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Case Report

Overcoming Logistical Delays and Resource Constraints: Achieving Complete Response in High-Risk Medulloblastoma with Delayed Metastatic Progression at a Newly Established Secondary Cancer Center

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Abstract

Introduction: High-risk Medulloblastoma (MB) requires time-critical, multimodal therapy. This report details the management of a high-risk MB case where critical logistical barriers necessitated treatment adaptation in a newly established, resource-limited secondary center.

Case Presentation: A 12-year-old female with Anaplastic/Large Cell MB suffered a critical two-month delay in initiating adjuvant therapy due to referral failures. This delay resulted in disease progression and confirmed M+ spinal drop metastases. The patient underwent second surgery, followed by intensive therapy.

Intervention and Adaptation: Initial resource deficits (radiotherapy immobilization equipment and skilled radiation therapists) were overcome through rapid inter-institutional collaboration. Due to institutional inpatient bed restrictions, a modified outpatient chemotherapy protocol (Carboplatin, Etoposide, Cyclophosphamide, Vincristine) was successfully delivered. While the patient experienced significant hematologic toxicity (requiring transfusions and multiple hospitalizations for febrile neutropenia), the regimen was completed without life-threatening infections.

Conclusion: The patient achieved a Radiological Complete Response (CR) at all sites and demonstrated remarkable functional recovery (independent mobility, improved speech). This case validates the feasibility of safely delivering high-quality, intensive pediatric neuro-oncology protocols in a resource-limited setting through thoughtful protocol adaptation and robust multi-institutional collaboration.

Keywords: *Medulloblastoma, Pediatric Neuro-Oncology, Resource-Limited Settings, Multidisciplinary Collaboration*

Introduction

Medulloblastoma (MB) is the most prevalent malignant paediatric central nervous system tumor, accounting for approximately 15% to 20% of all childhood brain tumors. Optimal management for high-risk MB—typically defined by the presence of leptomeningeal dissemination (M+ stage) or subtotal resection (>1.5 residual tumor)—mandates a highly time-sensitive, multimodal approach involving surgical resection, Craniospinal Irradiation (CSI), and intensive adjuvant chemotherapy. The timeliness of initiating adjuvant therapy is a critical prognostic factor, with delays exceeding the established 4-6 week benchmark often leading to reduced progression-free survival (PFS) and overall survival (OS).

Several barriers can delay access to optimal care for paediatric brain tumor patients. These include clinical instability, long distances to specialized centers, limited availability of paediatric intensive care or neurosurgical services, and administrative or logistical challenges—sometimes even for patients presenting to the hospital for non-medical travel such as religious visits or occupational relocation. Consequently, even patients eligible for treatment may experience delays, which underscores the importance of early recognition, stabilization, and efficient referral to tertiary neuro-oncology centers.

Despite these critical needs, this case details the challenges faced by a high-risk MB patient who suffered a two-month (approximately 60 days) delay in starting therapy due to failed tertiary center referrals and limited treatment eligibility, resulting in documented disease progression (M+ stage). We present a case of high-risk pediatric medulloblastoma with limited access to tertiary care due to logistical constraints and restricted treatment eligibility, necessitating management under considerable challenges in a newly established center. This report analyzes the clinical and ethical implications of protocol modification and initiation of complex pediatric oncology care within a resource-limited secondary hospital infrastructure.

Case Presentation

A previously healthy 12-year-old female presented to the emergency department on August 5, 2024, reporting a several-week history of headache, change in activity, and progressive gait disturbance. Physical examination revealed significant neurological deficits, including vertical and horizontal nystagmus, dysmetria in upper and lower limbs, bilateral spastic lower limb weakness, hypotonia, absent Deep Tendon Reflexes (DTRs), and marked truncal ataxia. Initial CT imaging confirmed a large posterior fossa lesion causing severe compression of the fourth ventricle and obstructive hydrocephalus, necessitating the urgent insertion of an External Ventricular Drain (EVD) on August 6, 2024.

