Case Report

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Late-Onset Vertebral Metastasis from Gastric Cancer: The Role of Re Biopsy and MRI: Case Report and literature Review

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ABSTRACT

Background: Late relapse after curative gastrectomy for gastric cancer is rare (2–10%) and may be driven by tumor dormancy, immune evasion, and chronic inflammation. This case report aims to illustrate the clinical trajectory and diagnostic challenges of a late relapse, emphasizing the importance of extended surveillance, spinal imaging, and HER2 reassessment.

Methods: An 81-year-old male with HER2-positive gastric cancer underwent distal gastrectomy in 2015, with omental involvement. He received FOLFOX plus trastuzumab, which was paused due to neuropathy. In 2022, an MRI was performed for new-onset neurologic symptoms and revealed a destructive vertebral lesion. Biopsy and FISH analysis were used to confirm metastatic recurrence and reassess HER2 status.

Results: MRI identified spinal cord compression secondary to a vertebral metastasis. Biopsy confirmed metastatic gastric adenocarcinoma, HER2-negative by FISH. Palliative radiotherapy preserved neurologic function. Systemic therapy was withheld due to myocardial infarction and declining performance status. The case demonstrated HER2 discordance between primary and metastatic sites (a phenomenon observed in 5–20% of cases).

Conclusion: This case underscores the need for prolonged surveillance in high-risk gastric cancer patients, prompt MRI evaluation for suspected spinal metastases, and routine re-biopsy for HER2 reassessment. These steps are critical for guiding treatment decisions and optimizing patient outcomes in late relapse scenarios

Keywords: Late Relapses; Gastric Cancer; Vertebral Metastasis; Metastatic Spinal Cord Compression

Abbreviations: SII: Systemic Immune-Inflammation Index; ctDNA: Circulating Tumor DNA; MSCC: Metastatic Spinal Cord Compression; IHC: Immunohistochemistry; CGA: Comprehensive Geriatric Assessment; PS: Performance Status

Introduction

Late relapse of gastric adenocarcinoma (recurrence >5 years) after curative gastrectomy is uncommon but often causes diagnostic and therapeutic challenges. In the literature, late recurrence occurs in 2–10% of patients [1-3], with most relapses occurring within three years after surgery [1,2]. Proposed mechanisms include tumor dormancy, immune evasion, and chronic inflammation [4-6]. At the same time, an advanced pT stage, aggressive histology, and a high systemic immune-inflammation index confer a higher risk. [1,4,6] Spinal metastases causing metastatic spinal cord compression are rare oncologic emergencies; MRI is the diagnostic gold standard, and biopsy is essential for definitive diagnosis and treatment planning [7-9]. HER2 status may vary between primary and metastatic sites (5–20%), supporting the need for re-biopsy and molecular reassessment to guide targeted therapy [10-13].

Case Presentation

Our patient was an 81-year-old male who was diagnosed in December 2015 with gastric adenocarcinoma. Initially, he underwent Distal gastrectomy and Roux-en-Y gastrojejunostomy with D2 lymph

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node resection. Omental deposits were positive for adenocarcinoma on frozen section. He received 11 cycles of FOLFOX with trastuzumab in the first-line metastatic setting, then treatment was kept on hold because of severe neuropathy along with altered general status. Regular follow-up of the patient did not show any evidence of metastases until October 2022, when an MRI of the spine done for neck pain was suspicious for vertebral metastases. PET scan later showed no FDG-avid lesions in the spine. A vertebral biopsy was done and initially came inconclusive for malignancy, then the patient refused to repeat any invasive procedure. In July 2023, the patient had progressive worsening neck pain, and a new MRI spine showed a spinal cord compression with a destructive bony lesion. Vertebral biopsy was done and came positive for metastatic adenocarcinoma (Figure 1) with an immunoprofile consistent with a gastric primary. The cancer cells were positive for CK7 and CK20, and focally positive for CDX2, and negative for NKX3.1 (Figure 2). The molecular profile of the new biopsy showed MMR proficiency, HER2 negativity by FISH, and a TMB of 4.7. Palliative RT to the spine was done, and the patient was kept free of neurological deficit. No further chemotherapy was given to the late relapsing tumor due to a further decline in performance status after the patient developed a myocardial infarction, which was managed medically. Writing consent was taken from the patient for publication purposes.

