Case Report:

Carcinomatous meningitis complicating carcinoma of uterine cervix: an uncommon presentation

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ABSTRACT

Carcinomatous meningitis is a rare clinical entity associated with gynaecological malignancies. However, it is an unusual occurrence in carcinoma of uterine cervix. Here we report a case of a 55-year-old female who was diagnosed to have carcinoma of uterine cervix stage IIB and was started on radiotherapy to whole pelvis with curative intent. One week later she complained of sudden onset of headache,vomiting and neck rigidity. Contrast enhanced computed tomography (CECT) brain showed diffuse meningeal enhancement of sulci. Cytopathological examiniation of cerebrospinal fluid revealed malignant cells which confirmed the diagnosis of carcinomatous meningitis. She received palliative whole brain radiotherapy and intrathecal methotrexate that resulted in symptomatic improvement during and immediately following treatment. She died four weeks after discharge from the hospital.

Key words: *Carcinomatous meningitis, Carcinoma, Uterine cervix*

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INTRODUCTION

Carcinomatous meningitis also known as neoplastic meningitis is a rare clinical entity occurring in 3% - 8% of all cancer patients.[1] With the evolution of effective therapeutic strategies for primary cancer sites which is augmented by advanced diagnostic imaging of neuraxis and a greater promptness to undertake cerebrospinal fluid cytopathological exmaination, its incidence appears to increase with proportionate rise in the overall survival. Carcinomatous meningitis is most commonly associated with haematological malignancies and solid tumors like breast cancer, lung cancer and melanoma.[2] Neoplastic seeding of meninges is very much unusual in gynecologic cancers and if present, most cases occur in ovarian cancers.[3] Uterine cervical squamous cell carcinoma presenting with carcinomatous meningitis is an exceedingly rare metastatic event with very few cases have been reported so far in English literature.[2-6] This prompted us to report the present case.

CASE REPORT

A 55-year-old postmenopausal lady with no significant comorbidities presented with complaints of bleeding and white discharge per vaginum of three months duration. On per vaginal and per rectal examination, an ulceroproliferative growth of 4 x 3 cm arising from uterine cervix was seen involving anterior and posterior vaginal walls upto upper one-third and bilateral parametria were involved medially. Punch biopsy from lesion was reported to be poorly-to-undifferentiated carcinoma of uterine cervix possibly of squamous cell origin (Figure 1). Immunohisto-chemistry revealed cyto-plasmic positivity for cytokeratin 5 (CK5), cytokerative 6 (CK6) and

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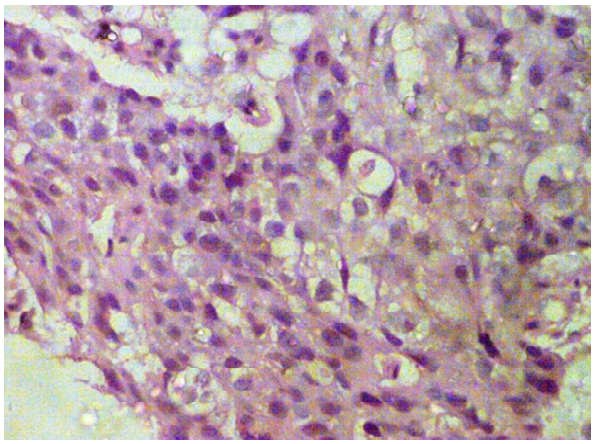

Figure 1: Photomcirograph showing poorly to undifferentiated carcinoma showing oval to polygonal neoplastic cells arranged diffusely (Haematoxylin and eosin, × 100)