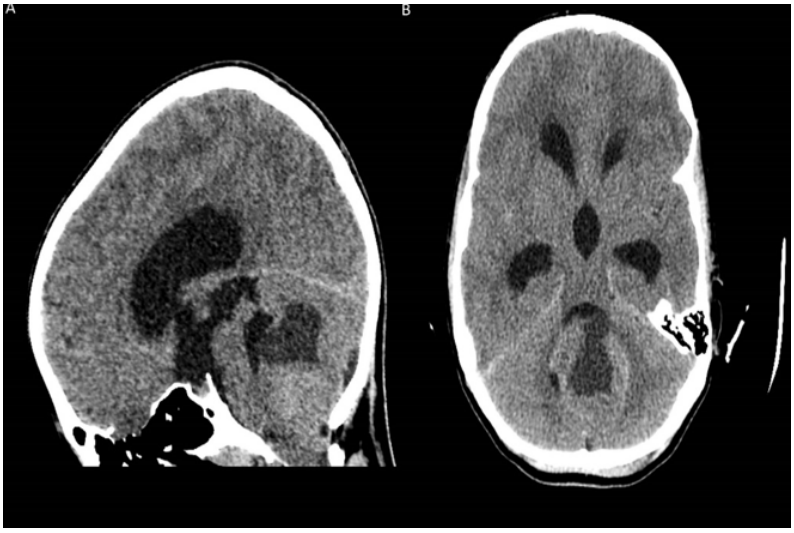

Figure 1. Initial CT examination.
Non-contrast CT images in the sagittal and axial planes demonstrate a heterogeneous midline posterior fossa mass centered within the fourth ventricle, containing both solid and cystic components. The lesion causes obstructive hydrocephalus.

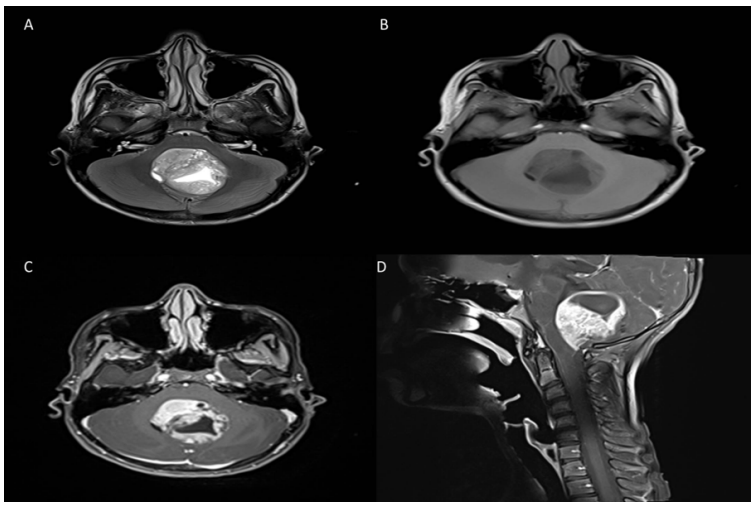

Figure 2. Initial MRI examination.
Selected axial T2-weighted, axial T1-weighted, and axial and sagittal post-contrast T1-weighted images of the brain and cervical spine demonstrate a heterogeneous midline posterior fossa mass centered within the fourth ventricle. The lesion contains solid and cystic components. The solid component demonstrates heterogeneous intermediate-to-low signal intensity on T2-weighted images, low signal intensity on T1-weighted images, faint diffusion restriction (not shown), and avid heterogeneous contrast enhancement. The cystic component demonstrates high T2-weighted signal intensity and low T1-weighted signal intensity, with fluid signal slightly higher than cerebrospinal fluid on FLAIR imaging. The mass exerts significant mass effect on the brainstem and causes obstructive hydrocephalus. Whole-spine MRI demonstrates no evidence of spinal leptomeningeal ("drop") metastases.

First Surgical Resection and Initial Risk Stratification

The patient underwent urgent tumor resection on August 11, 2024.

Post-operative MRI confirmed a Subtotal Resection (STR) with significant residual enhancing tumor measuring approximately 1.5 cm 2.2 cm 2.5 cm. The scan also identified a tiny, 3 mm enhancing nodule in the left cerebellar hemisphere.