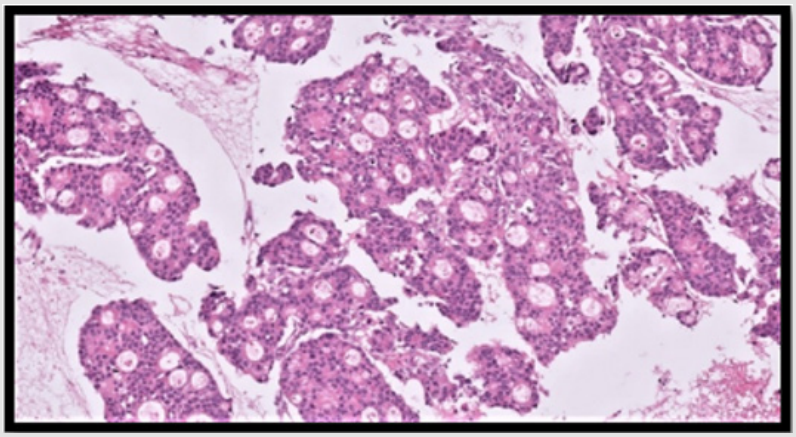

Figure 1: H&E(x100), The tumor cells infiltrating the vertebral column arranged in cribriform pattern with eosinophilic cytoplasm. The inset highlights pleomorphic vesicular nucleus with 2 to 3 prominent nucleoli.

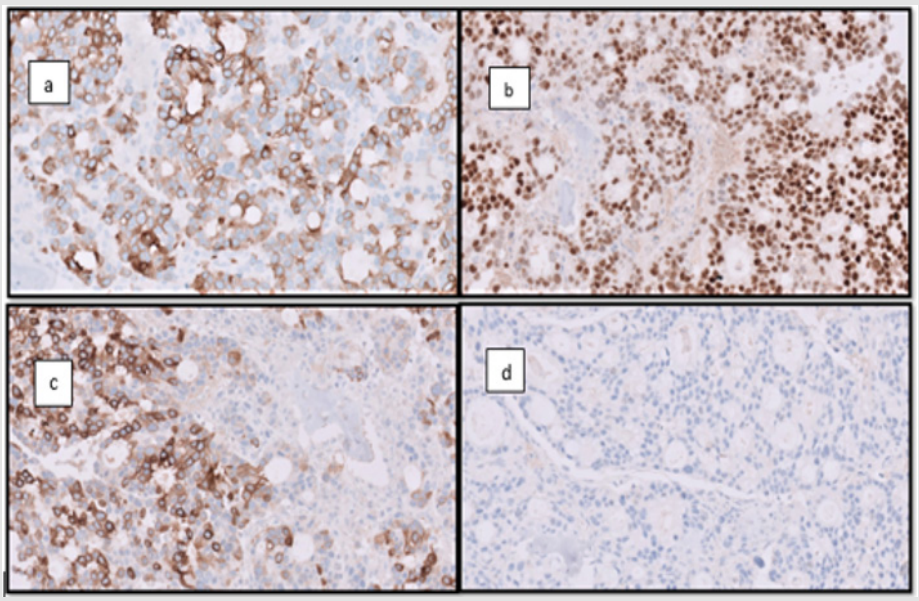

Figure 2: IHC(x200): a: CK7 shows diffuse membranous expression in all the tumor cells, b: CDX2 shows nuclear expression, c: CK20 shows focal membranous expression in tumor cells - d: NKX3.1 is negative in tumor cells.

