

Beyond the Spine: A Rare Case of Myxopapillary Ependymoma With Extraneural Metastases

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Abstract

Objective. Myxopapillary ependymoma (MPE) is a rare tumor of ependymal origin that commonly arises within the spinal canal. It is rather benign and slow-growing; however, it tends to recur along the central nervous system (CNS), usually after incomplete resection or tumor seeding due to surgical manipulation. Extraneural metastases of MPE are extremely rare, with only a few documented cases in the literature. **Case Report.** We describe a case of a middle-aged female patient with sacrococcygeal MPE, which was initially misdiagnosed as a pilonidal cyst and subjected to surgical excision. Over the following years, she experienced three local recurrences in the sacrococcygeal region, which were treated with surgery and radiotherapy. Ten years after the initial excision, the patient complained of dyspnea and hemoptysis, and imaging studies revealed multiple right lung nodules. A core biopsy of a lung lesion was performed, and histopathology was consistent with metastatic MPE. The patient was started on chemotherapy with per os temozolomide and has not experienced disease progression for nearly 3 years. **Conclusion.** Extraneural metastases of MPE represent an exceptionally rare and diagnostically challenging entity and should be considered in patients with a history of MPE who present with distant lesions, even years after the initial diagnosis.

Key Words: Myxopapillary Ependymoma ■ Spinal Neoplasms ■ Extraneural Metastasis ■ Central Nervous System.

Introduction

Myxopapillary ependymoma (MPE) is a distinct subtype of ependymoma that originates from ependymal cells within the central canal of the spinal cord (1). It is an exceptionally rare tumor, with an estimated incidence of 0.01 per million individuals, accounting for approximately 27% of spinal cord tumors (1, 2). MPE is predominantly located in the conus medullaris, cauda equina, or filum terminale and is typically encountered in the pediatric population and adults during the third and fourth decades of life, with a slight male predominance (1, 3).

This tumor has a high propensity for local recurrence along the central nervous system (CNS), whereas extraneural metastases are extremely rare (2). We present a case of MPE in an adult female patient who presented with secondary lung metastases 10 years after her initial diagnosis.

We aim to enhance the understanding of the diverse clinical manifestations, pathological characteristics, and treatment challenges associated with distant recurrence in MPE, which is very rare and often results from tumor dissemination during prior surgical procedures.

Case Report

A 45-year-old woman presented with lower back pain for the past month and underwent surgical excision of a sacrococcygeal lesion that was initially presumed to be a pilonidal cyst. No preoperative MRI was performed, and the surgeon proceeded directly to surgical excision without prior biopsy. Histopathological examination of the resected specimen revealed a sacrococcygeal myxopapillary ependymoma (MPE) measuring 35 mm with capsule violation. Following the diagnosis, the patient was placed on regular surveillance with serial

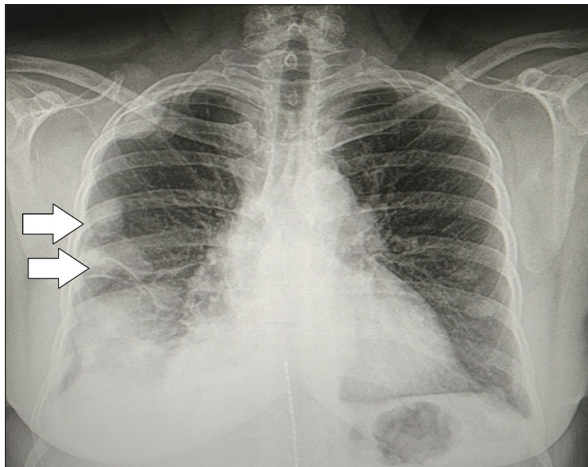


Figure 1. Chest X-ray showing multiple lung nodules in the right middle lobe.

magnetic resonance imaging (MRI) of the spine. Postoperative MRI scan of the spine demonstrated no evidence of a residual tumor.