Histopathology confirmed the diagnosis as Medulloblastoma, Anaplastic/Large Cell Histologic Subtype (WHO Grade IV). Based on the combination of Anaplastic histology and STR, the patient was immediately classified as High-Risk Medulloblastoma.

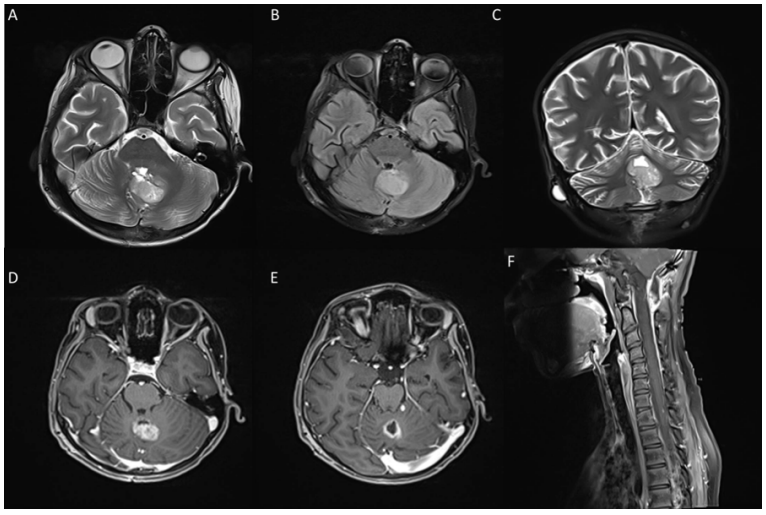

Figure 3. One-month postoperative follow-up MRI.
Axial T2-weighted and FLAIR, coronal T2-weighted, axial post-contrast T1-weighted, and sagittal post-contrast cervical spine images following subtotal tumor resection. Residual enhancing tumor is identified along the posterior and superior margins of the surgical cavity. A newly developed small enhancing nodule is also seen within the superior aspect of the left cerebellar hemisphere, suspicious for metastatic disease. In addition, a new small enhancing nodule is identified at the T1 vertebral level, consistent with spinal leptomeningeal metastasis.

Treatment Delay and Confirmed Metastatic Progression

Adjuvant therapy was critically delayed for nearly two months (45 days post-resection) due to systemic logistical constraints and repeated unsuccessful referral attempts to specialized tertiary centers. This delay resulted in definite disease progression, documented by a follow-up MRI performed on September 24, 2024.

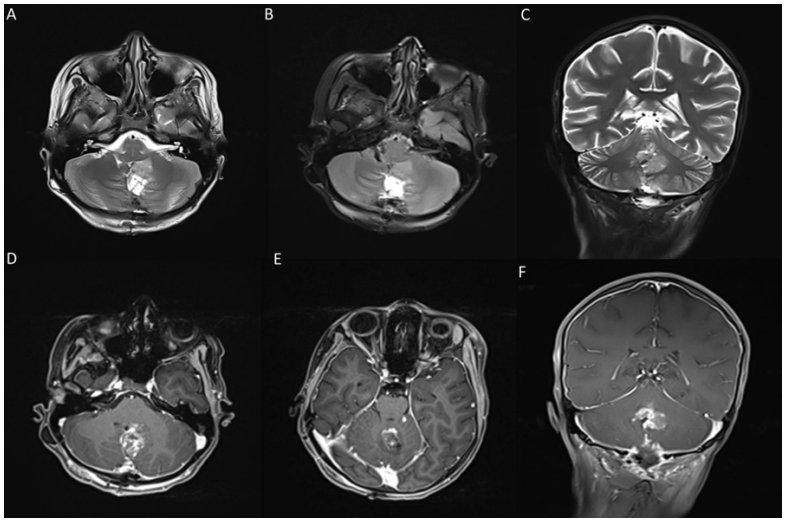

Figure 4. MRI following the second surgical resection.
Axial T2-weighted, FLAIR, coronal T2-weighted, and axial and coronal post-contrast T1-weighted images demonstrate postoperative changes following repeat tumor resection. Small residual enhancing tumor persists along the margins of the surgical cavity. The enhancing metastatic nodule within the superior aspect of the left cerebellar hemisphere remains stable in size.

