An Isolated Penile Mass in a Young Adult Turned Out To Be a Primary Marginal Zone Lymphoma of the Penis. A Case Report and a Review of Literature

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Abstract. *Aim: to discuss the rationale of the management of penile MALT lymphoma. Case Report: A 24-year-old patient presented with a painless and mobile nodule localized in the ventral part of the penis. The lesion was firstly evaluated through Doppler ultrasonography, which showed a hypoechoic and vascularized solid mass, a subsequent magnetic resonance confirmed size and position of the lesion. Subsequetly the patient underwent a surgical excision of the mass, the pathological diagnosis was consistent with penile lymphoma, MALT-type. The patient underwent a consolidative immunotherapy with rituximab. Disease re-staging was performed through a MR without any detection of local or systemic recurrences. Conclusion: To our knowledge, no cases of MALT lymphoma involving the penis have been reported in the literature so far. Surgical excision with organ sparing and immunotherapy with rituximab, successfully induced a complete response. Based upon this experience, we may recommend a conservative surgery associated with a systemic approach*

Extranodal marginal zone B-cell non-Hodgkin's lymphoma arises from mucosa-associated lymphoid tissue (MALT); it has been observed at a wide variety of extranodal sites, although in most cases, the anatomical site involved lacks proper native MALT. In these situations, the lymphoma is related to an acquired MALT that develops as a consequence of a persistent stimulus, such as a chronic inflammatory disorder, a chronic infection or an autoimmune process. In the setting of prolonged lymphoid proliferation, a malignant clone may emerge (1-3).

The presenting symptoms of MALT lymphoma are non-specific, and mainly related to the primary localization of the tumor. The disease may remain localized for a prolonged period within the tissue of origin, like many other slow-progressing, low-grade urogenital diseases (4), and for this reason the diagnosis may be delayed. Dissemination to multiple mucosal sites or bone marrow, in fact, is not so uncommon, even many years after the primary treatment (5).

Lymphomas arising in the urinary tract and male genital organs – including kidney, bladder, prostate, testis, ureter, urethra and penis – account for lower than 5% of extranodal lymphomas (6). Lymphomas involving the penis are very rare, mainly of B-cell origin, and have only been cited in isolated case reports, with diffuse large B-cell lymphoma being the most common subtype (7-11). Although most of the lymphomas reported at this site have been seen in adults, there is a case report of a primary penile lymphoma in a 4-year-old boy who presented with a painless penile mass (12). T-Cell lymphomas have also been reported (6, 13, 14). The diagnosis of this rare lymphoma can be difficult and the treatment options are controversial.

To our knowledge, no cases of MALT lymphoma involving the penis have been reported in literature so far: herein we describe the case of a primary penile MALT lymphoma and discuss the rationale of its management by means of surgery and systemic therapy.

Case Report

A 24-year-old Asian man presented in April 2012 to our Andrology Unit with a painless and mobile nodule localized in the ventral part of the proximal shaft of the penis,

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measuring 1 cm in its major diameter. On physical examination, testicular (12 of Prader) and inguinal lymph nodes were normal; no superficial lymphadenopathies were documented, nor any hepatosplenomegaly. The patient was totally asymptomatic, no general symptoms of lymphoma, such as fever, night sweats, weight loss or itching were reported. Moreover, the patient did not complain of difficulty in urination, priapism or urethral bleeding.

The nodular lesion was firstly evaluated through Doppler ultrasonography, which showed a hypoechoic and highly vascularized solid mass of 13×6 mm in diameter involving the distal part of the shaft of the penis, localized in the *corpus spongiosum* of the urethra and causing urethral compression; the lesion also protruded externally in the subcutaneous layer of the penis. Subsequent magnetic resonance imagine (MRI) of the penis, performed after the injection of 5 μg of prostaglandin-E^1 in the *corpora cavenosa*, confirmed the size and the position of the lesion, which appeared to be cleaved from the *corpus spongiosum* of the urethra after contrast infusion, however, determining a dislocation of the urethral canal (Figure 1, A). Findings were similar to those previously reported elsewhere (15).

One month later, the patient underwent surgical excision of the mass: a circular mucosal incision distant 1 cm from the *glans penis* was performed, with subsequent penile degloving; after a bilateral incision of Buck's fascia, the lesion was found to be in close contact with the ventral part of the distal urethra (Figure 1, panel B). The lesion was excised; it appeared completely capsulated and friable, and it did not seem to incorporate the *corpus spongiosum*, not to be adherent to the cavernous bodies (Figure 1, C and D). Upon histological examination, a diffuse proliferation of small CD20-positive lymphocytes was described, along with accompanying monotypic plasma cells expressing immunoglobulin λ light chain. The diagnosis was consistent with extranodal marginal zone B-cell non-Hodgkin's lymphoma, MALT-type (Figure 2). Evidence of re-arrangement of the immunoglobulin light chain genes was a proof of clonality of the lymphoproliferative process.

