoma, with medium-sized hyperchromatic nuclei and scant cytoplasm. Immunostaining for cytokeratin and leukocyte common antigen is helpful to resolve such a difficult distinction.

In our case, the morphological and immunophenotypic characteristics of the tumor cells fulfilled the criteria of typical nasal-type NK/T cell lymphoma. Unlike other extranodal NK/T cell lymphomas, the squamous epithelium and tubular glands were free of invasion by the tumor cells; presumably because lymphoma cells originated from the cervical stroma and were mostly located in the deeper wall of the cervix. Some nasal NK/T cell lymphomas are EBV positive, as in the present case. Although most cases have not shown T cell receptor chain gene rearrangement in previous studies [3,4], our case did show T cell receptor γ chain gene rearrangement, presumably corresponding to the cytotoxic T lymphocyte derivation.

Studies with large samples are not available due to the low incidence of primary cervical lymphoma and the standard treatment method. One important study recommended chemotherapy alone, radiotherapy alone, or radiotherapy combined with either chemotherapy or surgery [10]. In the present case, the patient and her family members refused further treatment because of the following symptoms of renal failure.

We reported this rare case mainly in the aspect of pathological analysis, which showed variable presentation compared with typical NK/T cell lymphoma. This case may be of value in the differential diagnosis of lymphoid lesions and other small cell tumors of the cervix.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

References