Given the failure of transfer and the urgent high-risk status, the patient underwent a second surgical intervention to manage the residual mass on October 15, 2024, immediately followed by the commencement of the intensive multimodal therapy protocol at the secondary center.

Post-Second Surgical Intervention

Following the urgent second surgical intervention (October 15, 2024), post-operative MRI confirmed a smaller residual component (measuring 2.2 x 2.3 x 1.9 cm). Crucially, the MRI Whole Spine confirmed the presence of two enhancing nodules in the thoracic spine (at levels D1 and D10-11), reinforcing the status of M+ CSF drop metastasis immediately prior to commencing chemoradiotherapy.

Radiotherapy Service

The Radiation Oncology Department had been operational for only three months when this child was referred for treatment. At that time, the department was not yet fully established to deliver paediatric radiotherapy services. The implementation of a paediatric radiotherapy programme requires coordinated multidisciplinary collaboration involving paediatric oncology, nursing, anaesthetics, play specialists, and social services, together with specialised equipment and workflows, which typically take many months to establish.

The referral therefore presented a significant clinical and logistical challenge, particularly as treatment had not been possible at other centres. In addition to the absence of specialised paediatric immobilisation equipment, the department had not yet recruited a senior radiation therapist (RTT) and relied on a senior Medical Physicist from a tertiary referral centre. Given the complexity of paediatric radiotherapy, particularly the need for consistent daily immobilisation, image verification, and treatment delivery, the involvement of an experienced senior RTT was considered essential to ensure safe and high-quality care.

To address this challenge, an urgent recruitment effort was undertaken to identify an appropriately experienced senior RTT who could join the team for the duration of the patient's treatment. Simultaneously, the radiotherapy team collaborated with colleagues across multiple radiotherapy centres in the Kingdom of Saudi Arabia to source the specialised immobilisation equipment required for treatment.

Several essential immobilisation devices required for the safe planning and delivery of paediatric radiotherapy were unavailable. These included a Posi Board for patient positioning, appropriately sized paediatric thermoplastic head and neck masks for customised immobilisation, and a vacuum cushion to ensure stable, accurate, and reproducible positioning on the treatment couch. In addition, the vacuum pump required to mould and activate the cushion was not available.

To address these limitations, the radiotherapy team collaborated with colleagues across multiple radiotherapy centres in the Kingdom of Saudi Arabia to source the required equipment. Within one week, a Posi Board was obtained from Riyadh (approximately 400 km from our centre), a paediatric head and neck thermoplastic mask from Dhahran (approximately 180 km away), and a vacuum pump from a private hospital within our city.

This collaborative effort enabled the department to rapidly assemble the necessary immobilisation equipment, allowing simulation CT to be performed using appropriate paediatric immobilisation techniques and facilitating timely commencement of radiotherapy treatment. The experience highlights the importance of inter-institutional collaboration in overcoming resource limitations during the establishment of new specialised oncology services.