nuclear positivity for (P 63 protein) in tumour cells suggestive of poorly differentiated squamous cell carcinoma (Figure 2). Laboratory investigations, such as, haemogram, liver function and renal function tests were within normal limits. Ultrasonography of abdomen and pelvis showed 4.6 x 4 cm growth in cervix with fat planes maintained with urinary bladder and bilateral grade 1 renal pelvis dilatation changes. No evidence of significant pelvic and abdominal lymphadenopathy was seen. Chest radiograph revealed mild bilateral pleural effusion for which general medicine consultation was taken; oral diuretic treatment was instituted for one week. Repeat chest radiograph after one week was within normal limits. She was staged as carcinoma of uterine cervix stage IIB and started on external beam radiotherapy to whole pelvis with curative intent. After one week of commencement of treatment, she complained of a gradual onset of low grade fever; bilateral pitting oedema, facial puffiness over three days; and an abrupt onset of headache, giddiness and neck rigidity. After adminsitration of 14Gy to the whole pelvis further radiotherapy treatment was withheld. Her blood pressure was 160/90 mm Hg which increased 190/120 mm of Hg over 24 hours even after antihypertensive medication to was started. Cardiology consultation was taken and the cardiologists advised work-up to rule out non-cardiac cause of uncontrolled hypertension including raised intracranial pressure. Contrast-enhanced computed tomography (CECT) brain showed diffuse meningeal enhancement of brain sulci and no evidence of focal lesion suggesting the possibility of meningeal carcinomatosis (Figure 3). Lumbar puncture and cerebrospinal

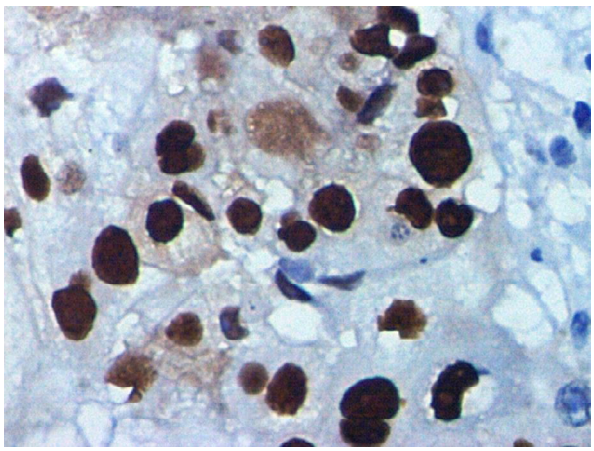

Figure 2: Photomcirograph showing p63 nuclear positivity in tumour cells (Immunohistochemistry,×200)

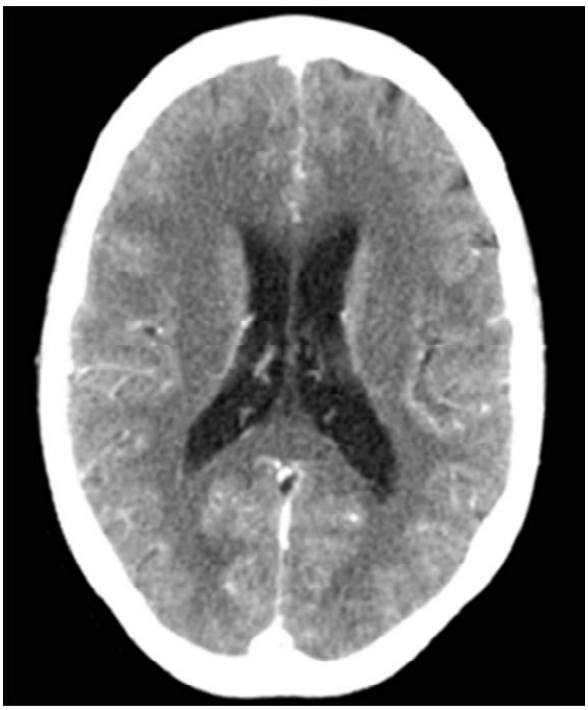

Figure 3: Contrast-enhanced computed tomography of the head showing diffuse meningeal enhancement in brain sulci and across sinuses

fluid (CSF) cytopathological examination was negative for malignant cells. Patient was started with conservative treatment with antioedema measures and anti-tuberculosis drugs with a strong clinical suspicion of TB meningitis. BacT/ALERT culture of CSF was negative. With progression of symptoms on the above treatment, at one week repeat CSF cytology which later revealed presence of malignant cells which confirmed the diagnosis of carcinomatous meningitis (Figure 4). Anti-TB treatment was discontinued and palliative whole brain radiotherapy (WBRT) and intrathecal methotrexate were adminsitered. This had resulted in symptomatic improvement during and immediately following treatment and the patient was dischared from the hospital. She died four weeks later at her home.

