International Journal of Women's Health

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE SERIES

Beyond the Pelvis: Brain Metastases in Cervical Cancer – A Case Series from a Low-Middle-Income Country

Candra Novi Ricardo Sibarani[1], Dodi Suardi[1], Siti Salima[1], Nathania Nathania[2], Nicholas Adrianto[3]

[1]Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Padjadjaran University, Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia; [2]Department of Obstetrics and Gynecology, Padjadjaran University, Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia; [3]School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, North Jakarta, Daerah Khusus Ibukota Jakarta, 14440, Indonesia

Correspondence: Candra Novi Ricardo Sibarani, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Padjadjaran University, Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, Email candra23001@mail.unpad.ac.id

Abstract: Brain metastases from cervical cancer are exceedingly rare and pose significant clinical challenges, particularly in low- and middle-income countries (LMICs), where access to advanced diagnostics and therapies may be limited. We report two cases of cervical carcinoma with brain metastases managed at a tertiary center in Indonesia, each illustrating distinct histopathologic subtypes and metastatic trajectories. The first case involved a 31-year-old woman with a grade II neuroendocrine carcinoma who developed intracranial recurrence 11 months after achieving a complete response to concurrent chemoradiotherapy. In the second case, a 46-year-old woman with poorly differentiated non-keratinizing squamous cell carcinoma developed progressive brain and pulmonary metastases during adjuvant radiotherapy. Both patients underwent craniotomy for gross total resection of symptomatic brain lesions, followed by adjuvant radiotherapy. The surgical intervention led to substantial neurological improvement in both cases, underscoring the role of symptom-directed neurosurgical palliation even in the setting of disseminated disease. These cases highlight the need for heightened clinical vigilance, individualized multidisciplinary management, and strategic application of available resources to improve outcomes in patients with central nervous system involvement from cervical cancer, especially within resource-constrained healthcare systems.

Keywords: cervical cancer, brain metastasis, neuroendocrine carcinoma, squamous cell carcinoma

Introduction

Cervical cancer remains a major global health burden, particularly in low- and middle-income countries (LMICs), where advanced disease presentations are common due to delays in diagnosis and limited access to healthcare facilities.[1,2] While cervical carcinoma typically metastases via lymphatic spread to pelvic lymph nodes, hematogenous dissemination leading to distant organ involvement, particularly brain metastases, remains exceedingly rare, occurring in less than 2% of cases.[3] However, when brain metastases do occur, they significantly alter prognosis and therapeutic strategies, presenting substantial challenges to clinicians.[4] Histologically, cervical cancer predominantly consists of squamous cell carcinoma (SCC), adenocarcinoma, adenosquamous carcinoma, and less commonly, neuroendocrine carcinoma (NEC). Neuroendocrine carcinoma of the cervix (NECC), characterized by aggressive behavior and early dissemination, particularly warrants attention for its propensity to metastasize beyond regional nodes.[5,6]

Despite advances in multimodal therapy including radical surgery, concurrent chemoradiotherapy (CCRT), and targeted agents the management of cervical cancer with central nervous system (CNS) involvement remains controversial, especially regarding the roles of surgery, radiotherapy, and systemic therapy.[7] Thus, understanding how best to integrate these modalities into effective therapeutic regimens, particularly in resource-limited settings, is paramount. In

Received: 14 June 2025
Accepted: 1 September 2025
Published: 22 November 2025

this report, we present two illustrative cases of cervical carcinoma with rare brain metastasis managed aggressively at a tertiary care center in Indonesia. These cases highlight distinct histopathological entities poorly differentiated squamous cell carcinoma and grade II neuroendocrine neoplasm and exemplify tailored multidisciplinary management approaches employed to achieve curative intent, underscoring the necessity of vigilance and strategic adaptation in LMIC oncology practice.

Case Presentation

Case 1

A 31-year-old multiparous woman (P2A0) presented to our gynecologic oncology clinic in March 2023 with a two-month history of persistent contact bleeding and leucorrhea. Pelvic examination revealed an exophytic cervical mass measuring approximately 5×4×4 cm without evident vaginal or parametrial involvement on clinical assessment. However, pelvic MRI demonstrated parametrial infiltration, consistent with FIGO stage IIB cervical carcinoma.

Histopathologic evaluation of cervical biopsy specimens confirmed a poorly differentiated neuroendocrine carcinoma (Figure 1A and B). Immunohistochemistry revealed strong chromogranin positivity, with negative expression of cytokeratin (CK) and synaptophysin, and a Ki-67 proliferation index of less than 20%, consistent with a grade II neuroendocrine neoplasm (Figure 1C–F).

The patient underwent definitive concurrent chemoradiotherapy (CCRT), comprising 25 fractions of external beam radiotherapy (EBRT), three sessions of intracavitary brachytherapy, and six cycles of weekly cisplatin. By October 2023, both clinical and radiologic assessments indicated complete response. In September 2024, she developed progressive headaches and visual disturbances. Brain MRI identified multiple intra-axial, irregularly bordered, inhomogeneous solid lesions predominantly located in the right temporoparietal and parieto-occipital regions, with necrotic and hemorrhagic components. These lesions exerted significant mass effect, compressing the Sylvian fissure, right lateral and third ventricles, right thalamus, midbrain, and pons, resulting in a leftward midline shift. Post-contrast imaging revealed irregular rim enhancement, consistent with intracranial metastases (Figure 2).