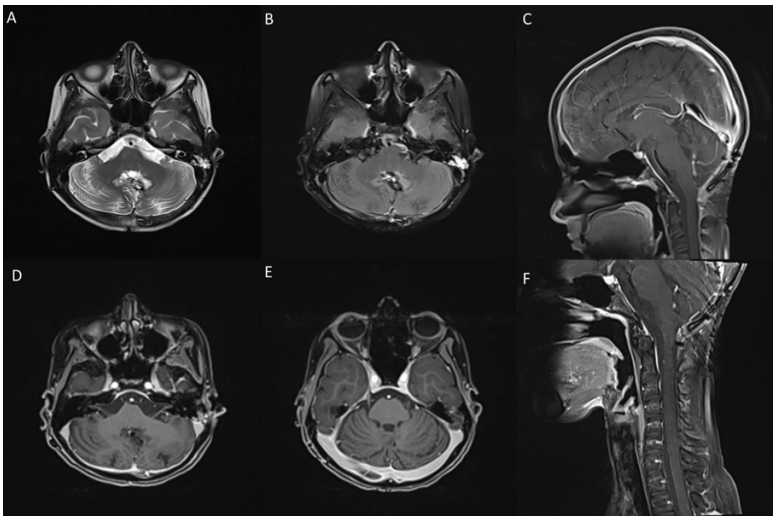

Figure 5. Final follow-up MRI after chemoradiotherapy.
Axial T2-weighted and FLAIR images together with axial and sagittal post-contrast T1-weighted images demonstrate near-complete resolution of the residual tumor. Only a tiny residual T2/FLAIR hyperintense nodule along the posterior aspect of the pons remains, which has further decreased in size and conspicuity and demonstrates no appreciable contrast enhancement, with complete disappearance of the metastatic nodules in the cerebellum and cervical spine, consistent with sustained treatment response.

Radiotherapy Treatment technique

The patient underwent CT simulation in the supine position; this allowed for better immobilisation and set-up reproducibility. We used the aforementioned immobilisation devices, custom head and neck shell and vacbag.

The patient was agitated and required anxiolytics during this process, this was facilitated by the paediatric oncology team.

CT images were obtained in the treatment position, with CT slice thickness 2mm.

MRI registration: registration of pre-operative and post-operative MRI to treatment planning CT was done.

Radiotherapy Target volume

The treatment protocol adopted was based on the SIOP High-Risk Medulloblastoma International trial (1)

Target volumes were defined according to International Commission on Radiation Units and Measurements (ICRU) 50/62/83 guidelines. (2,3,4)

Delineation of all target volumes were based on a planning CT and CT-MRI image fusion and outlined on each slice of the planning scan.

Radiotherapy volumes were outlined taking into account information delineating disease extent at diagnosis (pre- and post-operative MRI) as well as at the time of MRI re-evaluation before radiotherapy.

Delineation followed the SIOP High risk Medulloblastoma trial (1). Although the patient had spinal metastatic disease, the volume of this did not qualify for boost dose to the spinal metastasis. All Organs at Risk were contoured as per trial protocol.

Radiotherapy Treatment Planning

Our center delivers radiotherapy using a Varian VitalBeam® medical linear accelerator system (Varian, Palo Alto, CA, USA). The specific treatment approach used is a 6 MV photon volumetric modulated arc therapy (VMAT) delivery technique. VMAT is an advanced type of intensity-modulated radiation therapy (IMRT) that delivers a precise radiation dose with sparing healthy tissues while the treatment machine moves in an arc around the patient.

A senior medical physicist from a regional tertiary care referral hospital performed radiotherapy treatment planning for CSI-VMAT. Eclipse treatment planning system V16.12 (Varian, Palo Alto, CA, USA) was used. In this case, an effective radiotherapy treatment plan was developed using multiple VMAT arcs with three isocenters for the CSI region, along with an additional VMAT boost plan targeting the primary site. This meticulous planning ensures comprehensive target volume irradiation while accounting for factors like tissue heterogeneity and feathering the cranial and spinal fields with precise dose calculations and implementation. A carefully designed dose gradient is also applied over the vertebral bodies to promote symmetrical bone growth.

To ensure successful and safe radiation dose delivery, rigorous quality assurance (QA) measures are in place. In addition to the routine mechanical and dosimetrical QA tests performed on our linear accelerators, physicists conduct patient-specific quality assurance (PSQA) tests for every VMAT plan. These PSQA tests use the machine-integrated portal image dosimetry system to verify the accuracy of the planned dose delivery.