During the following five years, she developed three local recurrences, which were managed with two lumbar spine surgeries and adjuvant radiotherapy (40 Gy delivered in 20 fractions). Post-radiotherapy, she developed chronic L5 radiculopathy associated with muscle pain and motor weakness, which required treatment with opioid analgesics and peripheral nerve stimulation. Ten years after the initial surgical resection, at the age of 55, she presented to our department with progressive dyspnea and episodes of hemoptysis for the past month. Physical examination was unremarkable, and routine laboratory investigations were within normal limits. Chest radiography demonstrated multiple peripheral lung nodules in the right middle lobe (Figure 1).

Computed tomography pulmonary angiography (CTPA) revealed multiple peripheral lung nodules in the right middle lobe, in contact with the pleura (Figure 2A).

A computed tomography (CT)-guided biopsy of a lung nodule was performed, revealing small cuboidal cells with a basophilic cytoplasm, radially arranged around the blood vessels (perivascular pseudorosettes), suggestive of a myxopapillary

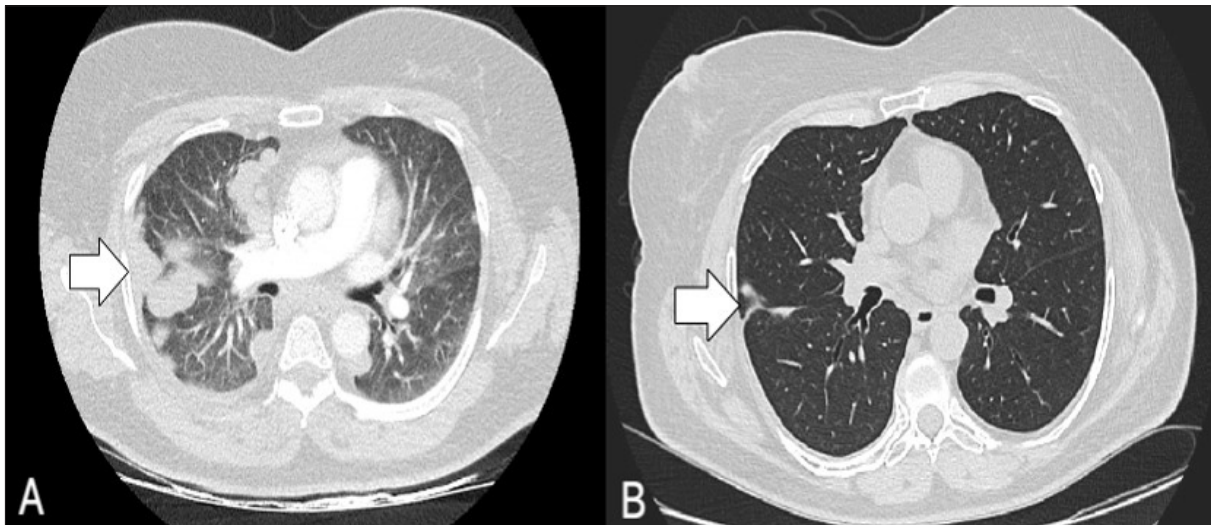


Figure 2. Axial CT scan of the chest demonstrating multiple peripheral lung nodules, as per MPE metastases (white arrow - panel A). Axial CT scan of the chest following 5 cycles of chemotherapy with temozolomide showing a significant disease response (white arrow - panel B).

