Testicular Metastasis in Prostate Adenocarcinoma: a Rare and Incidental Diagnosis on Histopathology

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Sir,

Testicular metastasis is a rare phenomenon and occurs at a relatively older age compared to primary testicular tumors. Tumors showing testicular metastases include renal cell carcinoma, colonic carcinoma, transitional cell carcinoma, bronchogenic carcinoma and esophageal carcinoma [1]. Prostatic adenocarcinoma, though the most common malignancy in the males, rarely metastasises to the testes [1]. The morphology of the metastatic disease can be atypical, thus posing a diagnostic difficulty. Immunohistochemistry (IHC) plays an important role in confirming the diagnosis.

We report a 62-year-old male who presented with bilateral lower limb deep venous thrombosis (DVT). On digital rectal examination, he was found to have a hard nodular prostate. On evaluation, serum PSA was markedly elevated, i.e. 243 ng/ml (normal <4.5 ng/ml). Trans-rectal ultrasound (TRUS) guided prostatic biopsy revealed adenocarcinoma with a Gleason score of 9 (4 + 5). Contrast-enhanced computed tomography (CECT) of the pelvis revealed enlarged pelvic lymph nodes. He was put on warfarin (3 mg/day) for DVT. As a part of hormonal ablation, bilateral orchiectomy was planned. Clinically, both the testes were of normal size. Grossly, both the testes were of normal size and cut surface did not reveal any tumor deposits. However, microscopically, the right testis

showed tumor cells arranged in the cribriform pattern, small glands, single cell infiltration and lymphovascular emboli (Fig. 1a). On IHC, the tumor cells were positive for PSA (Fig. 1b). Hence, a diagnosis of metastatic adenocarcinoma from prostate was confirmed.

Testicular metastasis is an uncommon phenomenon with the lungs and kidneys being the most common primary sites. Rare primaries are the stomach, pancreas, urinary bladder and rectum. One of the factors hypothesised for this low incidence is the relatively low temperature of the scrotum [2]. Lioe and Biggard evaluated 85 testicular tumors and found that secondaries comprise 10 % of testicular tumors [3]. Garcia-Gonzalez et al. found a 0.68 % incidence of metastases to the testes with solid malignant extragonadal neoplasms in their autopsy series of 738 males [4]. Prostatic adenocarcinoma though has a high frequency of dissemination, metastasis to the testes is extremely rare. Patel SR et al. in their study of 20 cases of testicular metastases, however, found prostate as the most common primary site [5]. This may be explained by a high percentage of therapeutic orchiectomy in their series as in our patient. Most cases are unilateral testicular metastasis occurring in the fifth to sixth decades of life and diagnosed incidentally at histopathology or autopsy with rare symptomatic presentation. Inaba Y et al. reported a case of testicular metastasis from prostatic adenocarcinoma presenting with scrotal swelling [6]. Persistent or recurrent urinary symptoms have also been reported. The testes are usually normal in bulk and shape, rendering difficult detection of tumor. The PSA levels are elevated in most cases though low levels do not exclude this diagnosis [7].

The most common mechanism postulated is invasion into lymphovascular spaces which also explains a high frequency of metastasis to the regional pelvic lymph nodes as in our case.

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Fig. 1 Low-power microphotograph (a) showing interstitial infiltration by tumor cells in cribriform pattern (*broad arrows*) and single cell and glandular infiltration pattern (*long arrow*). Normal seminiferous tubules

(*arrow heads*) are also noted in the surrounding testis. H&E, $\times 100$. Immunohistochemistry (b) demonstrating cytoplasmic prostate-specific antigen (PSA) positive tumor cells within the testis

The tumor may also spread from the prostatic urethra via retrograde extension into venous or arterial system with resultant embolisation or via direct invasion of the vas deferens. Menon S et al. highlighted the role of Hyaluronan and its receptor CD 168 in progression and metastasis of androgen-independent prostate cancer [8]. Since prostatic adenocarcinoma has variable morphology, the diagnosis of testicular metastasis could be challenging on histopathology. Primaries from the stomach, and the lung can mimic prostate adenocarcinoma based on morphology [2]. Besides, the morphology at primary versus secondary site can be quite different. This is particularly true in cases with a high Gleason score and a widely disseminated disease as was seen in our case too. The commonly reported patterns include ductal pattern involving the rete testis with large atypical cells in the interstitium and intertubular pattern with the neoplastic cells showing prominent nucleoli with abundant cytoplasm and loosely cohesive cells mimicking a seminoma. Thus, immunohistochemical markers are necessary to confirm the diagnosis to exclude these entities. Few rare cases of testicular involvement mimicking lymphoma have also been reported. Haupt B et al. reported a case where the testis showed infiltration by tumor cells morphologically resembling lymphoma, however, confirmed on IHC [9]. The discriminative IHC markers include positivity for cytokeratins AE1/AE3 and PSA.

The clinical implication of testicular metastasis in prostatic adenocarcinoma is though not well established; Korkes et al. concluded that testicular metastasis implies an aggressive behaviour and poor prognosis [10]. Thus, increased awareness among the urologists and pathologists is required to identify testicular metastasis in prostatic adenocarcinoma undergoing orchiectomy for hormone ablation. This is important for

further follow-up for instituting prompt therapy, thereby, reducing mortality.

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