


Case Study: Neurological Conundrums Complicating Management of Patients with Cervical Cancer

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Abstract

Background: Serious neurological events in patients with Carcinoma of the Cervix (Ca. cervix) are uncommon and are often misattributed to brain metastases. However, the incidence of Brain Metastasis (BM) in Ca. cervix remains low (0.45-2.3%). Other rare yet critical neurological complications that may complicate the primary management of cervical cancer include Cerebral Venous Thrombosis (CVT), Cerebrovascular Accidents (CVA), synchronous primary or benign brain tumors and parasitic neuro-infestations. The current report describes neurological conundrums that mimic brain metastasis in patients with cervical cancer.

Methods and Findings: Two patients diagnosed with Ca. cervix undergoing Concurrent Chemoradiotherapy (CCRT) who developed acute neurological symptoms, initially suspected to be brain metastases. However, detailed neuroimaging revealed alternate diagnoses: CVT and Neurocysticercosis (NCC). Each required tailored management strategies and significantly altered the course of oncologic treatment.

Conclusion: These cases highlight the need for a broad differential diagnosis in cervical cancer patients presenting with neurological symptoms to ensure appropriate and timely management.

Keywords: Cerebral Venous Thrombosis; Brain Metastasis; Cervical Cancer

Abbreviation

CA: Carcinoma; BM: Brain Metastasis; CVT: Cerebral Venous Thrombosis; CVA: Cerebrovascular Accident; CCRT: Concurrent Chemoradiotherapy; DVT: Deep Vein Thrombosis; NCC: Neurocysticercosis; FIGO: International Federation of Gynecology and Obstetrics; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; EBRT: External Beam Radiation Therapy; SWI: Susceptibility-Weighted Imaging; CCRT: Concurrent Chemoradiotherapy; TEE: Thromboembolic Events

Introduction

Cervical cancer remains a major global health burden, ranking fourth worldwide in terms of both incidence and cancer-related mortality, while it continues to be the second most common malignancy among women in India [1]. Despite a gradual decline in incidence due to improved screening and vaccination efforts, cervical cancer still accounts for nearly 10% of all female cancers in the country, with a significant proportion of patients presenting at a locally advanced stage [2,3]. Definitive Concurrent Chemoradiotherapy (CCRT), followed by intracavitary brachytherapy, constitutes the standard of care for Locally Advanced Cervical Cancer (LACC) [4]. More recently, neoadjuvant chemotherapy has also been explored and recommended in selected patients to improve disease control and survival outcomes [5]. Patients with malignancy who develop acute neurological symptoms such as seizures, focal neurological deficits, altered sensorium or loss of consciousness are often presumed to have intracranial metastases unless proven otherwise. This assumption is clinically relevant, as brain metastases significantly impact

prognosis and treatment intent. However, brain metastasis from carcinoma of the cervix is relatively uncommon, with reported incidence ranging from 0.45% to 2.3% [6]. Consequently, attributing neurological symptoms solely to metastatic disease may lead to misdiagnosis and inappropriate modification of oncological treatment.

Several alternative and less common etiologies can present with similar clinical manifestations and radiological appearances in patients with cervical cancer. These include Cerebral Venous Thrombosis (CVT), ischemic or hemorrhagic Cerebrovascular Accidents (CVA), synchronous primary intracranial tumors and parasitic infections such as Neurocysticercosis (NCC), particularly in endemic regions [7-10]. The prothrombotic state associated with malignancy, combined with chemotherapy-induced endothelial injury, dehydration, anemia and infections, further predisposes these patients to vascular neurological events such as CVT and stroke. The coexistence of such non-metastatic neurological conditions in patients with cervical cancer poses significant diagnostic and therapeutic challenges, as they can closely mimic metastatic brain disease both clinically and radiologically. Failure to recognize these entities may result in unnecessary cessation or alteration of curative-intent therapy. In this article, we present two illustrative cases of patients with non-metastatic carcinoma cervix who developed neurological symptoms during concurrent chemoradiotherapy, which were ultimately attributed to alternative, non-metastatic causes. These cases highlight the importance of maintaining a broad differential diagnosis and emphasize the need for careful clinicoradiological correlation in the evaluation of neurological events in cervical cancer patients.