Discussion

In this case report, we present an 81-year-old man with prior HER2-positive gastric cancer who presented seven years later with spinal cord compression. Biopsy showed metastatic gastric adenocarcinoma, HER2-negative. Palliative RT to the spine was done. Lately relapse in gastric cancer recurrence occurring more than 5 years after curative surgery is rare but clinically significant [1-3]. Late relapses are thought to result from dormant cancer cells that evade immune detection and remain quiescent for years before reactivation. Chronic inflammation and immune system changes may trigger reactivation and metastatic spread, particularly to the peritoneum and bone marrow [4-6]. Advanced T stage (especially pT4), aggressive histology, and high systemic immune-inflammation index (SII) are associated with a higher risk of late recurrence. Genetic alterations, such as PIK-3CA amplification and MSI-H status, can also influence the timing and pattern of recurrence [1,4,6]. Peritoneal dissemination is the most common pattern of late recurrence, followed by distant metastases (e.g., bone, pleura) [1,14,15]. Late recurrence (>5 years) occurs in 2–10% of patients after gastrectomy [1,15], with most relapses occurring within 8 years [1,15]. Patients with high-risk features may benefit from extended surveillance beyond the standard 5 years [1,4]. Circulating tumor DNA (ctDNA) monitoring can detect molecular residual disease and predict recurrence months before radiographic evidence, offering a promising adjunct to imaging and clinical follow-up [16].

Current guidelines focus on intensive surveillance for the first 2–3 years; however, evidence suggests that high-risk patients may require longer follow-up [1,17]. Spinal metastases and metastatic spinal cord compression (MSCC) from gastric cancer are rare but represent oncologic emergencies with high morbidity and mortality. Early diagnosis and multidisciplinary management are crucial for preventing irreversible neurological damage and improving outcomes. MRI is the gold standard for diagnosing spinal cord compression, handing detailed visualization of soft tissue, spinal cord, and the extent of metastasis. It is essential for detecting both epidural and intramedullary lesions, as well as for surgical planning [7-9]. PET/CT can help identify systemic metastatic disease and bone involvement, but is less sensitive than MRI for evaluating the degree of cord compression and soft tissue extension [9]. In rare cases, the radiological diagnosis of intramedullary metastasis can be challenging, and both modalities may be necessary for a comprehensive assessment [8]. Biopsy is critical for confirming the diagnosis, especially when the primary cancer is unknown or when imaging findings are atypical. Histopathology can reveal specific features such as signet ring cells in gastric adenocarcinoma, guiding targeted Therapy [8,18]. In select cases, surgical removal of the spinal lesion allows for both decompression and tissue diagnosis [8]. Radiotherapy is a mainstay for palliation, pain relief, and local tumor control, especially in patients with limited life expectancy or poor surgical candidates [7,9,18].

Surgery (decompression and stabilization) is indicated for patients with good performance status, rapid neurological decline, or spinal instability. Surgery can improve neurological function and quality of life, though overall survival remains limited. [8,9] Systemic Therapy (chemotherapy, targeted agents) may be considered based on tumor biology and patient status. However, evidence for efficacy in MSCC from gastric cancer is limited [8,9]. HER2 status can vary between primary and metastatic gastric cancer sites because of tumor heterogeneity and clonal evolution. Discordance rates range from 5% to 20%, [10-13] impacting treatment eligibility and supporting re-biopsy in select cases [10-13]. Intratumoral and intertumoral heterogeneity in HER2 expression leads to discordance between primary and metastatic sites. Clonal selection, genetic evolution, and microenvironmental factors play a role in these differences during metastasis [10-13]. Discordance can result in patients with HER2-negative primaries developing HER2-positive metastases, making them eligible for HER2-targeted therapies (e.g., trastuzumab) [10,19-21]. Conversely, loss of HER2 in metastases may render targeted Therapy ineffective. Some studies suggest that discordant patients may have worse outcomes, although the findings are not constantly statistically significant [22]. Re-biopsy of metastatic or recurrent lesions is warranted, given the discordance rates, up to 20% of patients showing HER2 gain in metastases, especially if the primary tumor was HER2-negative or if treatment decisions depend on HER2 status [10,13,19,21].