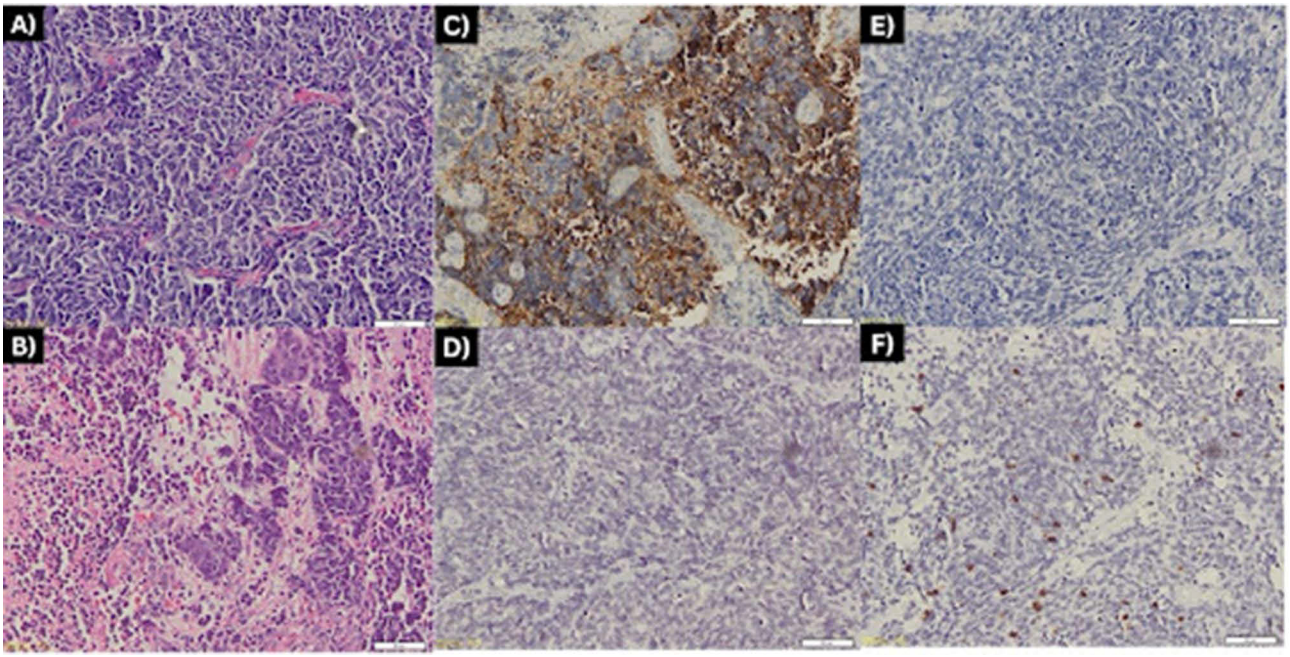

Figure 1 Histopathological features of neuroendocrine carcinoma of the cervix. (**A** and **B**) Hematoxylin and eosin (H&E), 200× magnification: Tumor composed of densely packed hyperplastic cells arranged in clusters, exhibiting polymorphic and hyperchromatic nuclei with frequent mitotic figures. The fibrous stroma shows prominent lymphocytic infiltration and areas of hemorrhage. (**C**) Chromogranin: positive immunoreactivity. (**D**) CK: negative. (**E**) Synaptophysin: negative. (**F**) Ki-67: positive in less than 20% of tumor cells.

