Unveiling the Unseen: A Rare Case of Brain Metastatic Ewing Sarcoma Originating in the Spinal Cord

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ABSTRACT

Ewing sarcoma (ES) with brain metastasis is an uncommon clinical occurrence, generally arising from primary tumours located in the skull or the long bones of the extremities. This report documents an extraordinarily rare instance of brain metastatic ES (BMES), with the primary neoplasm situated in the lumbosacral spinal canal. A middle-aged woman was admitted to the emergency room for disturbance of consciousness. She had a history of pelvic-lumbar ES diagnosed four years ago and a cerebral haemorrhage two months earlier. Upon admission, a computed tomography (CT) scan was performed, which identified a right cerebellar haemorrhage. The patient, with recurrent right cerebellar haemorrhage and a history of ES, underwent emergency surgery for suspected neoplastic haemorrhage, later confirmed as BMES. After two weeks in the hospital, the patient regained consciousness and showed no tumour recurrence at the one-year follow-up. This case represents the first documented instance of BMES originating in the spinal cord, suggesting the possibility that primary ES of the central nervous system may disseminate *via* cerebrospinal fluid. Furthermore, this case suggests that in patients with cerebral haemorrhage and a history of ES of the central nervous system, increased vigilance for the potential occurrence of neoplastic haemorrhage is warranted.

Key Words: *Ewing sarcoma, Brain metastases, Cerebellar haemorrhage, Lumbosacral vertebrae, Chemoradiotherapy*.

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INTRODUCTION

Ewing sarcoma (ES) is a highly aggressive cancer primarily affecting adolescents and children, and rarely adults. It usually develops in the long bones of the limbs but can also occur in the spine, pelvis, chest wall, skull, and other tissues.[1] The cancer mainly spreads through the bloodstream to the lungs or other bones.[2] Metastasis to the brain is extremely rare. Most patients with metastatic ES (MES) experience symptoms such as headache, nausea, and vision changes, though a few are asymptomatic at diagnosis. Total resection and chemoradiotherapy are key treatments for brain metastatic ES (BMES) and significantly extend patient survival. We present a 40-year woman with primary lesions in the L1-S2 spinal canal who developed a cerebral haemorrhage and was diagnosed with metastatic cerebellar ES post-surgery. This is the first reported case of BMES originating from the spinal canal, prompting us to consider whether tumour cells metastasised *via* cerebrospinal fluid.

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CASE REPORT

A 40-year female presented to the emergency department exhibiting a disturbance of consciousness. Upon physical examination, her vital signs were stable, and she demonstrated confusion with a Glasgow coma scale (GCS) score of 12. Pupillary assessment revealed equal pupils with intact direct and consensual light reflexes. No additional positive findings were noted. Following admission, pertinent laboratory tests and examinations were conducted, revealing through CT imaging (Figure 1N) that the patient had a right cerebellar haemorrhage. A review of the patient's medical history disclosed that the patient had been diagnosed with intramedullary lesion of the spinal cord from the L1 to S2, without brain metastases four years prior (Figure 1 A-D), causing symptoms of numbness, pain, and urinary dysfunction, for which surgical intervention was performed. Postoperative pathological analysis confirmed a diagnosis of ES (Figure 2A). Subsequently, the patient received radiation therapy and completed 16 courses of chemotherapy. After about a four-year follow-up period, no recurrence was observed (Figure 1 E-J). Notably, the patient had experienced a cerebral haemorrhage two months prior (Figure 1K), with the haemorrhage occurring at the same site as the current episode. Regrettably, the MRI results obtained at that time failed to identify any tumour lesions (Figure 1 I-M).

Given the propensity for ES to metastasise to the brain, along with the patient's medical history and pertinent examination

findings, the authors hypothesised the presence of MES with haemorrhage in the right cerebellar hemisphere. To evacuate the haematoma and establish a definitive diagnosis, an emergency craniotomy was performed. Postoperative CT and MRI assessments confirmed the complete excision of the tumour (Figure 1 O-R). Histopathological analysis post-surgery was consistent with a diagnosis of MES (Figure 2B). Furthermore, the immunohistochemical evaluation identified the presence of specific markers, CD99 (+), ki-67 (+, 67%). Following approximately two weeks of recuperative treatment, the patient regained full consciousness without any significant sequelae. Subsequent to the surgical intervention, the patient underwent radiotherapy. After one year of follow-up, there was no evidence of tumour recurrence.