Patients with HER2-positive metastases (even if the primary was negative) should be considered for HER2-targeted Therapy, as they may derive similar benefit to those with HER2-positive primaries [19]. Multiple studies and meta-analyses support routine HER2 reassessment in advanced or metastatic disease to optimize patient selection for targeted Therapy [13,23,24]. Immunohistochemistry (IHC) and molecular profiling are essential for classifying gastric cancer, guiding prognosis, selecting targeted or immunotherapy, and improving outcomes. Markers such as CK7, CK20, CDX2, MMR status, TMB, and HER2 are central to this approach, with direct implications for treatment. [25,26] Most gastric cancers are CK7-positive and CK20-negative or variably positive for CK20. This pattern helps distinguish gastric origin from other GI or metastatic tumors. [25,27] CDX2 is often positive in intestinal-type gastric cancers and negative in diffuse-type, aiding subtype classification. [25,27] MMR Status (MLH1, PMS2, MSH2, MSH6): Deficiency (dMMR/MSI-H) is found in 5–20% of gastric cancers and is associated with better prognosis and strong response to immune checkpoint inhibitors [25,27,28]. High TMB is more common in MSI-H tumors and may predict immunotherapy (e.g., pembrolizumab, nivolumab) response, though its predictive value is not absolute [29,30]. HER2 overexpression/amplification occurs in 10–20% of cases, especially in intestinal-type tumors, and identifies candidates for trastuzumab and other HER2-targeted therapies [25,31,32].

HER2 positivity enables trastuzumab-based regimens; MET, EGFR, and CLDN18.2 are emerging targets for treatment [25,30,31]. Treatment for frail elderly patients with gastric cancer requires individualized decisions that weigh functional status, patient values, and the potential benefits and burdens of Therapy. Comprehensive geriatric assessment and supportive care are central to optimizing outcomes and respecting patient autonomy [33,34]. Chronological age alone should not dictate treatment. Comprehensive geriatric assessment (CGA) and performance status (PS) are better predictors of treatment tolerance and outcomes than age, helping to identify frailty and guide the intensity of therapy [33-36]. Frailty is common (prevalence ~29%) and is associated with higher risks of complications, prolonged hospital stays, readmission, and mortality. CGA tools (e.g., G8, MFS) are recommended for risk stratification and treatment planning. [34,35,37-40] Treatment should align with the patient's goals, quality of life, and preferences. For severely frail patients, best supportive care or symptom management may be the most suitable strategy [25,34,41]. Clinical decisions should weigh therapeutic benefit against potential harm, prioritizing patient autonomy and minimizing interventions unlikely to bring meaningful outcomes [25,34,41,42]. In advanced disease settings where curative options are modest, palliative radiotherapy remains a beneficial modality, particularly for symptom control in cases of bleeding, pain, or obstruction, and when surgery or systemic therapy are contraindicated [25,41,42] due to frailty or comorbidities.

Short-course, low-toxicity regimens are preferred to minimize treatment burden and maintain quality of life [25,41]. Effective gastric cancer management relies on coordinated input from oncology, pathology, radiology, and palliative care, with robust documentation and shared decision-making enhancing outcomes. [43,44] Oncology leads systemic therapy planning, integrates input from other specialties, and ensures guideline-concordant care. Pathology provides definitive diagnosis, molecular profiling (e.g., HER2, MMR), and guides re-biopsy verdicts [17,25,43,45]. Radiology is central for precise staging, restaging, and monitoring, enhancing diagnostic precision and treatment choice [43,46-47]. Palliative care manages symptom management, quality of life, and psychosocial support, and is best integrated early through multidisciplinary planning [48,49]. Regular multidisciplinary meetings increase survival, improve staging accuracy, and ensure evidence-based, patient-centered decisions even for elderly or frail patients [47,50-53]. Standardized documentation (e.g., surgical details, staging, treatment plans) and clinical algorithms enhance audit readiness and adherence to guidelines [20,43,54,55]. Interventions such as standardized care pathways and regular audits lead to measurable improvements in care quality and process metrics [54]. Multidisciplinary teams promote re-biopsy and molecular reassessment at the time of progression or recurrence, ensuring up-to-date biomarker status (e.g., HER2, PD-L1) and eligibility for targeted therapies [17,20,43]. Tumor boards and MDTs serve as platforms for ongoing education, dissemination of new evidence, and reinforcement of the importance of molecular reassessment.

Conclusion

This case demonstrates a rare late isolated vertebral relapse of gastric adenocarcinoma causing metastatic spinal cord compression, treated with palliative radiotherapy. Extended surveillance for high-risk individuals is crucial. MRI is the gold standard for assessing spinal cord compression, and re biopsy is advised to guide targeted therapy eligibility.

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