

Metastatic inguinal lymph node, squamous and urothelial cell carcinoma in origin: a rare case of carcinoma of unknown primary with two different histopathologic deposits

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Summary

Cancer of unknown primary (CUP) sites constitutes approximately 5% of all cancers.^{1,2} The standard treatment for these patients typically involves empirical chemotherapy. However, specific subsets of CUP with unique clinical or pathological features, such as solitary metastatic lesions or isolated nodal CUP, may present a more favourable prognosis and can be effectively managed with excisional surgery or radiation therapy alone.³⁻⁵ Metastatic inguinal lymphadenopathy mainly originates from the genitalia and anorectal areas. In this case report, we describe an uncommon case of two different histological types of metastases in inguinal nodes with unknown primary sites.

Keywords: carcinoma of unknown primary, metastatic SCC, metastatic UCC, lymph nodal mass

Case report

A 65-year-old male, five-pack-year bidi smoker and tobacco chewer since past three years, presented with right inguinal swelling since past two years. He had no history of penile lesions, warts, or lower urinary tract symptoms. On examination, multiple 50 × 30 mm matted lymph nodes (LN) palpable at the right inguinal region were found (Figure 1). There were no penile lesions or urethral stricture.

Anoscopy showed no suspicious pigmentation or visible growth. Urethrocystoscopy was performed to rule out any suspicious bladder or urethral lesions. Contrast magnetic resonance imaging of the pelvis was suggestive of at least three partially necrotic LNs in the right inguinal region (largest 43 × 35 mm), with a possibility of a neoplastic secondary deposit more likely than infective. Contrast-enhanced computed tomography (CECT) of the thorax abdomen and pelvis was suggestive of enlarged, heterogeneously enhancing necrotic LNs (41 × 27 mm) in the right inguinal region. A fluorodeoxyglucose-18 (FDG) positron emission tomography (PET) scan was suggestive of a few metabolically active and enlarged necrotic LNs at the right inguinal region. There was no other metabolically active lesion in the rest of the scanned body segment.

The patient underwent fine needle aspiration cytology, which was suggestive of metastatic squamous cell carcinoma (SCC). For better categorisation, he also underwent incisional biopsy, which was suggestive of a metastatic deposit of urothelial carcinoma given the immunohistochemistry, which was negative for cytokeratin 17 and 20 and positive for P40, P63, and GATA-3. Serum carcinoembryonic antigen, cancer antigen 19-9, alpha-fetoprotein, prostate-specific antigen, and beta-human chorionic gonadotropin levels were within normal ranges.

Urine cytology for malignant cells was negative, undetected by the GeneXpert for MTB. Following the tumour board discussion, ilioinguinal LN dissection was advised. The patient underwent open right standard pelvic LN dissection and right radical inguinal lymphadenectomy (ILND) (Figure 2).

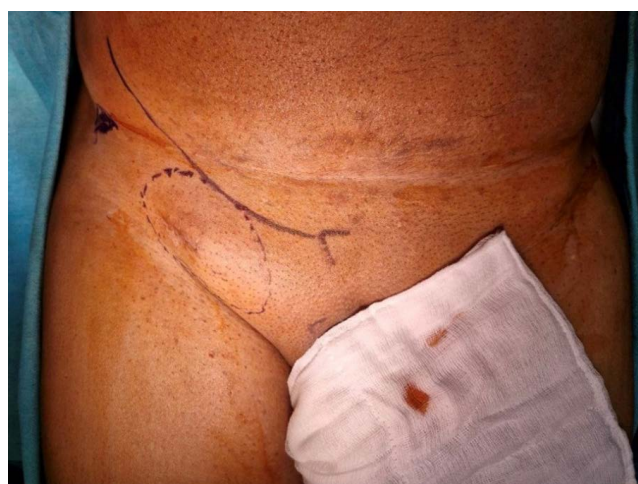


Figure 1: Incision for right standard pelvic lymph node dissection and radical inguinal lymphadenectomy

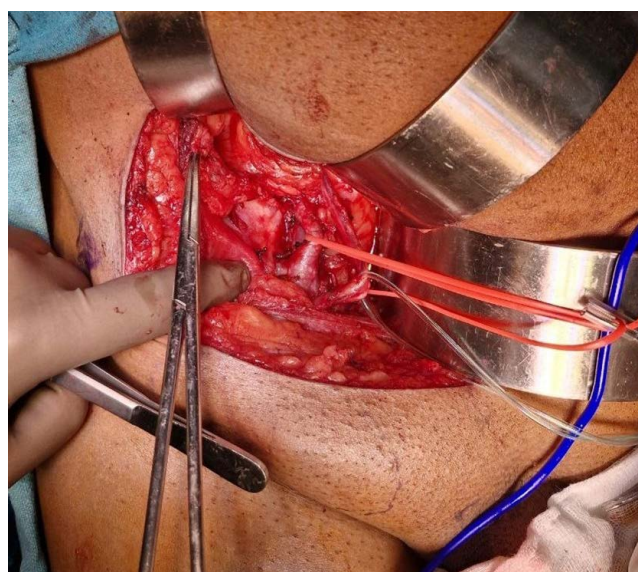


Figure 2: Open right standard pelvic lymph node dissection up to bifurcation of common iliac artery