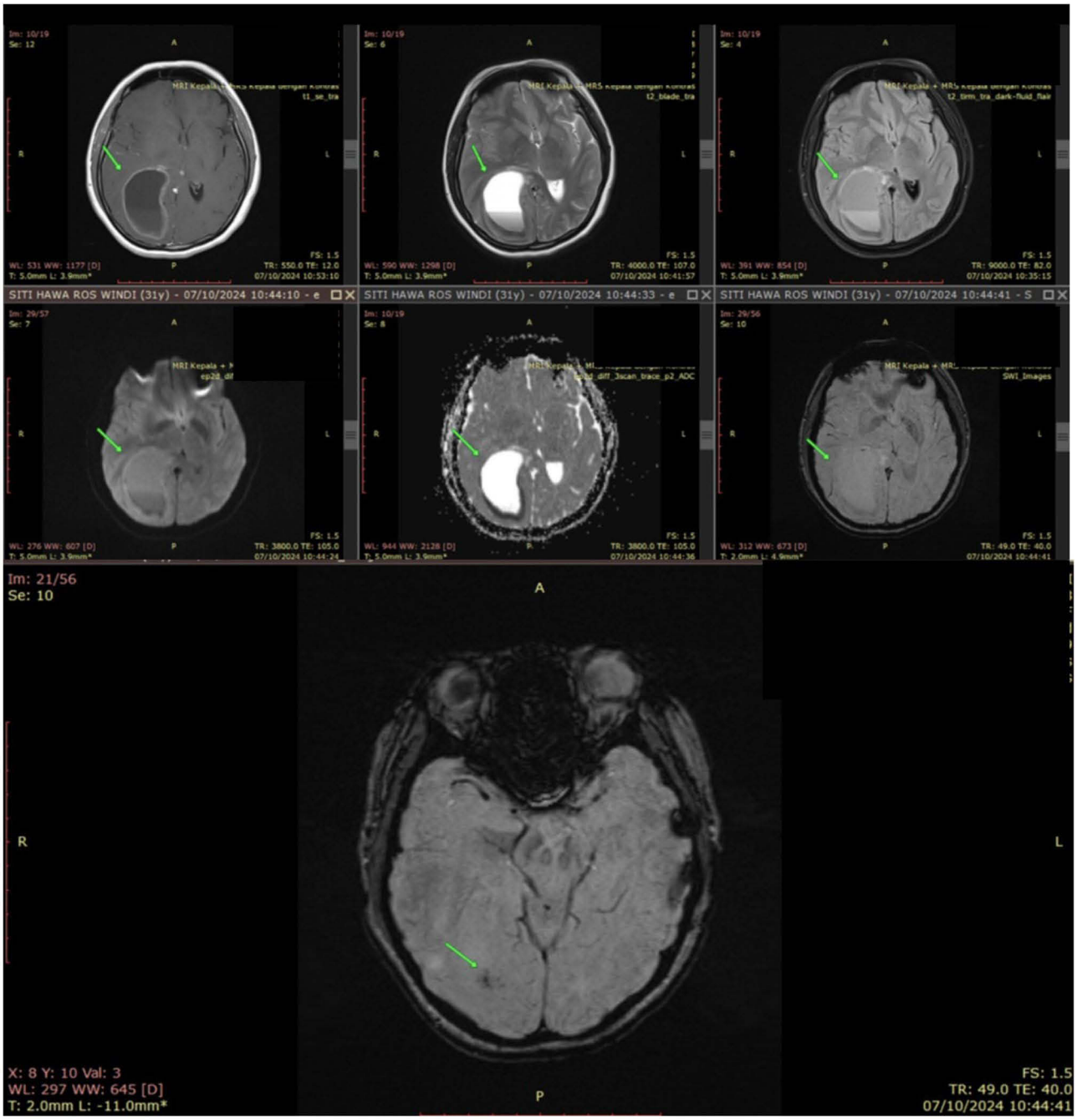

Figure 2 Axial MRI of the brain demonstrating multiple inhomogeneous solid masses within the right temporoparietal lobe, marked by irregular borders, central necrosis, and hemorrhagic components. Surrounding vasogenic edema significantly compresses the adjacent sulci, right Sylvian fissure, lateral ventricles, and deep brain structures, producing a mild leftward midline shift. Lesions exhibit hypointense T1-weighted signal intensity and hyperintense T2-weighted and T2-FLAIR signals with restricted diffusion and susceptibility artifacts. Post-contrast imaging revealed irregular rim enhancement, consistent with metastatic deposits. Orientation markers: A = anterior; P = posterior; H = head (superior); F = foot (inferior); AF = anterior foot; PF = posterior foot; RFP = right foot posterior; LHA = left head anterior; PH = posterior head.

A right-sided craniotomy was performed for gross total resection of the accessible supratentorial lesions. Intraoperatively, the tumor appeared moderately vascular, yellowish-white, and well-circumscribed. Approximately 10 mL of reddish turbid fluid was aspirated. Histopathologic evaluation confirmed metastatic grade II neuroendocrine carcinoma, composed of round-to-spindle-shaped hyperchromatic cells with prominent mitoses and vascular congestion (Figure 3A–C). Cytologic analysis of the aspirate supported the diagnosis, revealing cohesive tumor clusters with coarse chromatin and scant cytoplasm against a necrotic and lymphocytic background. The patient had an uneventful

