Primary penile malignant lymphoma: report of a rare case

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Abstract

A 73-year-old male presented with a 3-month history of two penile masses: one on the shaft and one on the glans penis. Both lesions were poorly defined, fixated and without tenderness. The sizes were 1.0 × 1.0 × 1.0 cm and 1.2 × 1.5 × 1.5 cm, respectively. The patient underwent lumpectomy of the glans penis; we confirmed malignant lymphoma of the glans penis (B-cell derived; diffused large B-cell) by postoperative pathological examinations. CHOP (cyclophosphamide-hydroxydaunorubicin-oncovin-prednisone) chemotherapy was administered. The patient was tumour-free at the 33-month follow-up.

Primary penile malignant lymphoma is very rare, there are only 26 reported cases worldwide.

A 73-year-old male presented with a 3-month history of penile mass; he was otherwise healthy. Physical examinations indicated the following: normal vital signs, with no enlarged superficial lymph nodes; no abnormalities in cardiopulmonary examination; flat abdomen; liver and spleen were impalpable, with no palpable mass; kidney was impalpable, with no tenderness. Digital rectal examination revealed a hyperplastic prostate, with no nodule. Two masses were discovered on the shaft of penis and glans penis; the masses were firm, poorly defined, fixated and no tenderness. Their respective sizes were: 1.0 × 1.0 × 1.0 cm and 1.2 × 1.5 × 1.5 cm. Routine blood/urine tests, liver and kidney function tests were normal. His prostate-specific antigen was 3.05 ng/mL. Upon ultrasound and computed tomography (CT) scanning, his prostatic hyperplasia measured 3.0 × 4.0 × 4.5 cm and was 28.08 mL; there were no abnormalities with the liver, gallbladder, pancreas, spleen, kidneys and ureter, and no enlargement of the retroperitoneal lymph nodes. A plain chest radiograph showed no abnormalities.

The patient underwent lumpectomy of the glans penis. At surgery, the mass on the shaft was unable to be resected, and thus only a biopsy tissue was taken. The mass on the glans penis was completely resected with some surrounding normal tissue, and primary suturing of the glans was performed. Pathological examinations indicated malignant lymphoma of the glans penis (B-cell derived; diffused large B-cell), and the mass margins on the glans were tumour-free; immunohistochemistry tests (Fig. 1, Fig. 2) indicated: CD3(-), CD792(+), LCA(+), L26(+), BCL6(-), BCL10(-), UCHL1(-), KP-1 cell(+). Postoperative bone marrow biopsy showed trilineage hyperplasia; lymphocyte showed no significant abnormalities in percentage and morphology. Chemotherapy was administered after the operation: CHOP (500 mg/m^2 cyclophosphamide and 30-50 mg/m^2 adriamycin and l-2 mg oncovin intravenously infused on day 1; and 40 mg prednisone taken orally on days 1-5, with an interval of 3 weeks between two courses of treatment). Physical examination, routine blood/urine tests, liver and kidney function tests, serum electrolytes, serum tumour makers, plain chest radiograph, abdominal and pelvic CT were examined to exclude recurrence and metastasis at each follow-up (postoperative month 3, 6, 9 and years 1 and 2. The follow-up showed regression of the mass on the shaft of penis and no signs of recurrence.

Discussion

Primary malignant lymphoma is mostly observed in lymph nodes. However, it can also occur in lymphoreticular and nonlymphoreticular systems outside the lymph nodes, which is primary extra-nodal lymphoma (PENL). PENL is mostly observed in the gastrointestinal tract, followed by Waldeyer's lymphatic ring, liver, spleen, nasal cavity, skin, central nervous system, bone, tonsil and thyroid gland. It is uncommon in the urogenital system. Primary penile lymphoma is rare, with only 17 reported cases in foreign countries[1-12] and 9 cases in China,[13-20] with unidentified pathogenesis. Patients were between the ages of 3 to 77 years (mostly adults, only 2 cases in children).[7-14] Among these 26 patients with penile lymphoma, 17 were located on the shaft, 5 on the glans