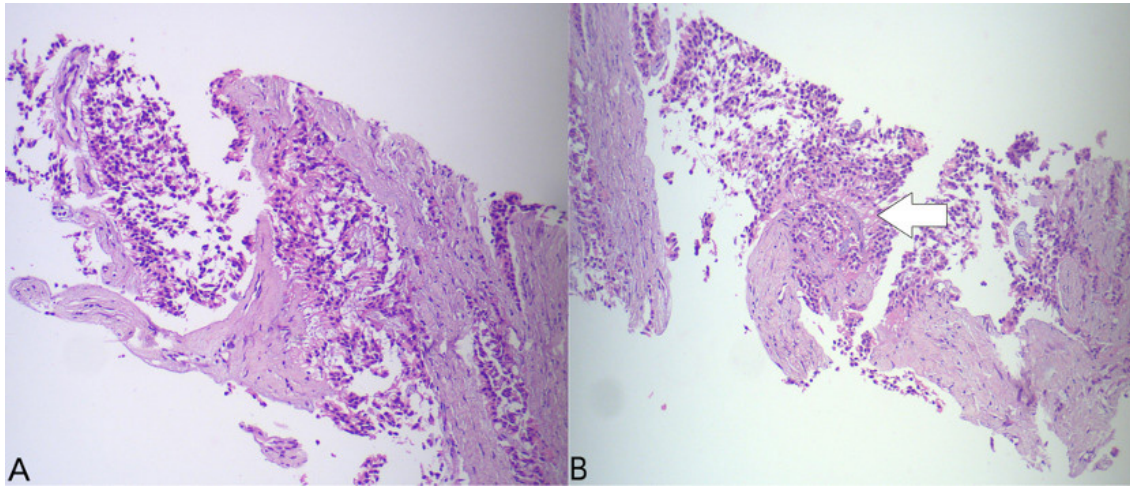


Figure 3. Hematoxylin/eosin staining, $\times 10$ magnification. Radial arrangement of cuboidal to epithelioid elongated glial tumor cells around hyalinized fibrovascular cores in a papillary configuration. Accumulation of basophilic myxoid material around blood vessels (myxoid stroma) is usually observed; however, it is not particularly evident in this case, which is characterized mostly by hyalinization of the papillary cores (panel A). Focal presence of a perivascular pseudorosette, which is the hallmark of ependymomas (white arrow - panel B).

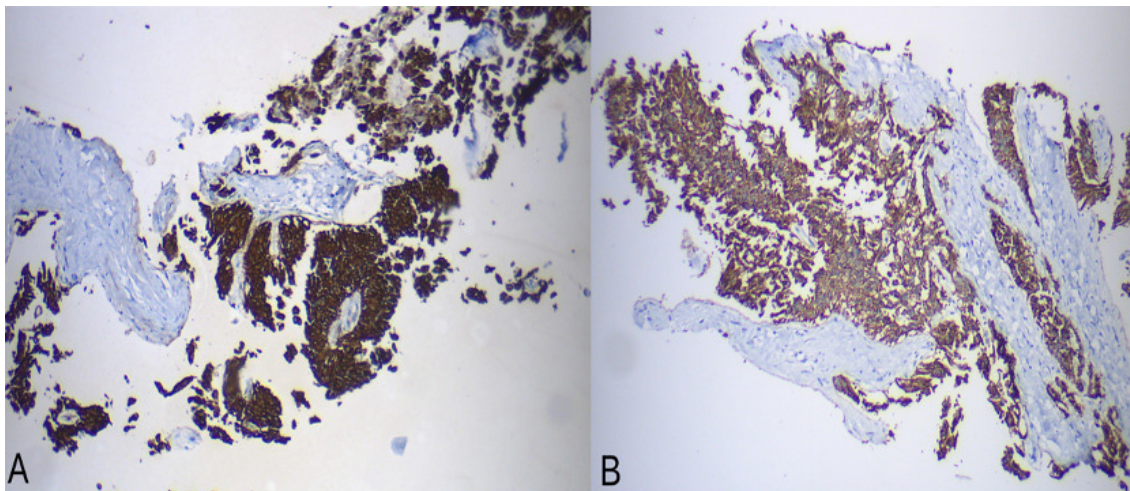


Figure 4. Immunohistochemical examination reveals diffuse positive GFAP (panel A) and CD56 (panel B) staining of the tumor cells.

ependymoma (Figure 3). Immunohistochemically, the cells stained strongly positive for G-FAP and CD56 (Figure 4), focally positive for TTF-1, and negative for chromogranin-A, synaptophysin, EMA, p40, and Napsin A. The Ki67 index was 5%, indicating a low cell proliferation rate. A review of both the initial surgical specimen biopsy and the recent lung nodule biopsy confirmed the diagnosis of metastatic MPE. No additional tissue was available for molecular profiling. Cranial and

whole-spine MRI scans were negative for signs of CNS dissemination.