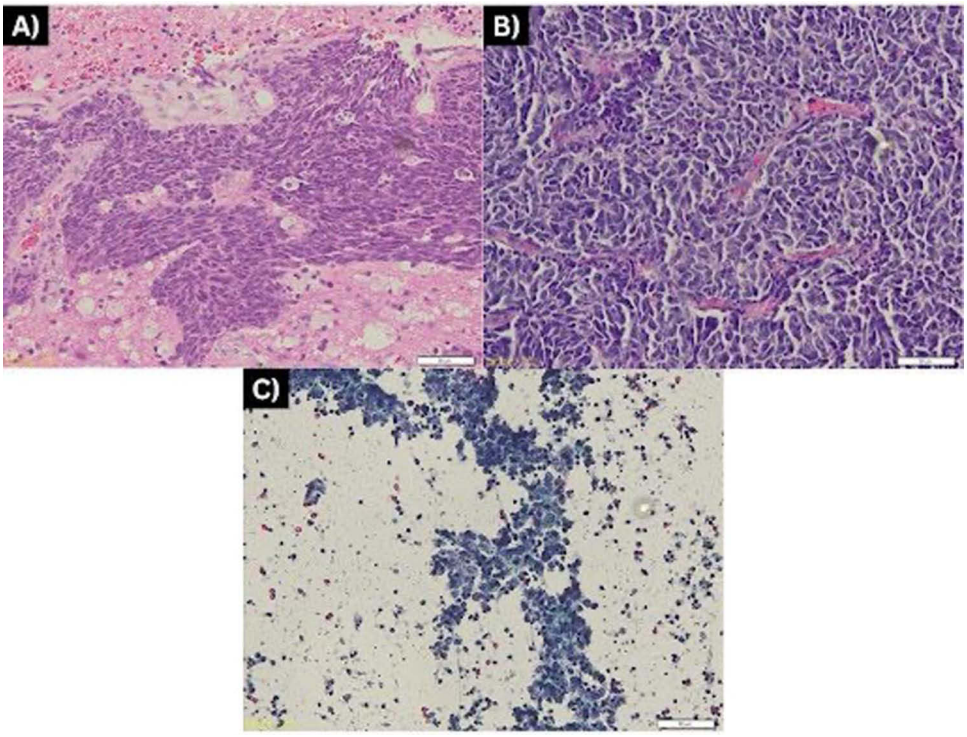

Figure 3 Histopathological and cytological features of a neuroendocrine neoplasm from the parieto-occipital region. (**A** and **B**) Hematoxylin and eosin (H&E), 200× magnification: The tumor exhibits nests of round to oval and spindle-shaped cells demonstrating hyperplastic growth. The nuclei are pleomorphic and hyperchromatic, with frequent mitotic figures observed. (**C**) Cytological analysis of tumor fluid reveals cohesive clusters of round to oval cells with coarse chromatin, irregular nuclear contours, and scant cytoplasm, set against a necrotic background with numerous lymphocytes findings consistent with neuroendocrine differentiation.

postoperative course without ICU admission. Neurological symptoms, including headache and visual impairment, markedly improved following surgery. A multidisciplinary tumor board recommended adjuvant cranial irradiation and systemic chemotherapy in view of confirmed CNS dissemination, underscoring the aggressive clinical trajectory of neuroendocrine carcinoma of the cervix.

Case 2

A 46-year-old multiparous woman (P2A1) presented in May 2024 with contact bleeding. Cervical biopsy confirmed a poorly differentiated non-keratinizing squamous cell carcinoma. She underwent radical hysterectomy with bilateral pelvic lymphadenectomy on July 3rd, 2024. Histopathologic analysis revealed poorly differentiated non-keratinizing squamous cell carcinoma of the cervix with bilateral parametrial invasion and lymphovascular space involvement, consistent with FIGO stage IIB (pT2bN0Mx) (Figure 4A and B). There was no involvement of the uterine corpus, adnexa, or pelvic lymph nodes.

Adjuvant EBRT was initiated in October 2024, approximately three months postoperatively. Prior to treatment, follow-up chest imaging on September 15th and 20th revealed multiple bilateral pulmonary nodules consistent with intrapulmonary metastases. During the 17th EBRT session, the patient developed a firm occipital scalp mass and was noted to be drowsy and difficult to awaken (Figure 5A). She was referred to the neurology emergency unit. Contrast-enhanced head CT and MRI on November 6th and 12th showed multiple intra-axial, inhomogeneous solid masses in the right frontoparietal and left frontal lobes, associated with perifocal edema, sulcal and ventricular compression, and a mild subfalcine herniation (Figure 6). Post-contrast sequences demonstrated rim enhancement, suggestive of intracranial metastases.

A biopsy of the occipital mass on October 29th confirmed metastatic squamous cell carcinoma. Craniotomy and tumor resection were performed on November 13th. The lesion appeared yellowish-white, vascular, and was completely excised. Histopathology confirmed metastatic non-keratinizing squamous cell carcinoma involving the frontoparietal lobes (Figure 5B and C). On November 13th, 2024, the patient underwent craniotomy for excision of the intracranial

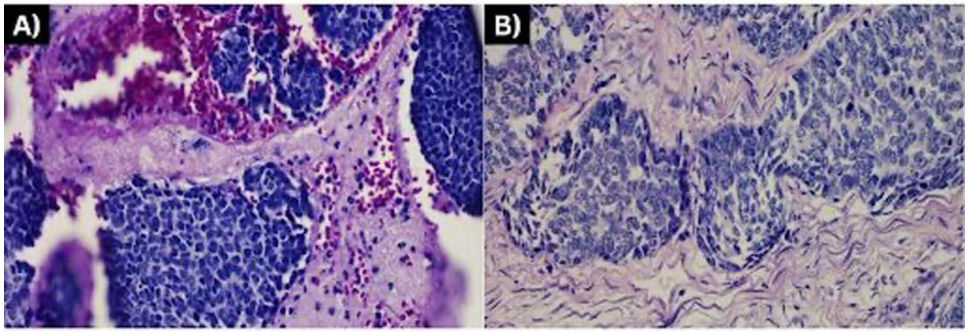

Figure 4 (**A** and **B**) Histopathological sections of the cervix showing non-keratinizing squamous epithelium transformed into a tumor mass composed of hyperplastic, densely clustered round to polygonal cells with pleomorphic, hyperchromatic nuclei and prominent mitoses. No keratin pearl formation was observed. The stroma exhibited lymphohistiocytic infiltration and hemorrhagic features.