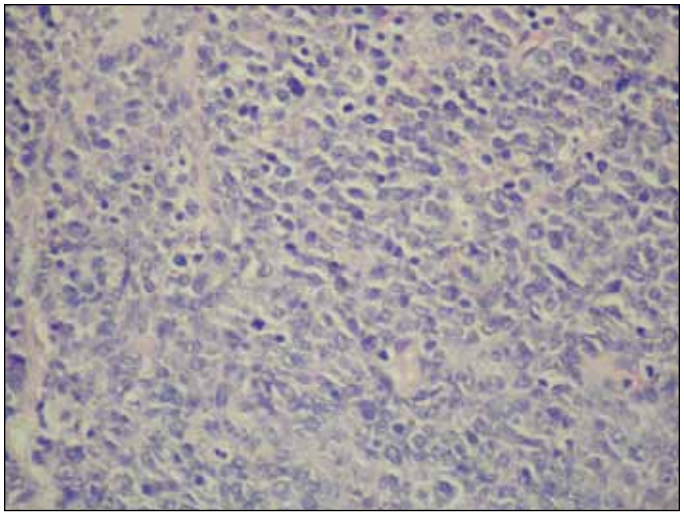

Fig. 1. Hematoxylin and eosin staining of primary penile lymphoma, ×400.

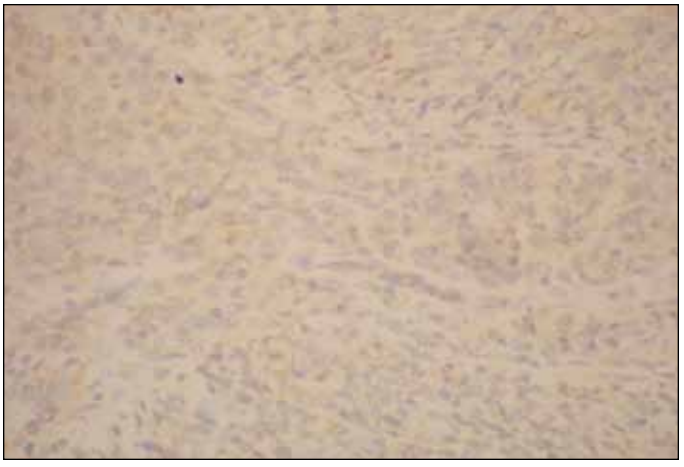

Fig. 2. Immunohistochemistry: leukocyte common antigen-positive tumour cells presented brown, ×400.

penis, 3 on the prepuce and 1 with unidentified location. In our case, the tumours were located on the shaft and the glans penis.

The major manifestation of primary penile lymphoma includes painless mass and ulcer on the corpus cavernosum penis, glans penis and penile skin. Symptoms, such as pruritus or dysuria, may also occur. Painless mass is most common, ulcer comes second, and dysuria is rare. When the lesion is on the shaft of the penis, the corpus cavernosum penis is involved and causes erectile dysfunction; penile swelling may also occur. Phallobase, inguinal lymph nodes and scrotum are often involved, which may affect distal blood flow of the penis and lead to preputial edema, usually without systemic symptoms.[17] The imaging examinations of primary penile lymphoma show no characteristic changes, and ultrasonography often shows vascularized mass, spot or ulcer of the penile skin.[21] A definitive diagnosis is made through biopsy and immunohistochemical examinations. However, ultrasonography, CT and bone marrow biopsy should be applied to identify distal metastasis and rule out lymphoma in other locations.

Due to the low incidence of penile lymphoma, a standardized diagnosis and treatment plan are yet to be established. Some researchers have developed a standard for diagnosing primary penile malignant lymphoma.[1,10] A diagnosis is made if the tumour is confined to the penis with no evidence of leukemia; and if there is a long interval between the primary and secondary tumour. In cases where the lesions are confined to the penis or if they are prominent in the penis, despite other locations, the penile lymphoma would still be considered a primary tumour. Upon reviewing other papers and our own case, we have come up with our own diagnostic standard: (1) penile mass and pathological confirmation; (2) no hypertrophy of superficial lymph nodes; (3) no signs of bone marrow suppression or leukemic hemogram; and (4) no visceral lymphatic masses or lymph node hypertrophy other than the penile mass. Our case report fits this diagnostic standard.