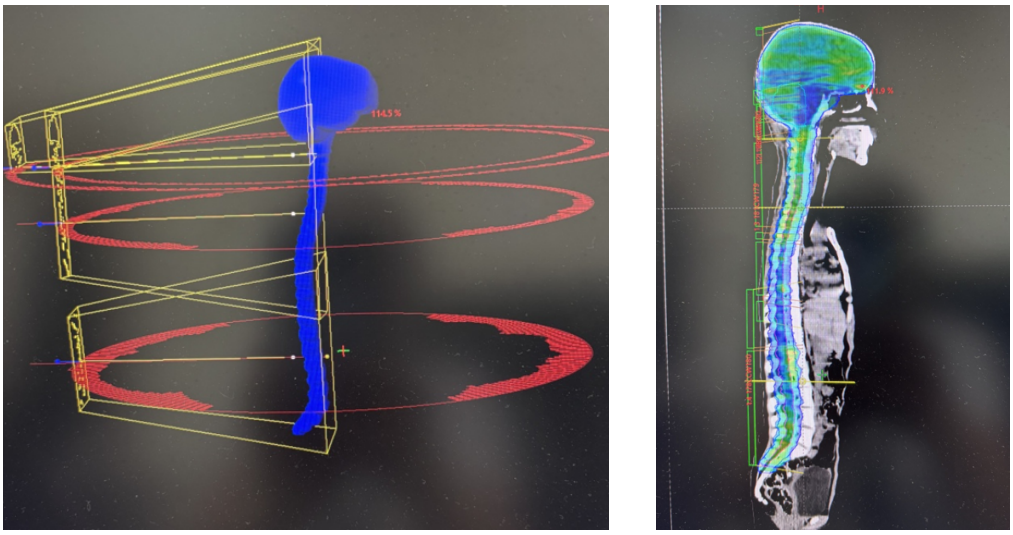

Figure 6 & 7. VMAT plan demonstrating three iscocentres for Craniospinal Irradiation with >=95% dose colour wash, with arm avoidance.

Radiotherapy Prescription:

The dose to the craniospinal axis was 36Gy in 20 daily fractions- 1.8Gy per fraction followed by boost of 18Gy in 10 daily fractions to the posterior fossa tumour bed -1.8Gy per fraction.

Daily Radiotherapy delivery

The patient attended the radiotherapy department daily from the inpatient unit, accompanied and supported by her family throughout the treatment course. Mild sedation was required on several occasions to alleviate treatment-related anxiety, primarily associated with immobilisation using the thermoplastic mask and associated claustrophobia.

Radiotherapy fractions (thirty in total) were delivered without complication. Daily cone beam computed tomography (CBCT) was performed to verify patient positioning and ensure accurate treatment delivery.

The patient developed expectant side effects from the radiation including hair loss, skin eryethema and dryness.

As this was the first paediatric patient treated at our centre, a structured positive reinforcement programme was introduced to enhance the treatment experience and promote adherence.

A treatment progress chart was created, allowing the patient to sign and stamp the chart following the completion of each radiotherapy fraction. This visual record of progress provided a tangible sense of achievement and encouraged engagement throughout the treatment course. In addition, the patient received a small gift after each treatment fraction, with further rewards provided upon completion of weekly treatment milestones. At the conclusion of the six-week treatment course, the multidisciplinary team and the patient's family marked the successful completion of therapy with a celebratory event.

This patient-centred approach helped foster a positive treatment environment, reduced treatment-related anxiety, and supported adherence throughout the prolonged course of radiotherapy.

Adjuvant Chemotherapy Protocol and Toxicity

The chemotherapy regimen utilized was a modified outpatient protocol- See Table 1 below. This adaptation was necessitated by institutional restrictions on administering chemotherapy in the inpatient setting, a critical logistical constraint in the newly established center, thereby aligning the protocol with the required shared-care model. The treatment included a concurrent phase of oral Etoposide administered alongside radiation.

The intensive adjuvant chemotherapy phase commenced following a standard post-radiation recovery period, strictly adhering to the protocol schedule for six cycles. The regimen consisted of:

- Cycles 1, 3, and 5 (Carboplatin/Etoposide): Carboplatin (600 mg/m2/dose) was given on Day 1. Etoposide (150 mg/m2) was infused over 120 minutes on Days 1–3.

- Cycles 2, 4, and 6 (Cyclophosphamide/Vincristine): Cyclophosphamide (400 mg/m2 once daily) was administered on Days 1–5 with periprocedural hydration. Vincristine (1.5 mg/m2) was given on Days 1, 8, and 15.

Supportive Care: Filgrastim (5 mcg per kg) was administered subcutaneously starting 24 hours post-chemotherapy until ANC recovery.

Table 1. Chemotherapy regimen used.