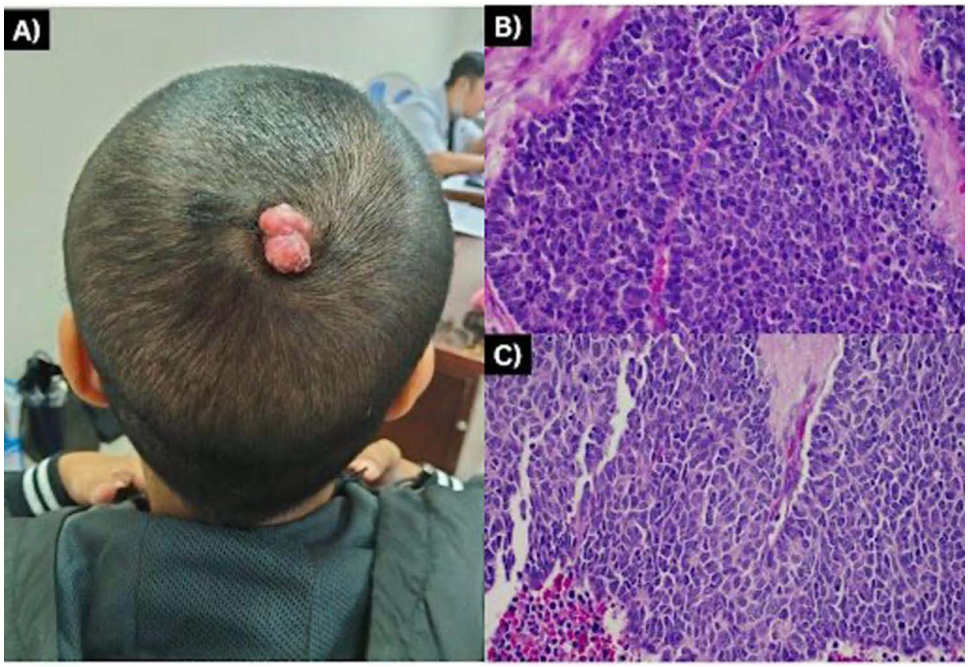

Figure 5 Lump in patient's head (**A**). Histopathology of occipital tumor biopsy revealing sheets of round-to-spindle shaped tumor cells with hyperplastic, dense growth patterns. The cells exhibited pleomorphic, hyperchromatic nuclei and frequent mitoses, forming cohesive sheets beneath stratified squamous epithelium. The underlying fibrous stroma showed lymphocytic infiltration (**B** and **C**).

lesion. A well-circumscribed, yellowish-white, moderately vascular tumor was identified on the right frontal dura and was completely resected. The dural defect was repaired, and the bone flap was secured. Histopathology confirmed metastatic non-keratinizing squamous cell carcinoma involving the frontoparietal lobes (Figure 7A and B).

In both case, we systematically assessed and documented the patient's quality of life and functional status following treatment. Improvements in performance status scores (ECOG and Karnofsky) reflected good neurological and daily functioning post-intervention. Serial laboratory evaluations—including renal and hepatic function tests—remained within normal ranges throughout follow-up, indicating that the multimodal therapy was well tolerated with no evidence of organ dysfunction. These findings support the safety and efficacy of aggressive individualized management, even in a resource-limited context.

Discussion

Brain metastases from cervical cancer are extremely rare, with reported clinical incidences ranging from 0.4% to 1.2%, while autopsy studies suggest higher rates between 3–10%.[7,8] This discrepancy likely reflects the underdiagnosis of CNS