Case Summaries

Two patients with histologically confirmed cervical carcinoma, undergoing CCRT as per institutional protocols, developed acute neurological symptoms during the course of definitive chemoradiotherapy. They presented with headache, seizures and focal neurological deficits. Initial management consisted of administration of corticosteroids and anticonvulsants under the suspicion of brain metastases. Magnetic Resonance Imaging with venography of the brain proved absolutely critical in establishing alternative diagnoses:

Case 1

A 40 year old patient of squamous cell carcinoma of the cervix FIGO stage IIB presented was undergoing concurrent chemoradiation planned to a total dose of 45 Gy in 25 Fractions along with weekly cycles of cisplatin at 40 mg/m². She presented with one episode of generalized tonic clonic seizures at the 18th fraction of radiotherapy, associated with post-ictal confusion. Serum electrolytes and random blood sugars were within normal range. CT brain was non contributory. MRI brain obtained post seizure was suggestive of few subcentimetric foci of doubtful hemorrhagic metastasis (Fig. 1). In view of a less likelihood of brain metastasis with early-stage cervical cancer, it was decided to continue definitive chemoradiation under the cover of antiepileptics. A repeat MRI was planned post completion of radiotherapy to the cervical lesion. However, she developed a severe holocranial headache, blurring of vision and acute onset weakness of the left upper limb. A repeat MRI brain was obtained with MR venogram, suggestive of venous infarction in conjunction with superior sagittal sinus thrombosis (Fig. 2). She was immediately started on low molecular weight heparin as anticoagulants and Mannitol as an anti-edema measure. No improvement was observed. She underwent a decompressive craniectomy. However, despite neurosurgical interventions, she succumbed to massive venous infarction.

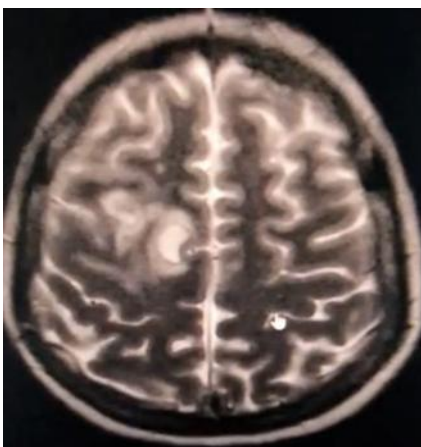


Figure 1: MRI Brain showing T2 hyperintense lesion resembling hemorrhagic brain metastasis.

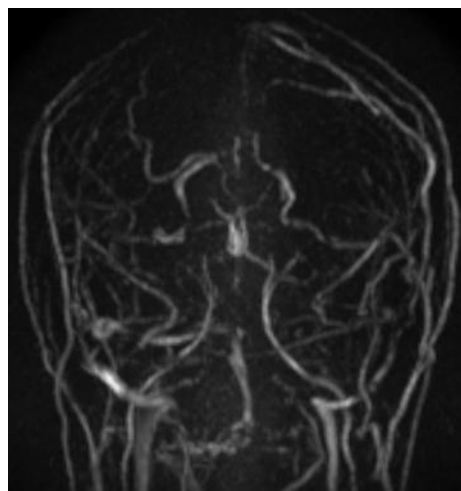


Figure 2: MRI Brain of same patient showing sagittal sinus flow void suggestive of progressive CVT.

