Case Report

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Late solitary testicular metastasis from rectal cancer

ABSTRACT

Isolated testicular metastasis from rectal cancer is rare. We describe the case of a patient who presented with a locally advanced rectal malignancy and underwent multimodality treatment with low anterior resection, postoperative radiotherapy and adjuvant chemotherapy. He developed a painless testicular nodule while on follow-up, five years after the diagnosis of primary rectal cancer. Histopathology and immunohistochemistry of orchidectomy specimen were compatible with a metastatic adenocarcinoma of rectal origin. We hypothesize that this phenomenon of isolated relapse in a sanctuary site could be due to the altered biology and pattern of metastasis as a result of effective adjuvant systemic chemotherapy. Treatment of late isolated relapse in the testis needs to be ascertained.

KEY WORDS: MeSH terms, rectal cancer, testicular metastasis

Ramachandran Venkitaraman, Mathew George[1], Suranga Weerasooriya[2], Sid Selva-Nayagam[3]

Ipswich Hospital NHS, UK, [1]Department of Medical Oncology, Tamworth Hospital, Australia, [2]Department of Medical Oncology, Royal Darwin Hospital, Darwin, NT, 0810, Australia, [3]Royal Adelaide Hospital, Australia

For correspondence: Dr. Mathew K. George, Department of Medical oncology, Tamworth Hospital, New South Wales, Australia. E-mail: doctormathekgeorge@yahoo.co.in

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INTRODUCTION

Metastatic testicular cancers are rare and often found incidentally at autopsy or therapeutic orchiectomy. Testicular metastasis have been reported in 0.02% to 2.5% of orchidectomy specimens in two large autopsy series, which included non-neoplastic deaths.[1,2] Patel *et al*. reported metastasis in 3.6% of 550 patients who had orchidectomy for testicular tumors, the common primary sites being prostate (60%), followed by melanoma (15%), sarcoma (10%), lung, colon and renal cancer (5% each).[3] Haupt *et al*. have studied testicular metastasis in 127 patients and have suggested that testicular tumors in older patients with extensive lymphatic and vascular invasion and an interstitial pattern, sparing the seminiferous tubules, is suggestive of a metastasis as opposed to primary testicular tumor.[4]

A few autopsy studies have reported rectal carcinoma with testicular secondaries.[1,3] A few reports of colon cancer with testicular metastases have been reported too, either at autopsies or as isolated case reports of advanced metastatic disease.[5-7] Very few cases of testicular metastasis from rectal cancer have been reported in the literature so far, but in all cases either at initial presentation or at relapse in the context of advanced disease.[8-11]

CASE REPORT

A 71-year-old Caucasian gentleman presented with rectal bleeding, and investigations revealed an ulcero-proliferative rectal growth 7 cm above anal verge. Rectal biopsy showed moderately differentiated adenocarcinoma. Carcino-embryonic antigen (CEA) level was three. He underwent low anterior resection and total mesorectal excision. Pathologic examination revealed Stage IIIA disease (pT3N1M0; two of 16 nodes positive; microscopic margins clear). The patient received adjuvant chemotherapy with 5 FU / Folinic acid for six cycles and postoperative radiotherapy (45 Gy in 25 fractions) to the rectum. He was on regular follow-up with no evidence of disease.

The patient represented in five years with a nodule in the right testis. Clinical examination was unremarkable except for the testicular swelling. CEA, CA 19.9, alfa fetoprotein (AFP) and beta human chorionic gonadotropin (HCG) levels were normal. Imaging studies including CT scan of the chest, abdomen and pelvis were normal. The patient underwent right orchiectomy. Histology of the orchidectomy specimen was consistent with infiltrating adenocarcinoma with a mucinous component involving the testis with CytoKeratin 7 and CytoKeratin 20 being patchy positive and CEA being positive [Figure 1 and 2]. The morphology of the tumor and the immunohistochemistry were consistent with metastatic rectal adenocarcinoma.

The patient subsequently developed secondaries in the lungs and liver six months later. The patient was treated with palliative chemotherapy with no appreciable response and minimal improvement in his condition and succumbed to death.

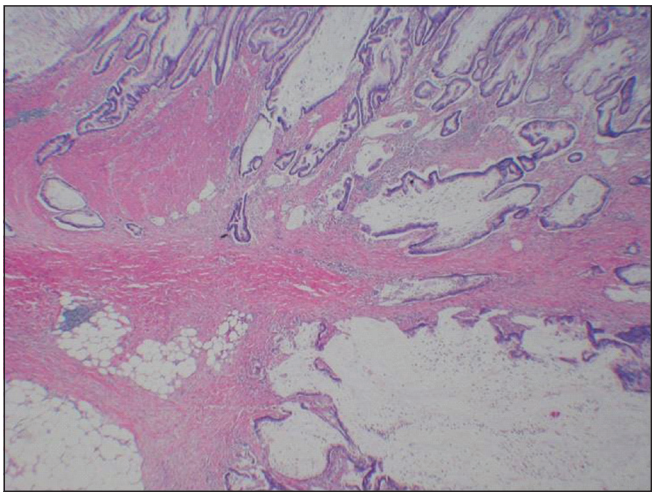

Figure 1: Histopathologic examination of the resected testicular tumor shows infiltrating adenocarcinoma with mucous production (H&E, ×40)