The case was discussed at a multidisciplinary tumor board, and the patient was initiated on chemotherapy with temozolomide (dose: 150 mg/m² PO daily on days 1–5 of a 28-day cycle) in October 2021. During treatment, the patient reported complete resolution of dyspnea and hemoptysis. The treatment was well tolerated overall, apart from grade 2 thrombocytopenia and neutropenia

requiring granulocyte colony-stimulating factor (G-CSF) support. Restaging CT scans after 5 cycles of treatment demonstrated a significant size reduction of the lung nodules, indicating a partial response according to the RESIST 1.1 criteria (Figure 2B). The patient is still on treatment with temozolomide and remains free of disease progression for nearly three years. She is under close follow-up with serial craniospinal MRI scans, in order to mitigate the risk of CNS recurrence. Treatment will be continued until disease progression or the development of unacceptable toxicity. In the event that temozolomide must be discontinued, management would be individualized based on disease status. Options would include close surveillance, consideration of targeted therapies, or enrollment in a clinical trial.

Discussion

Myxopapillary ependymoma is a tumor that originates from the ependymal lining of the spinal canal. It is an extremely rare tumor with an annual incidence of 0.01 per million (1, 4), predominantly affecting males during the third and fourth decades of life (5, 6). The most common sites of occurrence include the conus medullaris, cauda equina, and filum terminale regions (1). No specific genetic or environmental risk factors have been identified to date (1). MPE is classified as a grade II tumor according to the recent World Health Organization (WHO) Classification of Tumors of the Central Nervous System and is considered to have low metastatic potential (3, 7).

The clinical presentation of MPE is characterized by vague, nonspecific symptoms, including low back pain radiating to the lower limbs, occasionally accompanied by motor weakness or paralysis, altered sensation, and sphincter or sexual dysfunction (3, 4, 7). The clinical presentation of metastatic MPE varies according to the metastatic site. In our case, the patient presented with hemoptysis, dyspnea, and fatigue due to pulmonary metastases ten years after resection of a sacrococcygeal MPE initially misdiagnosed as a pilonidal cyst.

MRI scans with intravenous contrast remain the gold standard imaging method for visualizing the spinal canal. On MRI, sacrococcygeal myxopapillary ependymoma (MPE) appears as a well-circumscribed lesion with variable enhancement, depending on the presence of hemorrhage or calcifications (7, 8). On CT scan, spinal and extraneural MPEs typically present as hyperdense lesions with homogeneous contrast enhancement (9). In our case, lung metastases of MPE appeared as hyperdense, well-circumscribed nodules on CT.

Due to the lack of distinctive clinical and imaging features, definitive diagnosis relies on a tissue biopsy (7). The histopathological characteristics of MPE include papillary structures composed of cuboidal or columnar cells often embedded within a myxoid stroma, resulting in a characteristic myxopapillary appearance (10). These cells are radially organized around blood vessels, forming unique rosettes or pseudorosettes (8). Immunohistochemical studies reveal consistent expression of ependymal markers, such as GFAP, vimentin, CD99, and S-100, supporting their ependymal origin (11-13). Additionally, positive CD56 staining is observed in some instances (11).

Gross total resection (GTR), while preserving the integrity of the tumor capsule, is the mainstay of treatment for localized disease (3). Adjuvant focal radiotherapy is indicated in cases of subtotal resection (STR), capsule violation, or positive post-operative cerebrospinal fluid (CSF) cytology; however, its role in spinal ependymoma management beyond these indications is not well established (3, 14). Due to the rarity of metastatic MPE, no current guidelines exist for its management; however, various methods are employed, including metastasectomy, chemotherapy, radiotherapy, targeted therapy, and immunotherapy (4, 12-16). Systemic agents used in the management of metastatic MPE with reported durable responses include temozolomide (either as monotherapy or in combination with olaparib), tyrosine kinase inhibitors (TKI) such as imatinib, sorafenib, and pazopanib, and monoclonal antibodies such as bevacizumab and tislelizumab, among others (4, 10, 15-18).