Histopathology was suggestive of metastatic SCC. Immunohistochemistry was positive for P40 and P63 and negative for HMB-45 and GATA-3. The right pelvic nodes showed no evidence of metastasis. The right superficial and deep inguinal nodes showed metastatic deposits in three out of nine nodes.

A postoperative tumour board discussion was held, given the initial LN biopsy, which was suggestive of metastatic urothelial cell carcinoma (UCC) deposits and radical ILND specimen suggestive of metastatic SCC. A decision was made, and the patient underwent adjuvant radiation therapy to the groin and pelvis. Postoperative CECT of the abdomen and pelvis was done after six weeks, indicating postoperative changes in the right inguinal lesion, with no primary lesion visualised. The patient underwent 54 Gy in 27 fractions of volumetric modulated arc therapy (VMAT). The patient was on close follow-up for three months after the adjuvant radiotherapy.

Discussion

Inguinal LNs account for approximately 10% of cancer of unknown primary (CUP) cases in lymphatic tissue. Adenocarcinoma is the most prevalent histological type, while only 13.7–21.4% arise from squamous cell origins.^{6,7} The lymphatic drainage of the inguinal LNs is derived from the lower limbs, gluteal region, lower anterior abdominal wall, penis, scrotum, penile urethra, vulva, distal parts of the vagina, and the anal canal. The role of adjuvant radiotherapy to the bilateral inguinal, pelvic, and para-aortic regions with a dose of 55 Gy in 25 fractions over five weeks is to be considered.⁸

In one of the largest series involving more than 2 000 patients with inguinal nodal metastasis, the primary site could not be identified in 22 patients (1%), even after a significant follow-up period.⁸ In our case, the site could not be determined despite extensive attempts to locate the primary site. The clinical investigative approach towards CUP patients is primarily directed by histopathology, and every effort should be made to obtain a high-quality tissue sample for detailed immunohistochemical analysis.

Investigations should involve a multimodality approach. The role of a PET scan is yet to be established; however, it has the potential to modify the treatment in some patients whose tumour was localised with computed tomography.⁹ As early as 1979, it was emphasised that the analysis of tissue samples should help to eliminate the need for undirected investigations when screening for the primary site.⁹ Since then, significant advances in the molecular analysis of tumours have been made, and so the incidence of CUP has decreased.⁹

Because CUP in the inguinal region is rare, there is a paucity of literature on the management of such patients, and no clear guidelines are described. The mainstay of treatment is surgery, with complete surgical excision through systematic lymph nodal dissection being mandatory. Aggressive surgical treatment, including vascular resection and reconstruction with grafting, may be required to achieve tumour-free margins. Although the role of postoperative radiotherapy is not clearly defined, it is thought that, in the presence of extensive nodal involvement and/or extranodal tumour spread, postoperative radiotherapy should be used as in any known primary site with SCC.

A review article indicates that surgery with adjuvant irradiation was the preferred treatment for inguinal metastasis with an unknown primary site.⁹ A diligent follow-up is required for these patients. One case report described an occult carcinoma of the penis that manifested three years after the treatment of inguinal nodal metastasis.¹⁰ According to the authors, circumcision and random biopsy of the glans should be routine for such patients. The patient in our case was also followed up clinically and radiologically, with cystoscopy, due to the presence of transitional cell carcinoma.

Conclusion

CUP with inguinal metastasis is a rare entity. Investigations should be directed to identify the primary site according to histopathology. Our case is an even rarer occurrence, as two different histopathologies were identified from the metastatic deposit in the right inguinal node: UCC in the initial LN excision biopsy specimen and SCC in the radical ILND specimen with an unknown primary. Although there are no clear guidelines for the management of these patients, treatment should be multimodal, including aggressive surgical resection and postoperative radiotherapy. Our patient received 54 Gy in 27 fractions of postoperative VMAT. The possible role of chemotherapy is unknown. In the future, molecular studies, such as a final diagnostic panel of immunohistochemistry, may enhance our ability to distinguish subtypes of CUP and treat them differently.

Conflict of interest

The authors declare no conflict of interest.

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