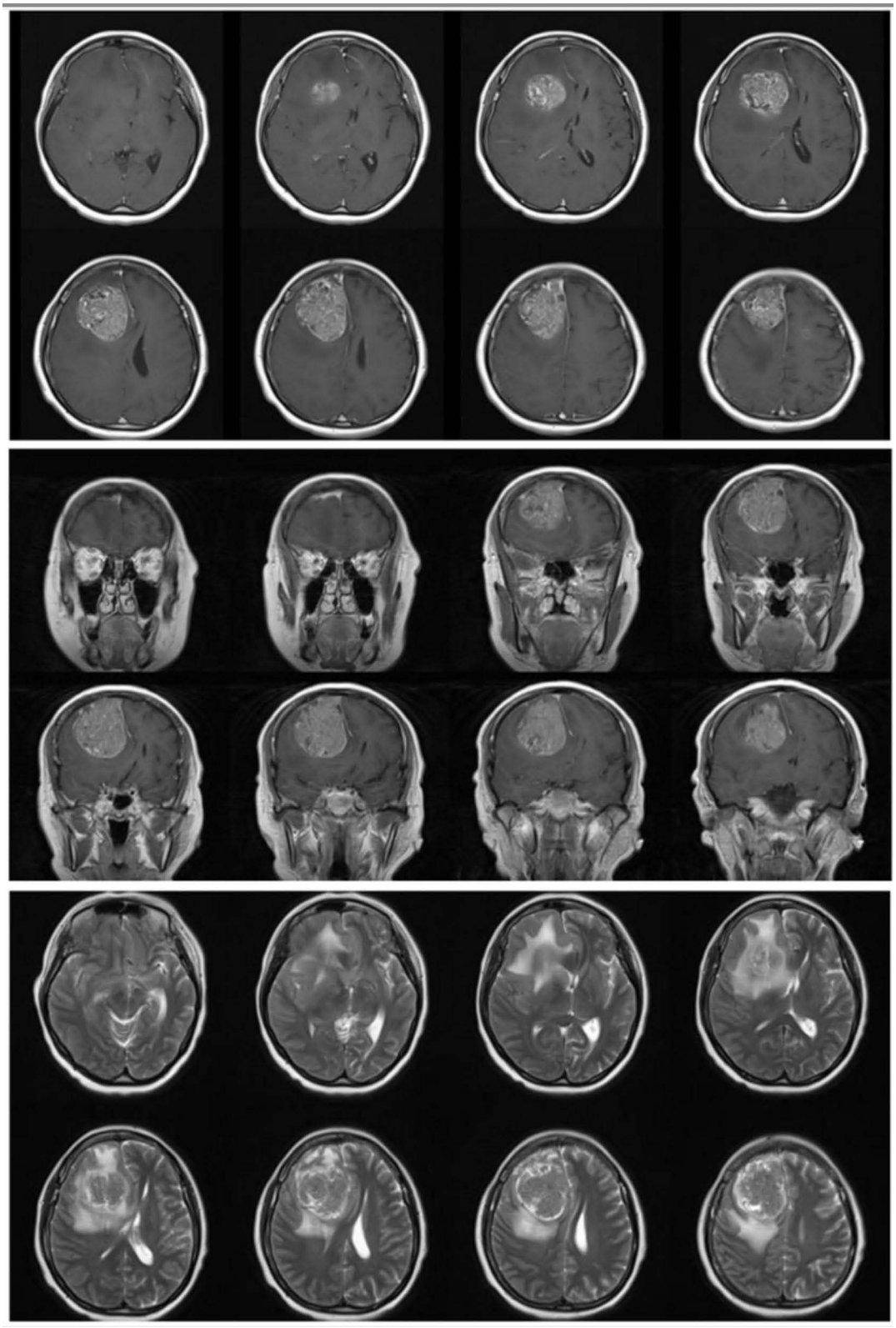

Figure 6 Axial MRI of the brain on T1-weighted imaging, multiple mixed-intensity lesions were observed in the right frontoparietal and left parietal regions, showing inhomogeneous enhancement following contrast administration. On T2-weighted imaging, the same multiple mixed-intensity lesions were noted in the right frontoparietal and left parietal regions, accompanied by positive perifocal edema.

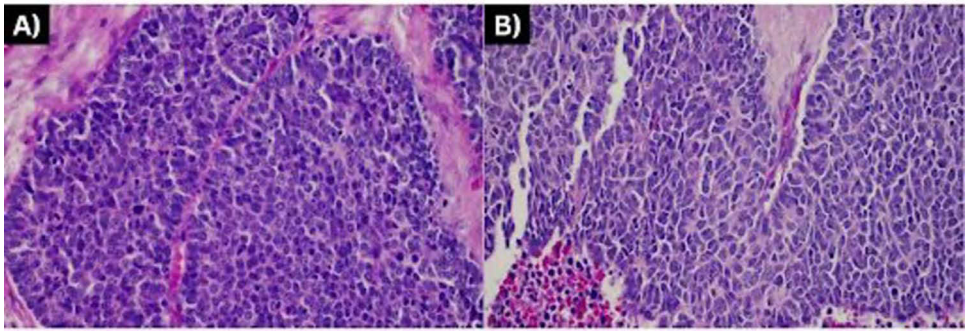

Figure 7 Histopathological features of brain metastasis from cervical squamous cell carcinoma (**A** and **B**). Tumor section from the frontoparietal lobe shows sheets of round to spindle-shaped tumor cells exhibiting hyperplastic, compact growth without keratin pearl formation. The nuclei are pleomorphic and hyperchromatic with frequent mitotic figures. The fibrillary stroma contains scattered lymphocytic infiltrates, dilated blood vessels, areas of hemorrhage, and extensive necrosis. These features are consistent with metastatic non-keratinizing squamous cell carcinoma.

involvement, as routine neuroimaging is not standard in asymptomatic patients.[9] Consequently, brain metastases often present late, typically in patients with advanced or aggressive histologic subtypes.[6,10] Although imaging currently remains the clinical standard for CNS surveillance, there is growing research interest in non-invasive biomarkers, such as circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs)—as potential tools for earlier detection of metastatic spread, but these approaches remain investigational in this context.[11]