In order to accomplish accurate disease staging, a computed tomographic scan of the chest, abdomen and pelvis was performed, showing no lymph node enlargement at mediastinal or retroperitoneal sites. A bone marrow trephine biopsy showed no evidence of disease infiltration. All the criteria for the diagnosis of primary – *i.e.* stage I_E A according to the Ann Arbor staging system (16) – MALT lymphoma were fulfilled.

The patient's complete blood counts and blood chemistry were all within normal ranges; serum immunoglobulin concentrations and free light chain κ/λ ratio were normal; no monoclonal components were documented on serum immunofixation. Serological tests for hepatitis B and C virus and human immunodeficiency virus were all negative; neither IgG nor IgM antibodies directed to *Treponema pallidum* were detected on immunoblot.

The patient underwent a consolidative immunotherapy with the anti-CD20 monoclonal antibody rituximab, which was administered once a week for four consecutive weeks at a dose of 375 mg/m^2. The treatment was perfectly tolerated, with no remarkable side-effects.

Disease re-staging was performed two months after the last rituximab administration through a penile MRI: neither residual neoplastic masses were detected, nor any recently developed focal lesions of the *corpora carvernosa* and *corpus spongiosum*. Inguinal lymph nodes were not enlarged. The penile shaft showed no pathological incurvation while erected.

Discussion

Penile tumors are essentially squamous carcinomas and are generally treated with total or partial penis resection based on the extension of the disease, or conservatively with interstitial brachytherapy (17). On the contrary, penile lymphomas are extremely rare and need a different approach. Their clinical appearance is variable, commonly presenting with nodules, ulcers or diffuse – and generally painless – penile swelling (18), but even simulating Peyronie's disease, with a bulky scrotal mass (19), priapism, inflammatory ulcers of the shaft or the glans, traumatic injury or dysuria (9). The discrimination between penile lymphoma, arising from the soft tissue of the penis, and urethral lymphoma, another very rare lymphoma of the genitourinary tract that can mimic the same symptoms and can determine obstruction of the urinary tract, is an important issue, as well as the differential diagnosis from other neoplasms, such as undifferentiated sarcomas or carcinomas. The surgical excision of the mass to locally eradicate the disease and to obtain a specimen for pathological examination and immunohistochemistry is, therefore, the most significant step required to achieve the diagnosis.

Literature about penile lymphoma is scarce, and about 20 cases have been reported in English, with no cases of primary penile MALT lymphoma previously described as far as we are aware of. Multiple treatment options, including surgical amputation, radiotherapy and chemotherapy, even in combination, are available for the treatment of this peculiar type of lymphoma; however, due to the rarity of the disease, specific recommendations regarding the best treatment choice are unavailable, and follow-up data are lacking.

More specifically, as in other extranodal MALT lymphomas, the indolent nature of the disease justifies a conservative approach, with local treatments to be considered as the first option (2, 20). The surgical approach should be of choice to treat small lesions, thus avoid mutilating or demolishing interventions most times (21). Radiation is a

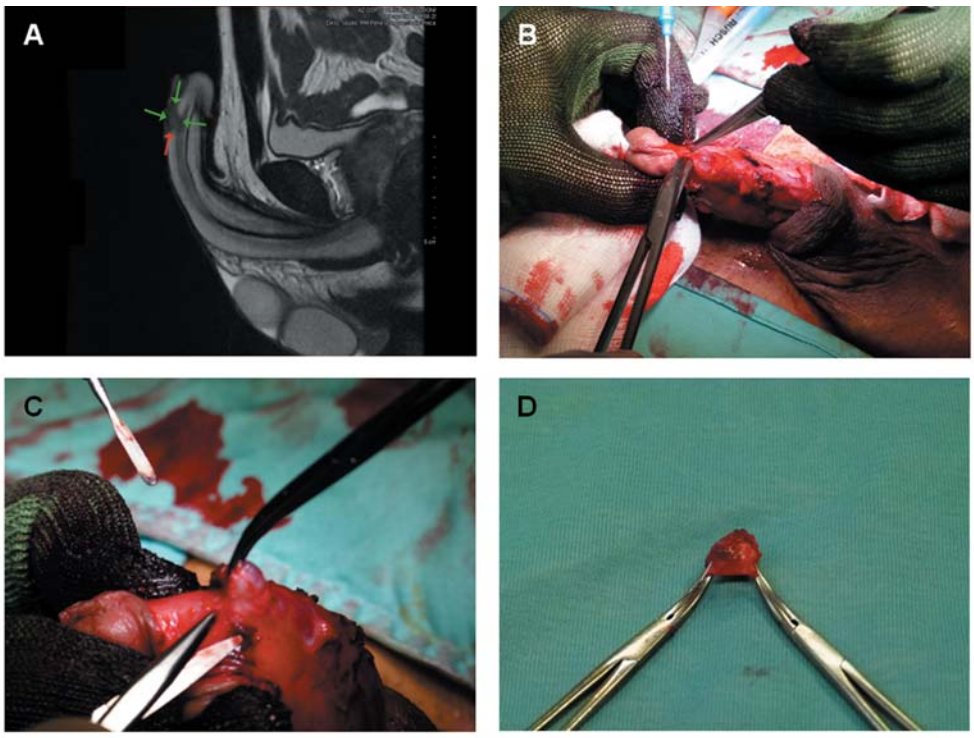

Figure 1. *Magnetic resonance imaging of the penis showing the lesion (surrounded by arrows) of the penile shaft (panel A); isolation (panel B) and surgical excision (panel C) of the mass; the gross appearance of the excised nodule (panel D).*

