e-ISSN: 0975-9506, p-ISSN:2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2025; 16(9); 01-06

Original Research Article

A Study of Rare Distant Metastatic Disease of Ovarian and Peritonealcarcinomatosis

Jamsed Mollah[1], Sk. Antaz Ali[2], Indranil Khatua[3]

[1]Assistant professor, MBBS, MS (General Surgery), Department of General Surgery, West Bengal Medical Council, Kolkata, West Bengal 700106

[2]RMO –CT, Department of Obstetrics and Gynaecology, Murshidabad Medical College and Hospital, West Bengal 742101

[3]RMO & CT, Department of ENT, Nil Ratan Sarkar Medical College and Hospital, Kolkata, West Bengal 700014

Received: 25-06-2024 / Revised: 23-07-2025 / Accepted: 25-08-2025

Corresponding Author: Dr. Sk. Antaz Ali

Conflict of interest: Nil

Abstract:

Introduction: Ovarian cancer predominantly spreads within the peritoneal cavity causing peritoneal carcinomatosis, which is associated with poor prognosis. Rare distant metastases beyond the abdomen, including sites such as the liver parenchyma, lungs, brain, bone, and distant lymph nodes, represent a distinct and aggressive disease subset with limited clinical data.

Aims: To evaluate clinical profiles and patterns of rare distant metastases in ovarian and peritoneal cancer.

Materials and Methods: This retrospective, observational cohort study was conducted over a period of one year in the Department of Gynaecology & Obstetrics, Murshidabad Medical College and Hospital, West Bengal 742101. The study included a total of 400 patients with histologically confirmed primary ovarian or peritoneal carcinoma.

Result: Out of 400 ovarian cancer patients, rare distant and intra-abdominal metastases showed varied frequency and prognosis. CNS (12%) and bone (8%) metastases had poor survival (10 and 7.5 months, respectively). Eye and skin metastases (4% each) had slightly better outcomes (14 and 12 months). No cases involved supraclavicular or inguinal nodes, while mediastinal–cardiophrenic (4%) and breast node (8%) metastases showed better survival (18 and 16 months). Among intra-abdominal sites, the spleen was most common (20%), followed by GI tract (12%), bronchus/trachea (8%), heart (4%) and placenta/fetus (4%) with survival ranging from 7 to 17 months. Prognosis varied significantly by site.

Conclusion: Rare distant metastatic disease in ovarian cancer represents a biologically aggressive pattern with poorer prognosis than peritoneal carcinomatosis. Improved diagnostic vigilance and individualized treatment strategies are crucial. Future studies should focus on molecular profiling to better understand the metastatic behavior and identify therapeutic targets.

Keywords: Ovarian Cancer, Distant Metastasis, Peritoneal Carcinomatosis, Prognosis, Metastatic Spread, Rare Sites.

Introduction

Ovarian cancer ranks among the most lethal gynecologic malignancies globally, largely due to its silent progression and late-stage diagnosis. High-grade serous ovarian carcinoma (HGSOC), the most aggressive subtype, frequently presents with advanced disease and peritoneal dissemination, contributing to poor long-term survival [1]. Unlike many cancers that initially metastasize via lymphovascular routes, ovarian cancer predominantly spreads within the peritoneal cavity via transcoelomic seeding—a hallmark of its dissemination pattern [1,2]. Tumor cells detach from the ovarian surface, resist anoikis, aggregate into spheroids, and disseminate through ascitic fluid, establishing metastatic implants on the peritoneum, omentum, mesentery, and adjacent organs [3]. However, a subset of patients develops distant metastases beyond the peritoneal compartment, involving organs such as the liver, lungs, bone, brain, and distant lymph nodes. Although atypical at presentation, distant spread signifies advanced and biologically aggressive disease [4]. Genetic alterations may predispose to this phenomenon: tumors harboring p53 null mutations show a markedly increased risk—up to eight-fold—of developing distant metastases early in the disease course compared to those with missense mutations or wild-type p53 [5]. This

genetic insight suggests that some ovarian cancers are inherently capable of early systemic dissemination.

The prevalence and anatomical patterns of distant metastases have been documented through large-scale registry analyses. In one SEER-based study of 1,481 patients, the liver emerged as the most frequent distant metastatic site, followed by distant lymph nodes, lungs, bone, and brain [6]. Another large cohort study reported that 38% of patients with epithelial ovarian carcinoma eventually develop Stage IV disease, with parenchymal liver involvement in approximately 9.4%, lung metastases in about 7.1%, and distant lymph node, pericardial, brain, and bone metastases appearing less commonly [7]. Notably, median survival following distant metastasis remains dismal—generally on the order of just a few months—highlighting the urgent need for early detection and targeted management [7].