Malignant lymphoma is classified into B, T or NK cell lineage. Immunophenotyping identifies the derivation of lymphomas, which is significant in guiding clinical treatment and prognosis.[18] CD20(+) and CD3(-) indicate B-cell derivation. NK cells and cytotoxic T-cells have common functions and cell markers. NK-cell lymphomas express CD2, CD7, CD8, CD56 and CD57 – all of which are also observed in certain subgroups of T-cells. Immunoenzyme labelling of the most common NK/T-cell malignant lymphoma suggests CD2(+), CD56(+), surface CD3(-) and cytoplasmic CD3(+), with cytotoxic granule proteins positive in most cases. Clonal immunophenotypic markers are still unavailable for T-cell lymphomas. Although CD56 is a useful marker for NK/T-cell lymphomas, it is not specific. Therefore, the World Health Organization applies multiple parameters for lymphoma classification, including cell morphology, immunohistochemistry tests, genetics and clinical manifestations.[11] Studies indicate that NK/T-cell lymphoma accounts for 12% among all non-Hodgkin lymphomas.[11] NK/T-cell lymphoma is clinical invasive and has a poor response; survival time is shorter compared with B-cell lymphoma and Hodgkin lymphoma.[12] Our case is classified as B-cell lymphoma.

The treatment of primary penile lymphoma is still controversial due to its low incidence rate. Previous reviews suggested treatment patterns like surgery, radiotherapy or chemotherapy alone, as well as surgery combined with radiotherapy and/or chemotherapy. Some researchers believe that surgery alone or surgery combined with radiotherapy should yield ideal results; local dissection is applied instead of partial or total dissection due to the fact that penile lymphoma is usually a primary malignancy and rarely caused by metastatic invasion of systemic lymphomas.[4,22] Other researchers, however, argue that penile lymphoma is a manifestation of

systemic lymphoma, suggesting postoperative chemotherapy to enhance efficacy.[9,23] Yu and colleagues reported a case of a 6-year tumour-free survival with total dissection and chemotherapy.[23] There are also researchers suggesting that with clear diagnosis, chemotherapy alone could achieve good therapeutic results, with good preservation of the normal structure and function of the penis.[6,8,24] Recent developments in immunology has focused on biotherapy and made it a crucial component of the comprehensive treatment of lymphoma. Commonly applied biotherapeutic measures include monoclonal antibody therapy, radioimmunology therapy, active immunotherapy, adoptive immunotherapy, B-cell lymphoma-2-targeted therapy and specific micromolecular-targeted drug therapy. With rational application of these therapies and combination with other therapeutic measures, we can enhance the short-term efficacy and long-term survival rate. The most prominent development is the application of rituximab, a chimeric anti-CD20 monoclonal antibody. Rituximab changes the therapeutic pattern of B-cell lymphoma and kills tumour cells by complement activation, antibody-dependent cell-mediated cytotoxicity (ADCC) or apoptosis induction.[25] The combination of rituximab with chemotherapy and other bioactive drugs can enhance curative effects.[25] Other developments include great therapeutic potential of radioimmunological conjugates and oblimerson sodium (B-cell lymphoma-2 antisense oligonucleotide) to treat low-grade malignant lymphomas. Novel chemotherapy (bleomycin-etoposide-adriamycin-cyclophosphamide-oncovin-procarbazine-prednisone, BEACOPP) and new drugs like gemcytabine and anti-CD20 monoclonal antibody have been clinically applied.

Conclusion

The use of systemic chemotherapy and biotherapy is considered first-line therapy to achieve total alleviation and preservation of penile function and shape. Another widely accepted treatment is local radiotherapy, like systemic chemotherapy and biotherapy; this can also preserve the shape and function of the penis. In terms of surgery, local or total dissection of the genitalia are applied; local dissection is only used for biopsy or combining treatment and total dissection is applied only as a palliative method when radiotherapy and chemotherapy have failed. If the diagnosis is clear, a comprehensive treatment pattern of systemic chemotherapy, biotherapy and radiotherapy should be applied.

Competing interests: None declared.

This paper has been peer-reviewed.

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