The two cases presented illustrate divergent metastatic trajectories. The first patient experienced disease recurrence after initial complete response to chemoradiotherapy for NECC, whereas the second patient exhibited progressive disease with brain and lung metastases developing during the course of adjuvant treatment for poorly differentiated squamous cell carcinoma. The majority of reported cases involve poorly differentiated tumors, with squamous cell carcinoma being the most common histologic subtype.[4] In neuroendocrine cervical carcinoma, brain metastases are even more uncommon, and no standardized guidelines currently exist for their management.[12] NEC, although representing less than 5% of cervical cancers, is characterized by early and widespread hematogenous dissemination including to the CNS and exhibits a distinct metastatic pattern with a higher propensity for brain involvement compared to non-neuroendocrine subtypes.[13,14] NECC exhibits a distinct metastatic pattern characterized by a higher propensity for brain involvement compared to non-neuroendocrine subtypes. These characteristics underscore the importance of vigilant neurological assessment and may support consideration of prophylactic cranial irradiation in selected high-risk patients.[13] Brain metastases are most frequently identified in the presence of concurrent extracranial metastases, with reports indicating that the majority of cases (up to 86%) occur alongside involvement of other organ systems.[15]

While early-stage and locally advanced cervical cancer are managed with multimodal therapy, treatment for metastatic disease remains non-standardized and primarily palliative in intent.[16] Although both patients were classified as having palliative-stage disease due to distant metastases, the decision to proceed with surgery was guided by symptom burden and lesion accessibility. Importantly, this highlights the evolving role of neurosurgical resection as a form of symptom-directed palliation aimed at improving quality of life rather than achieving cure. In appropriately selected patients, the potential benefits in terms of neurologic recovery and functional status can outweigh the operative risks.[17]

For patients with brain metastases from cervical cancer, a multimodal treatment approach is generally utilized. Surgical resection and radiotherapy remain the primary strategies for managing intracranial disease. Whole brain radiotherapy (WBRT) is widely utilized for patients with multiple lesions, although its association with long-term neurocognitive decline is well-documented. In contrast, subsequent stereotactic radiosurgery (SRS) offers a more targeted modality with reduced collateral damage and is increasingly preferred in patients with a limited number of metastases. Aggressive treatment, incorporating surgery or SRS followed by adjuvant WBRT and, where appropriate, systemic chemotherapy, should be strongly considered, particularly in younger patients, as this strategy has been associated with improved overall survival.[18] In our series, surgical resection was undertaken to alleviate neurological symptoms and improve functional status, followed by adjuvant radiotherapy to enhance local disease control.

Postoperative adjuvant radiotherapy has been associated with improved survival, enhanced neurological outcomes, and reduced rates of CNS recurrence compared to radiotherapy alone.[4]

Overcoming the late identification of CNS involvement remains a significant challenge in cervical cancer with brain metastases. Based on our experience, future studies and clinical practice should prioritize improved patient and provider education to foster early recognition of new neurological symptoms. We recommend a risk-stratified surveillance strategy, potentially including selective neuroimaging, for patients with high-risk features such as neuroendocrine histology or rapid systemic disease progression.[19] Moreover, effective multidisciplinary collaboration is vital, ensuring that new clinical information is rapidly integrated to adapt therapeutic strategies in real time. This approach may help improve timeliness of diagnosis and optimize outcomes, particularly given the absence of formal screening guidelines and the rarity of CNS involvement in cervical cancer. In addition, one important limitation of our report is the absence of HPV subtyping data. Routine HPV genotyping is not performed at our institution due to national insurance constraints.

Despite the generally poor prognosis of cervical cancer patients with brain metastases, median survival ranging from 2 to 8 months, our cases demonstrate that aggressive, symptom-oriented intervention can yield meaningful clinical improvement. This is particularly relevant in LMICs, where access to advanced therapies may be constrained. Our experience underscores that timely diagnosis, collaborative management, and judicious use of available resources can still lead to favorable functional outcomes, even in resource-limited settings.

Conclusion

In conclusion, while brain metastases from cervical cancer are rare, they represent a serious complication that requires prompt and aggressive management. Clinicians should maintain a high index of suspicion for CNS involvement in patients with aggressive histological subtypes or new-onset neurological symptoms. Multimodal treatment approaches, including surgery, radiotherapy, and systemic therapy, should be considered to optimize patient outcomes. Further research is warranted to validate the use of non-invasive biomarkers for early detection and monitoring of brain metastases in cervical cancer, addressing challenges posed by the blood–brain barrier and the rarity of CNS involvement. Concurrently, accumulation of case reports and clinical data is essential to inform and develop evidence-based guidelines for optimizing management of this rare but complex clinical scenario. Future studies should focus on validating the use of circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs) as non-invasive biomarkers for early detection and monitoring of brain metastases in cervical cancer, while addressing challenges related to the blood-brain barrier and the rarity of CNS involvement.