Table 1. Reported Cases of Sacrococcygeal MPE With Extraneural Metastases, Compiled, Modified, and Updated From Mastantuoni et al., 2022 (7), and Jayawardena et al., 2025 (29)

Author/Year	Age/ Sex	Initial level	Metastatic site	Duration (presentation to metastases)	Treatment modality	Outcome (total f/up)
Weiss, 1955 (22, 23)	22/M	Cauda equina	Retroperitoneum, lungs, liver, hilar and tracheobronchial lymph node, mediastinum, IVC, pleura, chest wall, diaphragm, pelvis	10 years	None	Died (10 years)
Sharma, 1956 (7)	29/M	Cauda equina	Lungs, liver, mediastinum, paraaortic lymph node, IVC, pleura	4 years	N/A	N/A
Patterson, 1961 (23, 24)	28/F	Cauda equina	Vertebrae, mediastinum, pleura, lung, hilar lymph nodes	17 years	Radiation therapy	Died (17 years)
Wight, 1973 (7, 23)	20/M	Cauda equina	Para-aortic lymph nodes, pelvis, humerus, rib, pleura	38 years	Cobalt	Died
Bardales, 1994 (12, 25)	19/M	Sacrum	Inguinal lymph nodes	16 years	Resection	N/A
Newton, 1992 (7)	37/M	Cauda equina	Lungs, pleura	<1 year	N/A	N/A
Newton, 1992 (7)	16/M	Cauda equina	Abdomen	22 years	N/A	N/A
Bardales, 1993 (25)	19/M	Sacrum	Abdomen, subcutaneous tissue, inguinal lymph nodes	16 years	N/A	N/A
Graf, 1999 (26)	15/M	Cauda equina/ conus	Lungs, liver, abdominal and mediastinal lymph node, pleura, chest wall	36 years	Cisplatin/ Ifosfamide/ Etoposide	40 years
Rickert, 1999 (7, 27)	55/F	Cauda equina	Lungs	12 years	N/A	N/A
Satti, 2005 (2)	16/F	Gluteus	Lungs	9 years	-Carmustine/ etoposide -Oral etoposide -Radiotherapy	Alive (10 years)
Vega-Orozco, 2011 (7, 28)	22/M	Cauda equina	Inguinal lymph node	18 years	N/A	N/A
Fegerl, 2012 (16, 29)	39/F	Sacrum	Pleural	20 years	-Temozolomide -Imatinib -Sorafenib	Alive
Guzin, 2016 (29, 30)	23/F	Sacrum	Cervix	9 years	Surgical resection	Alive
Ekemen, 2018 (12)	17/F	Sacrum	Inguinal lymph node	19 years	N/A	N/A
Katz, 2018 (31)	38/M	Sacrum	Gluteus	2 years	- Lapatinib/ temozolomide -Radiotherapy -cytlophosphamide -Etoposide	Alive (6 years)
Katz, 2018 (31)	76/M	Sacrum	Retroperitoneal lymph nodes	N/A	N/A	Died (4.2 years)
Deniel, 2019 (17, 29)	30/F	Filum terminale	Lung, pleura, mediastinum	13 years	Temozolomide	Died (13 years)
Tapia Rico, 2020 (4, 29)	23/F	Sacrum	Lungs	De novo	-Tislelizumab -Temozolomide -Carboplatin	Alive (4 years)
Bruno, 2020 (21)	32/F	Sacrum	Lungs, gluteus	20 years	-Temozolomide -Platinum/Iomustin	Died (23 years)
Mastantuoni, 2022 (7)	9/M	Cauda equina	Paraspinal muscles	30 years	Surgical resection	Alive
Mahalingam, 2023 (10, 29)	28/F	Pelvis	Lungs	20 years	-Carboplatin-etoposide -Temozolomide -Vismodegib -Olaparib/ ctemozolomide	Died
Fecker, 2024 (29, 32)	29/F	Sacrum	Pleura, lung, intravascular space	De novo	None	Died
Riegel, 2024 (29, 33)	24/F	Sacrum	Pleura, lungs, pelvis	11 years	Temozolomide/ lapatinib	Alive
Jayawardena, 2025 (29)	24/M	Lumbar	Lungs	37 years	None	Died (39 years)

MPE exhibits a rather indolent course and a generally favorable prognosis, with a 10-year overall survival rate of approximately 93% after GTR (1, 19). However, literature reports suggest a high rate of local recurrence within the CNS, reported up to 15.5%, particularly after incomplete resection or surgical manipulations (1, 3, 6, 7, 20). Most local recurrences occur during the first 3-6 years after the initial excision, often necessitating subsequent debilitating surgeries that affect the patient's overall health and well-being (3). In our case, the tumor was initially resected under the assumption of a pilonidal cyst, raising the possibility of unplanned capsule disruption and tumor seeding, which may have contributed to the three local recurrences observed during the first five years after diagnosis.