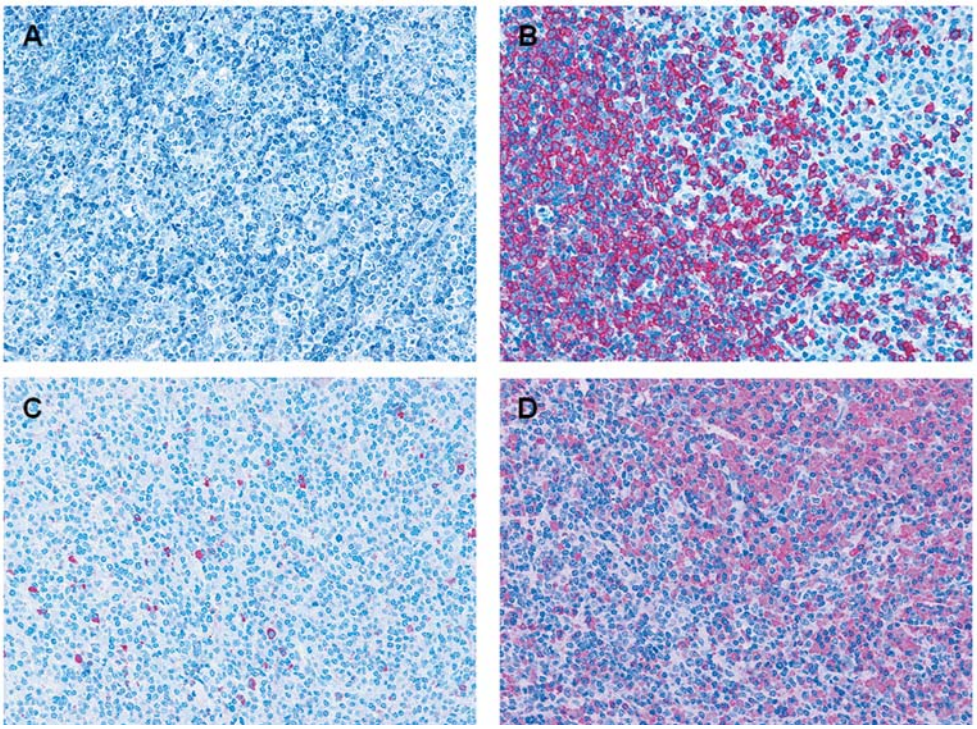

Figure 2. *Tissue sample (Giemsa staining), showing small lymphocytes and plasma cells (A); lymphocytes stain positively for CD20 (B), stain negatively for κ light chains (C). CD20-negative lymphoid elements show a strong immunohistochemical reaction for immunoglobulin λ light chain (D) (magnification ×200).*

highly effective modality, and in general it may be sufficient to achieve local control of the lymphoma with low morbidity (7), although it may determine late functional *sequelae* (such as flaccid and non-functional penis) if applied at doses higher than 400 cGy, as reported for squamous tumors (21).

As in other B-cell non-Hodgkin's lymphomas, rituximab is effective in MALT lymphoma, with a reported response rate of about 70%, and a very tolerable toxicity profile (22). For this reason, it appears a suitable option in the adjuvant setting as a single agent.

Although systemic chemotherapy is active, it should be reserved for advanced stage disease, when the involvement of other nodal or extranodal sites, or of the bone marrow is documented and the penile lesion is part of a systemic process, or for palliative purposes (2, 20). A chemotherapy approach should also be recommended in relapsing disease after local conservative treatment, and in all high-grade non-Hodgkin's lymphoma subtypes (namely diffuse large B-cell lymphoma) after surgical excision, with the concomitant use of rituximab.

Conclusion

In summary, to our knowledge this is the first reported case of primary MALT lymphoma of the penis. Surgical excision with organ-sparing approach and immunotherapy with rituximab successfully induced a complete response without any clinically significant *sequelae*. Because of the rarity of this pathological entity, there are no available guidelines for treatment and follow-up: based upon this experience, we would recommend conservative surgery associated with a subsequent systemic approach. Penile MRI appears useful both at disease staging and as a tool to detect possible residual neoplastic masses.

Conflicts of Interest

All Authors declare they have no conflicts of interest to disclose.

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