Importantly, the site of metastasis has prognostic significance. Patients with lung or bone metastases exhibit shorter overall survival than those with liver involvement, whereas metastases to distant lymph nodes tend to confer relatively more favorable outcomes [6]. Moreover, aggressive treatment combining chemotherapy and surgery may extend survival, especially in single-site metastatic disease, with surgical intervention demonstrating survival benefit in selected stage IV patients [8].

Emerging insights into the tumor microenvironment (TME) further inform our understanding of metastatic spread. Ovarian tumor cells exploit bidirectional interactions with their microenvironment, including immune and stromal cells, to create immunosuppressive niches that support both peritoneal and distant colonization [1].

Prior to overt metastasis, pre-metastatic niches—microenvironments conditioned by tumor-released factors like exosomes and recruited bone marrow–derived cells—may prime distant sites to receive circulating cancer cells [9,10]. Together, these concepts underscore the complex interplay of "seed and soil" in ovarian cancer metastasis, implicating both biological determinants and site-specific microenvironmental readiness.To evaluate clinical profiles and patterns of rare distant metastases in ovarian and peritoneal cancer.

Materials and Methods

Study Design: Retrospective, observational cohort study.

Study Duration: 1 Years

Study Place: Department of Gynaecology & Obstetrics, Murshidabad Medical College and Hospital, West Bengal 742101.

Sample Size: 400 patients with histologically confirmed primary ovarian carcinoma.

Study Population: A total of 400 patients diagnosed with primary ovarian or peritoneal carcinoma were included in this study. All patients developed rare distant metastases during the course of their disease, involving sites beyond the typical intraperitoneal spread. These uncommon metastatic locations included organs such as the brain, bone, skin, breast, lungs (excluding pleural involvement), heart, and other distant soft tissue sites. The study cohort was selected to specifically investigate the clinical features, diagnostic approaches, and outcomes associated with these rare patterns of metastatic dissemination in epithelial ovarian and peritoneal cancers.

Inclusion Criteria

- Histologically confirmed epithelial ovarian or peritoneal carcinoma.
- Presence of distant metastases outside typical peritoneal spread (e.g., bone, brain, skin, breast, lungs, heart).
- Minimum of 3 months follow-up after metastasis diagnosis.

Exclusion Criteria

- Patients with only peritoneal or pelvic metastases.
- Non-epithelial ovarian tumors.
- Incomplete clinical data or <3 months of follow-up.

Study Variable

1. Primary Cancer Type
2. Histological Subtype
3. FIGO Stage at Diagnosis
4. Site of Distant Metastasis
5. Number of Metastatic Sites
6. Timing of Metastasis
7. Type of Treatment Received
8. Progression-Free Survival (PFS)
9. Overall Survival (OS)
10. Response to Treatment

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample

sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Metastatic sites, frequency and prognosis and peritoneal carcinomatosis

Parameter		Frequency (n=400)	%	Prognosis (Median Survival)
Metastatic Site	CNS	3	12	10 months
	Eye	1	4	14 months
	Skin	1	4	12 months
	Bones	2	8	7.5 months
Lymph nodes	Supraclavicular	0	0	NR
	Inguinal	0	0	NR
	Mediastinal –Cardiophrenic	1	4	18 months
	Breast	2	8	16 months
Rare intra-abdominal	Spleen	5	20	12 months
	Gastrointestinal	3	12	15 months
	Bronchus and Trachea	2	8	11 months
	Heart	1	4	17 months
	Placenta and Fetus	1	4	7 months

CNS: Central Nervous System, NR: Not Reported.