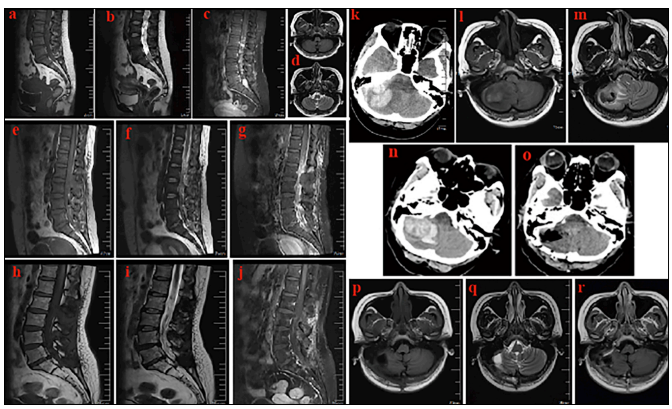

Figure 1: MRI revealed multiple nodular lesions in the L1-S2 spinal canal (A-C) but no brain metastases (D). The postoperative MRI (H-J) showed that the tumour was removed compared to preoperation (E-G). CT (K) and MRI (I and M) showed a cerebellar haemorrhage. Preoperative (N) and postoperative CT (O) or MRI (P-R) showed the lesion was largely resected.

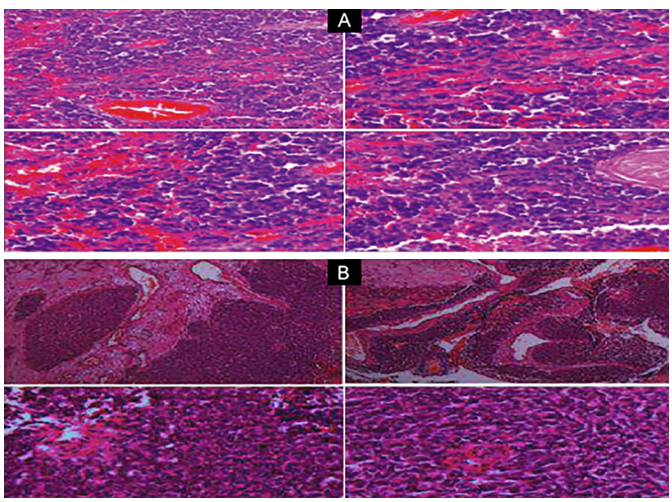

Figure 2: (A) The pathology revealed small round tumour cells. (B) Pathology confirmed brain metastasis from Ewing sarcoma.

DISCUSSION

ES is an aggressive small round blue cell malignancy affecting both bones and soft tissues. This neoplasm is exceedingly rare, constituting approximately 1% of all soft tissue tumours,[3] with a global incidence estimated at 1 in 1.5 million individuals. The incidence rate is notably higher in paediatric populations compared to adults, positioning ES as the second most prevalent bone malignancy in children, representing 34% of such cases.[4] Furthermore, it accounts for approximately 2% of all childhood malignancies. ES was initially reported and described by James Ewing[5] in 1920. Sixty years later, the characteristic t (11; 22) (q24; q12) chromosomal translocation was identified,[6] marking a significant advancement in the molecular diagnosis of ES. Currently, the diagnosis of ES primarily relies on morphological assessment and immunohistochemical analysis. The concurrent expression of CD99 and NKX2.2 is widely regarded by scholars to possess high specificity (98%) for the diagnosis of this type of tumour.[7] Advancements in genetic analysis have identified additional fusion genes such as *EWSR1-ERG* alongside the common *EWSR1-FLI1*,[8,9] significantly improving ES diagnosis rates. Mainstream treatments include surgical resection followed by chemoradiotherapy, boosting the five-year survival rate from 10 to 70% for responsive patients.[10,11] However, those with metastases at diagnosis have a five-year survival rate of less than 30%.

ES exhibits a high propensity for distant metastasis, commonly disseminating to the lungs, bones, and lymph nodes. Nonetheless, metastases to the brain are infrequent, with recent studies indicating that central nervous system involvement occurs in less than 5% of cases.[12] Typically, such metastases result from direct infiltration by a primary skull lesion or haematogenous spread. The authors present the first case of brain metastasis in ES originating from the lumbosacral region and subsequently, metastasising to the right cerebellum. Notably, this patient exhibited no metastases to other anatomical sites, prompting an investigation into the potential role of cerebrospinal fluid (CSF) in the metastatic process. Regrettably, due to patient-specific constraints, a comprehensive cytological analysis of CSF could not be conducted to substantiate this hypothesis.