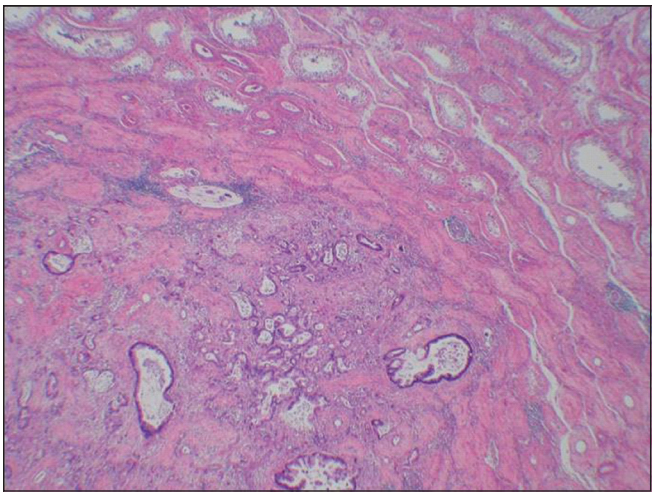

Figure 2: The orchidectomy specimen shows characteristic lymphovascular invasion by adenocarcinoma (H&E, ×40)

DISCUSSION

Testicular metastasis from rectal cancer is rare. To our knowledge this is the first instance of late solitary testicular metastasis from rectal cancer. Previous case reports have described testicular metastasis from rectal cancer as part of initial or advanced disease presentations.[2,5,11] There have been some reports of testicular metastasis from colon cancer as the initial site of distant relapse.[7]

Lower temperatures in the scrotum creating an unfavorable environment for the seeding of the metastatic cells could explain the relative rarity of testicular metastasis.[12] The routes of metastasis to the testis in solid tumors are thought to be retrograde arterial, venous or lymphatic embolization. Retrograde spread through spermatic veins from the renal veins or the retro peritoneum may be possible due to the absence of valves.

Testicular relapses after chemotherapy are considered to be due to the presence of 'the blood testis barrier' making it a sanctuary site impermeable to the cytotoxic drugs. The physico-chemical barrier consists of continuous capillaries, sertoli cells in the tubular wall, connected together with narrow tight junctions and a myxoid layer around the seminiferous tubules.[13] The efflux pump barrier contains p-glycoprotein in the luminal capillary endothelium and myxoid layer, and multidrug resistance associated protein-1 located basolaterally on the sertoli cells. The immunologic barrier consisting of the FAS ligand in the sertoli cells may also act as a deterrent to the optimal action of cytotoxic drugs.

In patients with lympho-proliferative disorders, isolated testicular relapses are common and are frequently salvaged with high dose chemotherapy which crosses the blood-testis barrier along with testicular radiotherapy.[14] Some studies have suggested that clinically overt testicular relapse may have a poorer outlook and may be the harbinger of widespread systemic relapse subsequently, while others have suggested that isolated testicular relapses may have a better prognosis than systemic relapse in other organs like liver and lung.

In this case report, the patient did not receive what is considered standard treatment i.e. preoperative chemoradiation. The inferior loco regional and systemic treatment may have resulted in an increase in risk of disease relapse. Isolated relapse of rectal primary after five years is uncommon, the usual sites, if it occurs, being the liver, lung and distant lymph nodes. Occult micro metastasis at the time of diagnosis or after surgery is thought to be the cause for distant systemic relapses. Adjuvant chemotherapy for solid tumors like colorectal cancer tackles systemic micrometastic disease and is proven to significantly reduce the incidence of relapses at these sites. Effective systemic treatment may have altered the biology of the disease leading to less systemic relapses, with an apparent increase in the frequency of late isolated relapses of solid tumors in sanctuary sites like the brain and testis.[15] In solid tumors like rectum, instances of delayed isolated testicular relapse may be more frequent in the future due to the altered relapse pattern arising from use of systemic chemotherapy which reduces relapses in the common sites. Testicular examination as a part of routine post-chemotherapy follow-up examination may be warranted in the future in patients with solid tumors like colorectal cancer, similar to patients with lymphoproliferative disorders. Salvage treatment for such isolate late relapses is in evolution and the prognosis is uncertain. Whether isolated testicular relapses have a better prognosis than systemic relapses in other organs may need to be ascertained by more information gained from pooled analysis of the outcomes of patients described in similar case reports. Also open to discussion is the need for high doses of salvage chemotherapy which could penetrate the blood testis barrier or the need for radiotherapy to contralateral testis.

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