Ethics Approval and Consent to Participate

The patient provided written informed consent for the publication of this case report, including all relevant clinical details and images. Documentation of this consent can be made available to the Editor-in-Chief upon request. Our institutional review board reviewed the submission and determined that this case report did not require formal ethical approval to publish.

Consent for Publication

Written informed consent was obtained from both patients for publication of the case details and the associated images.

Disclosure

The author(s) report no conflicts of interest in this work.

References

1. Hull R, Mbele M, Makhafola T, et al. Cervical cancer in low and middle-income countries. *Oncol Lett*. 2020;20(3):2058–2074. doi:10.3892/ol.2020.11754
2. Ali A, Mohan J, Nadaf TAA, Ravishankar H, Deepa KR. Bioinformatics-driven discovery of signaling pathways and genes influencing cervical cancer. *SN Comput Sci*. 2024;5(8):989. doi:10.1007/s42979-024-03347-6
3. Divine LM, Kizer NT, Hagemann AR, et al. Clinicopathologic characteristics and survival of patients with gynecologic malignancies metastatic to the brain. *Gynecol Oncol*. 2016;142(1):76–82. doi:10.1016/j.ygyno.2016.04.030

4. Fetcko K, Gondim DD, Bonnin JM, Dey M. Cervical cancer metastasis to the brain: a case report and review of literature. *Surg Neurol Int*. 2017;8:181. doi:10.4103/sni.sni_111_17
5. Vinh-Hung V, Bourgain C, Vlastos G, et al. Prognostic value of histopathology and trends in cervical cancer: a SEER population study. *BMC Cancer*. 2007;7:164. doi:10.1186/1471-2407-7-164
6. Salvo G, Meyer LA, Gonzales NR, Frumovitz M, Hillman RT. Neuroendocrine cervical carcinomas: genomic insights, controversies in treatment strategies, and future directions: a NeCTuR study. *Int J Gynecol Cancer*. 2025;35(3):101639. doi:10.1016/j.ijgc.2025.101639
7. Branch BC, Henry J, Vecil GG. Brain metastases from cervical cancer – a short review. *Tumori J*. 2014;100(5):e171–e179. doi:10.1177/1660.18186
8. Teke F, Tunc SY, Teke M, et al. The impact of the stage and tumor size on rare brain metastasis of cervical cancer. *Turk Neurosurg*. 2016;26 (6):818–823. doi:10.5137/1019-5149.JTN.13973-15.1
9. Takayanagi A, Florence TJ, Hariri OR, et al. Brain metastases from cervical cancer reduce longevity independent of overall tumor burden. *Surg Neurol Int*. 2019;10:176. doi:10.25259/SNI_37_2019
10. de Brito Rangel J, Giglio AG, Cardozo CL, Bergmann A, Thuler LCS. Prognostic factors for brain metastasis in women presenting cervical cancer. *J Neurooncol*. 2022;159(2):469–477. doi:10.1007/s11060-022-04082-9
11. Zhao X, Hou S, Hao R, Zang Y, Song D. Prognostic significance of circulating tumor DNA detection and quantification in cervical cancer: a systematic review and meta-analysis. *Front Oncol*. 2025;15. doi:10.3389/fonc.2025.1566750
12. Valenzuela F, Desai S. Isolated central nervous system metastasis from neuroendocrine carcinoma of the cervix without pulmonary metastasis. *Cureus*. 2020;12(9):e10728. doi:10.7759/cureus.10728
13. Park HK. Neuroendocrine carcinomas of the uterine cervix, endometrium, and ovary show higher tendencies for bone, brain, and liver organotrophic metastases. *Curr Oncol*. 2022;29(10):7461–7469. doi:10.3390/curroncol29100587
14. Villamar MF. Extensive cerebral and extracerebral metastases from a large-cell neuroendocrine cervical carcinoma. *Pan Afr Med J*. 2017;28(264). doi:10.11604/pamj.2017.28.264.14347
15. Salvo G, Gonzalez Martin A, Gonzales NR, Frumovitz M. Updates and management algorithm for neuroendocrine tumors of the uterine cervix. *Int J Gynecol Cancer*. 2019;29(6):986–995. doi:10.1136/ijgc-2019-000504
16. Li H, Wu X, Cheng X. Advances in diagnosis and treatment of metastatic cervical cancer. *J Gynecol Oncol*. 2016;27(4):e43. doi:10.3802/jgo.2016.27.e43
17. Li Q, Yu J, Yi H, Lan Q. Distant organ metastasis patterns and prognosis of neuroendocrine cervical carcinoma: a population-based retrospective study. *Front Endocrinol*. 2022;13. doi:10.3389/fendo.2022.924414
18. Gressel GM, Lundsberg LS, Altwerger G, et al. Factors predictive of improved survival in patients with brain metastases from gynecologic cancer: a single institution retrospective study of 47 cases and review of the literature. *Int J Gynecol Cancer*. 2015;25(9):1711–1716. doi:10.1097/IGC.0000000000000554
19. Tangella AV, Yadlapalli DC. Neuroendocrine carcinoma of cervix: a case series. *Cureus*. 2023;15(5):e39165. doi:10.7759/cureus.39165