Drug/Agent	Dose	Route	Schedule (days)	Maximum Dose
Carboplatin Etoposide Filgrastim (GCSF)	600 mg/m2/dose 150 mg/m2 5 mcg/kg/dose	IV over 60 minutes IV over 120 minutes SubQ once daily	Day 1 (Cycles 1, 3, and 5) Days 1-3 (Cycles 1, 3, and 5) Starting 24 hours after the last dose of chemotherapy and continuing until ANC >1500 **post nadir (at least 10 doses)**	
Cyclophosphamide	400 mg/m2/dose once daily	IV over 30-60 minutes	Days 1, 2, 3, 4, and 5 (Cycles 2, 4, 6)	
Vincristine	1.5 mg/m2/dose	IV over5-15 minutes	1, 8, and 15 of each cycle (cycles 2, 4, 6)	**2 mg**
Filgrastim (GCSF	5 mcg/kg/dose	SubQ once daily	Starting 24 hours after the last dose of chemotherapy and continuing until ANC >1500 **post nadir (at least 10 doses)**	

All doses were delivered exactly as per the protocol schedule without delay or modification.

Toxicity and Supportive Care:

Despite the outpatient approach, the patient experienced significant hematologic toxicity, requiring multiple hospitalizations for management of febrile neutropenia and necessitating repeated transfusions of platelets and red blood cells. Infectious complications included one episode of Clostridioides difficile infection and one episode of herpes simplex virus reactivation. Post-therapy, she developed localized herpes zoster. Despite the high demands for supportive care, the patient did not develop any life-threatening systemic infections and successfully completed the entire regimen.

Final Outcome:

The Final MRI Brain and Whole Spine performed upon completion of the intensive multimodal treatment (July 17, 2025) demonstrated definitive and sustained interval improvement. The small nodule previously attached to the dorsal aspect of the pons showed no enhancement in the follow-up scans. Crucially, the MRI Whole Spine showed no obvious enhancing nodule to suggest drop metastasis in the spine. These findings confirm a Radiological Complete Response (CR) at the metastatic sites and within the residual primary tumor bed, underscoring the success of the high-risk protocol delivery.

Clinical Recovery:

Clinically, the patient achieved a remarkable functional recovery. The severe initial neurological deficits, including truncal ataxia and significant gait disturbance, resolved significantly. The patient demonstrated marked improvement in speech fluency and regained the ability to mobilize independently without signs of significant residual neurological impairment. This combination of complete radiological response and robust functional recovery validates the feasibility and safety of delivering an intensive, high-quality treatment protocol in a resource-limited setting, achieved through thoughtful adaptation and collaborative care.

Discussion

1. The Clinical Impact of Treatment Delay and the Role of the Shared-Care Model

The management of this child with high-risk medulloblastoma in a newly established secondary hospital presented significant clinical and logistical challenges, reflecting the limited paediatric oncology infrastructure and the absence of an established specialised paediatric neuro-oncology service. The most significant obstacle was a two-month delay in initiating adjuvant therapy, resulting from repeated unsuccessful attempts to transfer the patient to a tertiary referral centre. This interval substantially exceeded the recommended timeframe for commencing postoperative therapy, which is generally within 4–6 weeks following surgical resection, and was associated with radiological disease progression, including the development of spinal drop metastases. Consequently, the patient's management shifted from planned adjuvant treatment to urgent treatment for progressive metastatic disease.

These challenges are consistent with those reported in resource-limited settings, where deficiencies in specialised infrastructure, workforce capacity, and timely access to tertiary care can compromise the delivery of multimodal therapy for paediatric central nervous system (CNS) tumours. The management of medulloblastoma requires close coordination between neurosurgery, paediatric oncology, radiation oncology, neuroradiology, pathology, and supportive care services. Delays in access to any component of this pathway may adversely affect disease control and clinical outcomes.