Case 2

A 40 year old patient of squamous cell carcinoma of the cervix FIGO stage IIB presented was undergoing concurrent chemoradiation planned to a total dose of 45Gy in 25 Fractions along with weekly cycles of cisplatin at 40 mg/m². After the last fraction of External Beam Radiotherapy (EBRT), she presented with acute onset weakness of the right upper limb and lower limb with no history of headache or seizures or loss of consciousness. Computerized Tomography (CT) scan of the brain was suggestive of left paracentral high parietal calcified granuloma with surrounding perilesional edema. MRI brain was suggestive of a peripheral enhancing lesion with calcification with central blooming on Susceptibility Weighted Imaging (SWI) (Fig. 2). She was commenced on Levipill 500 mg BD and Syp.Glycerol 30 ml twice daily as anti-edema measure i/v/o high probability of seizures due to the perilesional edema. High Dose Rate Brachytherapy was performed in three sessions under short general anaesthesia with no overnight stay with applicator in situ. A dose of 8 Gy in 3 Fr. was delivered (Fig. 3).

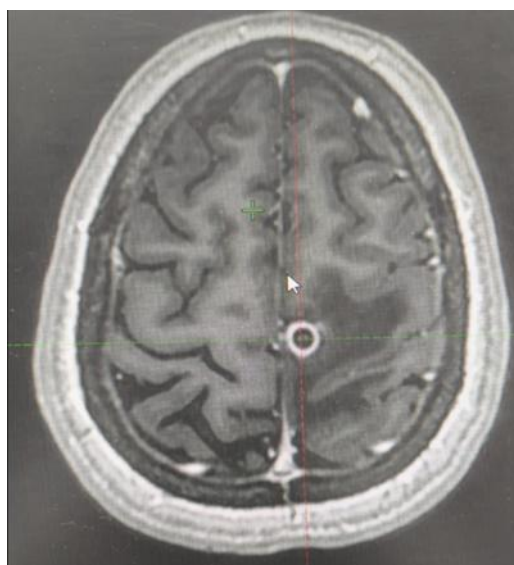


Figure 3: MRI brain showing calcified ring enhancing lesion suggestive of NCC.

Discussion

Neurological events in patients with malignancies are often presumptively attributed to metastatic disease, especially when involving the central nervous system. While brain metastases are indeed a frequent concern in advanced cancer, this assumption can lead to critical diagnostic oversights [11,12]. The incidence of Brain Metastasis (BM) in patients with primary cervical carcinoma is as low as 0.45-2.3 % [6]. Several potentially reversible yet life-threatening neurological conditions may mimic metastatic involvement and must be vigilantly considered during the management of cervical cancer patients undergoing concurrent Chemoradiotherapy (CTRT).

Cerebral Venous Thrombosis (CVT): An Underdiagnosed Emergency

Concurrent platinum-based chemotherapy forms the cornerstone of curative-intent treatment for locally advanced carcinoma of the cervix. However, platinum agents, particularly cisplatin, are associated with an increased risk of Thromboembolic Events (TEE), with an incidence reported between 6-13% across various studies [13-15]. It causes direct endothelial injury, leading to exposure of subendothelial procoagulant factors and activation of the coagulation cascade [13]. Cisplatin has also been shown to increase circulating levels of von Willebrand factor, fibrinogen and tissue factor, while reducing natural anticoagulants such as protein C and protein S, thereby promoting platelet activation and fibrin formation [13]. In addition, cisplatin is associated with metabolic and hematologic toxicities including hypomagnesemia, dehydration, anemia and nephrotoxicity, all of which contribute to endothelial dysfunction, hemoconcentration and increased blood viscosity, further predisposing patients to venous thrombosis [16].

While peripheral Deep Venous Thrombosis (DVT) is well-recognized in this patient population, often arising de novo or secondary to venous compression by bulky pelvic lymphadenopathy, cerebral venous thrombosis remains largely underdiagnosed.

CVT presents a particular diagnostic challenge due to its protean clinical manifestations, ranging from headache and seizures to focal neurological deficits and altered mental status. Patients with cancer have 4.9 times higher odds of CVT compared to non cancerous controls [17-19]. In the absence of overt neurological signs, the diagnosis requires a high index of suspicion and prompt radiological confirmation. This typically includes MRI venography or CT venography. Early identification is crucial as timely anticoagulation can be lifesaving.