DISCUSSION

Central nervous system (CNS) involvement in uterine cervical cancer is uncommon and is mainly attributed to intraparenchymal involvement. The incidence of brain metastases have been reported to be 0.5%–1.2% in various clinical study series.[4,5] However carcinomatous meningitis is an extremely rare clinical issue in relation to carcinoma cervix with a very few cases have been reported in English literature.[4-]

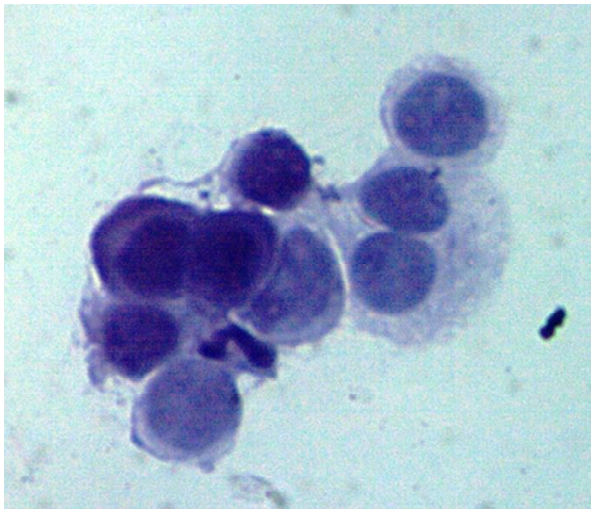

Figure 4: Photomicrograph of cerebrospinal fluid cytology smear showing tumour cells, neutrophil and mesothelial cells (Haematoxylin and eosin, × 400)

The possible mechanisms for such metastatic event may be due to meningeal seeding from previous brain metastasis, direct extension from subdural or extradural tumors, direct extension from sites outside but adjacent to CNS or haematogenous spread.[6]

The risk of hematogenous spread is more common in locally advanced and high grade cervical cancer. Patients present with focal neurological signs and symptoms such as headache, vomiting, giddiness, mental changes and gait difficulty. The gold standard investigation for diagnosing carcinomatous meningitis is identification of tumour cells in CSF. Repeated lumbar puncture and CSF examination often may be required due to false-negative results in the initially collected samples.[7] Imaging radiography may be useful in confirming diagnosis, mainly by gadolinium enhanced magnetic resonance imaging (MRI) than CECT brain that often displays diffuse meningeal enhancement of sulci or enhancement of basal cisterns and hydrocephalus without mass obstructing CSF outflow.

The prognosis of carcinomatous meningitis is poor due to fast progression of disease process and lack of effective therapeutic measures. Because of poor CSF or CNS penetration of most systemic chemotherapeutic agents, there is no standard systemic therapy for carcinomatous meningitis. Intrathecal chemotherapy with methotrexate, thiotepa, cytarabine have been tried with limited favourable outcome and localized treatments such as stereotactic radiotherapy, whole brain radiotherapy along with intrathecal chemotherapy have no significant influence on the course of the disease.[8] Treatment intent is not curative but rather aims at effective local control and palliation of neurological symptoms which in turn may improve the quality of life. Despite any modality of treatment, prognosis

remains poor with median survival of 3-4 months. Our patient was started on anti-TB drugs with strong clinical suspicion of TB meningitis in view of low grade fever, neck rigidity but was later discontinued with progression of symptoms on medication.

Though carcinomatous meningitis is an extremely rare event in uterine cervical cancer, this diagnosis should be strongly suspected in patients with unexplained neurological signs and symptoms, even though radiologic imaging of neuraxis is equivocal. The prognosis being poor and unpredictable, treatment with radiotherapy and/or intrathecal chemotherapy may ensure effective palliation and good quality of life.

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