This case highlights the potential value of a shared-care model, in which specialised expertise is integrated with treatment delivered closer to the patient's home through collaboration between tertiary referral centres and secondary hospitals. Such models may reduce delays in initiating time-critical therapy, expand access to specialised treatment, and strengthen regional paediatric oncology networks while maintaining appropriate standards of care. [1,2]

2. Overcoming Radiotherapy Challenges through Inter-Institutional Collaboration

The successful delivery of paediatric craniospinal irradiation (CSI) at a newly established radiotherapy centre presented substantial logistical, technical, and workforce challenges. At the time of referral, essential paediatric immobilisation equipment and experienced personnel required for the safe delivery of complex paediatric radiotherapy were not yet available. These limitations had the potential to compromise the reproducibility and precision required for craniospinal irradiation delivered over 30 treatment fractions.

These challenges were overcome through rapid inter-institutional collaboration. Essential immobilisation equipment was sourced from radiotherapy centres in Riyadh and Dhahran, together with additional resources from a local private hospital, allowing treatment preparation to proceed without significant delay. In parallel, an experienced senior radiation therapist (RTT) was recruited to provide specialist support throughout the patient's treatment course, ensuring consistent daily patient positioning, image verification, and treatment delivery.

Treatment planning was undertaken using volumetric modulated arc therapy (VMAT) by an experienced medical physicist from a regional tertiary oncology centre. Daily cone beam computed tomography (CBCT) was used to verify patient positioning before each fraction, enabling accurate and reproducible treatment delivery in accordance with the prescribed protocol.

This experience demonstrates that the successful implementation of complex paediatric radiotherapy in newly established or resource-limited centres is achievable through coordinated multidisciplinary collaboration, inter-institutional sharing of expertise and equipment, and robust quality assurance processes.

Such collaborative models may facilitate the safe integration of secondary hospitals into regional paediatric oncology networks, improving access to specialised radiotherapy while maintaining high standards of care. [3,4]

3. Justification for the Outpatient Chemotherapy Regimen

The outpatient chemotherapy regimen consisting of carboplatin, vincristine, cyclophosphamide, and etoposide was selected based on established clinical evidence supporting its efficacy and safety in patients with high-risk medulloblastoma.

Sirachainan et al (5). evaluated 23 newly diagnosed patients with high-risk medulloblastoma treated with this combination regimen and reported a 5-year overall survival (OS) of 60% and a 5-year progression-free survival (PFS) of 41.8%. Hematologic toxicity was the most common adverse event but was predictable and manageable with appropriate supportive care in the outpatient setting.

Similarly, Rutkowski et al.(6) investigated a comparable regimen in young children with medulloblastoma, particularly those who underwent gross total resection, and reported 5-year OS rates of up to 93% and 5-year PFS of approximately 82%, with an acceptable safety profile and no unexpected toxicities. Collectively, these studies provide a strong rationale for the use of a carboplatin-, vincristine-, cyclophosphamide-, and etoposide-based regimen in our patient, supporting both its efficacy and its feasibility for outpatient administration under close clinical supervision.

Although treatment was associated with significant hematologic toxicity, requiring multiple hospitalizations for febrile neutropenia and repeated blood product transfusions, infectious complications were limited to a single episode each of Clostridioides difficile infection and Herpes simplex virus infection reactivation, both of which were successfully managed. These findings demonstrate that this intensive high-risk chemotherapy protocol can be delivered safely in the outpatient setting when supported by comprehensive multidisciplinary care, vigilant monitoring, and timely management of treatment-related complications. [5,6]

Conclusion

The patient successfully completed the prescribed multimodal treatment protocol and achieved a radiological complete response at all disease sites, accompanied by significant functional recovery, including restoration of independent ambulation and improved speech.

This case illustrates that complex paediatric neuro-oncology care, including craniospinal irradiation, can be delivered safely and effectively within a newly established secondary hospital when supported by multidisciplinary expertise, rigorous quality assurance, and close collaboration with tertiary oncology centres.

Successful treatment was made possible through a shared-care approach that integrated specialist expertise, inter-institutional resource sharing, and coordinated multidisciplinary decision-making to overcome substantial logistical, technical, and workforce challenges.

This experience highlights the value of regional oncology networks in expanding access to timely, high-quality paediatric cancer care while maintaining adherence to established treatment protocols. Further studies are required to evaluate the reproducibility and long-term outcomes of this collaborative model in other resource-limited or developing radiotherapy services.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Acknowledgements

None.

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