Patients on therapeutic anticoagulants who require brachytherapy for gynecologic malignancies represent a unique clinical challenge owing to the competing risks of hemorrhagic and embolic events. Bridging therapy is the temporary cessation of long-acting anticoagulants such as warfarin with substitution using short-acting agents such as low molecular weight heparin. The goal of bridging anticoagulation therapy is to reduce the patient's risk for TTE while also minimizing their risk of bleeding during the procedure.

Intracavitary/Interstitial Brachytherapy for cervical cancer are best performed under spinal anesthesia. The risk of hemorrhagic complications is particularly high during such invasive procedures, necessitating a carefully coordinated approach between oncologists, anesthesiologists and hematologists to minimize both thrombotic and bleeding risks. According to the American College of Surgeon's guidelines for peri-operative management of antithrombotic medications, warfarin may be withheld five days prior to invasive procedure, 72 hours for Direct acting oral anticoagulants such as apixaban and rivaroxaban and 24 hours hold for therapeutic dose enoxaparin. These may be resumed 24 hours post removal of the applicator [20].

Neurocysticercosis (NCC): A Parasitic Mimic of Metastasis

Neurocysticercosis (NCC) is a critical differential diagnosis in cancer patients presenting with seizures or signs of raised intracranial pressure. NCC is endemic in parts of South and Central America, India, Southeast Asia, China and sub-Saharan Africa [21]. Given the demographic overlap between areas with a high burden of NCC and cervical cancer, clinicians must remain vigilant. NCC may manifest with generalized or focal seizures, persistent headaches due to raised intracranial tension and occasionally cranial nerve palsies symptomatology that closely mimics brain metastasis. Misdiagnosis may lead to inappropriate staging and therapeutic delays. Neuroimaging, particularly contrast-enhanced MRI or CT, is essential for distinguishing parasitic lesions from metastatic deposits [22].

The management of NCC typically involves high-dose corticosteroids to control inflammation, mannitol to manage cerebral edema and antiparasitic agents such as albendazole [22]. However, treatment is often staged, as initiation of antiparasitic therapy without adequate steroid cover can worsen symptoms due to inflammatory response [22]. Until the acute phase is stabilized, CRT and brachytherapy must be deferred, thereby delaying cancer treatment or increasing the overall treatment time. Multidisciplinary coordination is imperative to balance parasitic disease control with timely oncological intervention. Seizures during brachytherapy can be catastrophic, particularly if spinal anesthesia is employed. Therefore, patients with known epileptogenic foci are often managed with short general anesthesia during brachytherapy sessions to ensure safety [23]. This necessitates anesthesiology support and may influence scheduling and logistical planning within oncology departments.

Conclusion

Neurological complications in patients undergoing CTRT for cervical cancer extend far beyond metastatic brain disease. Cerebral venous thrombosis and neurocysticercosis are few clinical examples that may create unique diagnostic and therapeutic challenges. Given the potential for significant morbidity and treatment delays, a proactive, multidisciplinary approach is essential. From a therapeutic standpoint, increasing recognition of cancer- and treatment-associated hypercoagulability underscores the potential role of individualized thromboembolic risk assessment and prophylactic strategies in selected high-risk cervical cancer patients, particularly those receiving cisplatin-based chemoradiotherapy. Additionally, development of evidence-based guidelines for anesthesia selection and peri-procedural neurological risk stratification during brachytherapy may further enhance patient safety and treatment compliance.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Not applicable.

Ethical Statement

The study was approved by the Inter System Biomedica Ethics Committee (ISBEC).

Informed Consent Statement

Informed consent was obtained from participants before collecting the data.

Authors' Contributions

All authors have contributed equally to this work and have reviewed and approved the final manuscript for publication.

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