Common symptoms in patients with BMES typically include elevated intracranial pressure, manifesting as headaches and vomiting, as well as region-specific neurological symptoms depending on the tumour's location within the brain. However, the patient in question exhibited no symptoms indicative of nervous system involvement prior to the haemorrhage and was not diagnosed until after the second surgical intervention. This case suggests that certain instances of BMES may remain asymptomatic in the early stages. Consequently, comprehensive neuroimaging is essential to rule out the possibility of brain metastasis in patients with ES. Similar to other primary brain tumours, patients may present to the hospital with cerebral haemorrhage, and imaging of the haemorrhage often complicates the diagnosis of the tumour. Consequently, it is prudent to consider the possibility of neoplastic haemorrhage in patients with cerebral haemorrhage who have a history of ES.

PATIENT'S CONSENT:

Informed consent was obtained from the patient to publish the data concerning this case.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

CX: Conceptualisation, project administration, writing of the original draft, review, and editing.

YS: Formal analysis, visualisation, writing of the original draft, review, and editing.
QH: Conceptualisation, data curation, methodology, supervision, validation, visualisation, review, and editing.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Wright A, Desai M, Bolan CW, Badawy M, Guccione J, Korivi BR, *et al*. Extraskeletal Ewing sarcoma from head to toe: Multimodality imaging review. *Radiographics* 2022; **42(4)**: 1145-60. doi: 10.1148/rg.210226.
2. Zetouni NC, Sergi CM. Features of metastatic Ewing sarcoma. In: Sergi CM. Ed. Metastasis. Brisbane, Australia: Exon Publications; 2022. Chapter 13. doi: 10.36255/exon-publications.metastasis.matastatic-ewing-sarcoma.
3. Gereige R, Kumar M. Bone lesions: Benign and malignant. *Pediatr Rev* 2010; **31(9)**:355-62. quiz 363. doi: 10.1542/pir.31-9-355.
4. Sbaraglia M, Righi A, Gambarotti M, Dei Tos AP. Ewing sarcoma and Ewing-like tumours. *Virchows Arch* 2020; **476(1)**:109-19. doi: 10.1007/s00428-019-02720-8.
5. Ewing J. The classic: Diffuse endothelioma of bone. Proceedings of the New York pathological society. 1921;12:17. *Clin Orthop Relat Res* 2006; **450**:25-7. doi: 10.1097/01.blo.0000229311.36007.c7.
6. Zou YS, Morsberger L, Hardy M, Ghabrial J, Stinnett V, Murry JB, *et al*. Complex/cryptic EWSR1::FLI1/ERG gene fusions and 1q jumping translocation in paediatric ewing sarcomas. *Genes (Basel)* 2023; **14(6)**:1139. doi: 10.3390/genes14061139.
7. Shibuya R, Matsuyama A, Nakamoto M, Shiba E, Kasai T, Hisaoka M. The combination of CD99 and NKX2.2, a transcriptional target of EWSR1-FLI1, is highly specific for the diagnosisof Ewing sarcoma. *Virchows Arch* 2014; **465(5)**:599-605. doi: 10.1007/s00428-014-1627-1.
8. Sorensen PH, Lessnick SL, Lopez-Terrada D, Liu XF, Triche TJ, Denny CT. A second ewing's sarcoma translocation, t(21;22), fuses the EWS gene to another ETS-family transcription factor, ERG. *Nat Genet* 1994; **6(2)**:146-51. doi: 10.1038/ng0294-146.
9. Shing DC, McMullan DJ, Roberts P, Smith K, Chin SF, Nicholson J, *et al*. FUS/ERG gene fusions in Ewing's tumours. *Cancer Res* 2003; **63(15)**:4568-76.
10. Gupta A, Riedel RF, Shah C, Borinstein SC, Isakoff MS, Chugh R, *et al*. Consensus recommendations in the management of Ewing sarcoma from the national Ewing sarcoma tumour board. *Cancer Soc* 2023; **129(21)**: 3363-71. doi: 10.1002/cncr.34942.
11. Dos Santos RP, Roesler R, Gregianin L, Brunetto AT, Da Cunha Jaeger M, Lunardi Brunetto A, *et al*. Cancer stem cells and chemoresistance in Ewing sarcoma. *Curr Stem Cell Res Ther* 2023; **18(7)**:926-36. doi: 10.2174/1574888X17666220627114710.
12. Poh JZ. Secondary brain metastases of Ewing's sarcoma presenting with collapse after 6 years of complete remission. *Clin Case Rep* 2021; **9(1)**:560-5. doi: 10.1002/ccr3.3583.