Although MPE is typically considered a low-grade neoplasm, distant metastases may occur despite a low Ki-67 proliferation index, suggesting that conventional histologic features do not reliably predict metastatic potential. Proposed mechanisms of dissemination include cerebrospinal fluid spread with secondary extraneural extension and hematogenous dissemination, particularly following repeated surgical interventions. The relatively early development of pulmonary metastases in our patient, occurring ten years after the initial diagnosis compared with the reported average interval of more than 20 years, may reflect the cumulative impact of repeated local recurrences and prior surgical manipulation.

To our knowledge, fewer than 30 cases of adult MPE with extraneural metastases have been reported in the literature since 1955, highlighting the exceptional nature of such occurrences (2, 7, 15, 17, 21). Published cases of myxopapillary ependymoma with extraneural metastases are summarized in Table 1.

Extraneural metastases of MPE have been documented in the lungs, pleura, liver, bones, pelvis, or lymph nodes (2, 7, 15, 17, 21). The mean time from the initial presentation of MPE to extramedullary metastases can exceed 20 years, thus necessitating lifelong follow-up with serial MRI or CT scans (2, 6). However, unlike many reported cases in which metastases developed after two decades or more, pulmonary metastases in our patient

were detected ten years after the initial diagnosis, underscoring the variability in the timing of distant recurrence.

Given the risk of both local and distant relapse, long-term surveillance is essential. We suggest annual contrast-enhanced MRI of the brain and entire spine for patients with recurrent disease or prior subtotal resection. CT scans should be considered when extraneural symptoms develop or in patients with multiple recurrences and suspected distant dissemination.

Conclusion

Extraneural metastases of myxopapillary ependymoma are extremely rare. The majority of cases occur due to incomplete surgical excision or violation of the tumor capsule, leading to the dissemination of tumor cells along the spinal canal or to distant extraneural sites. To mitigate the risk of potential tumor seeding and subsequent local or distant recurrence, it is imperative to maintain a high index of suspicion for myxopapillary ependymoma and seek expert pathology consultation in select suspicious cases prior to proceeding with surgery for a pilonidal cyst.

What Is Already Known on This Topic:

Myxopapillary ependymoma (MPE) is a rare, slow-growing spinal tumor that arises from ependymal cells of the filum terminale and cauda equina. It is generally considered a low-grade neoplasm with a favorable prognosis following gross total resection. Despite its indolent behavior, MPE has a recognized tendency for local recurrence, particularly after incomplete excision or capsule violation. Extraneural metastases are extremely uncommon, with only a limited number of cases reported worldwide. When distant spread occurs, the lungs, lymph nodes, bones, and liver are the most frequently involved sites. Due to the rarity of metastatic disease, there are no standardized systemic treatment guidelines, and management is largely based on individual case reports and small series. Therefore, long-term surveillance is recommended, as metastases may develop many years after the initial diagnosis.

What This Study Adds:

This report describes a rare case of myxopapillary ependymoma presenting with extraneural pulmonary metastases ten years after initial diagnosis and multiple local recurrences. This case highlights the potential for very late distant dissemination and underscores the importance of lifelong follow-up in patients with MPE. Additionally, it demonstrates durable disease control with temozolomide chemotherapy, supporting its potential role as a therapeutic option in metastatic MPE when standard treatment strategies are lacking.

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Patient Consent: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Ethics Statement: All procedures in this study were approved by the Institutional Review Board of the 251 Air Force General Hospital (Approval No: 2025-354).

Conflicts of Interest: The authors declare that they have no conflict of interest.

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