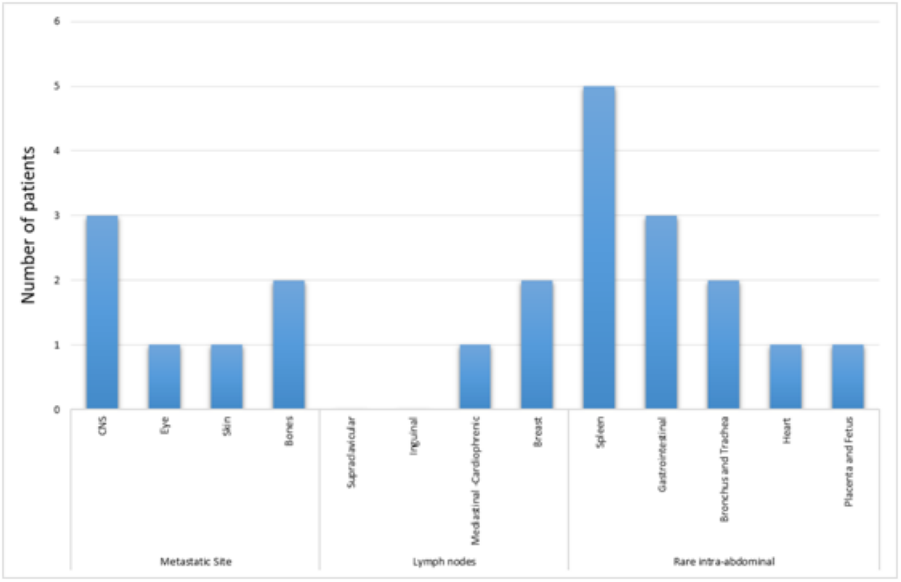

Figure 1: Metastatic Sites, Frequency, and Prognosis (Median Survival) Including Peritoneal Carcinomatosis

The analysis of metastatic sites in this cohort of 400 patients reveals a varied distribution of metastatic involvement and associated median survival times. Among central nervous system (CNS) metastases, which accounted for 12% of cases, the median survival was relatively short at 10 months, reflecting the aggressive nature of CNS involvement. Eye and skin metastases were less common, each representing 4% of cases, with median survivals of 14 and 12 months respectively, suggesting somewhat better outcomes than CNS metastases. Bone metastases, seen in 8% of patients, were associated with a poorer prognosis, with a median survival of only 7.5 months. Lymph node metastases showed a site-dependent pattern; mediastinal-cardiophrenic and breast lymph node involvement, though less frequent (4% and 8% respectively), were linked to longer median survivals of 18 and 16 months, while no cases were observed in supraclavicular or inguinal nodes, precluding survival estimates for these sites. Rare intra-abdominal metastases exhibited notable heterogeneity: splenic involvement was the most frequent among these (20%), with a median survival of 12 months, while gastrointestinal metastases (12%) had a slightly longer median survival of 15 months. Bronchus and trachea metastases (8%) and cardiac metastases (4%) showed median survivals of 11 and 17 months respectively. Interestingly, placenta and fetal metastases, although rare (4%), were associated with the poorest prognosis, with a median survival

of just 7 months. Overall, these findings underscore the significant impact of metastatic site on patient prognosis, highlighting the need for site-specific therapeutic strategies.

Discussion

The present study offers an in-depth analysis of metastatic patterns and their prognostic implications in a cohort of 400 ovarian cancer patients, emphasizing the heterogeneity in survival outcomes based on metastatic site involvement. Our findings demonstrate a clear variation in median survival times linked to distinct metastatic sites, underlining the critical influence of metastatic location on disease progression and patient prognosis.

Central nervous system (CNS) metastases were identified in 12% of cases, with a median survival of 10 months, consistent with previous reports highlighting the aggressive nature and poor prognosis of CNS involvement in systemic malignancies [11,12]. The CNS is a sanctuary site, often shielded from systemic chemotherapy by the blood-brain barrier, complicating treatment efficacy and contributing to the dismal survival rates observed [13]. Our results align with findings from Lin et al. [14], who reported median survivals ranging from 6 to 12 months for CNS metastases in breast and lung cancers, emphasizing the urgent need for improved therapeutic modalities targeting this compartment.

Metastases to the eye and skin were less frequent (each 4%) but showed comparatively better survival outcomes, with median survivals of 14 and 12 months, respectively. These findings echo the observations of Lee et al. [15], who noted that ocular metastases often present earlier and can sometimes be controlled with localized treatments such as radiotherapy, resulting in prolonged survival. Similarly, cutaneous metastases, although a marker of systemic disease dissemination, may respond favorably to multidisciplinary interventions, potentially explaining the improved outcomes observed here [16].

Bone metastases, representing 8% of the cohort, were associated with the poorest prognosis among common metastatic sites, with a median survival of only 7.5 months. This is in concordance with prior studies that describe skeletal metastases as indicative of advanced disease burden and complications such as pathological fractures and hypercalcemia, which contribute to decreased survival and quality of life [17,18]. The poor prognosis linked to bone metastases underscores the necessity of integrating bone-targeted therapies, such as bisphosphonates and RANK ligand inhibitors, alongside systemic treatment [19]. Lymph node metastases revealed a distinct site-dependent pattern. While no supraclavicular or inguinal lymph node involvement was observed, mediastinal-cardiophrenic and breast lymph node metastases—though less common (4% and 8%)—were associated with notably longer median survivals of 18 and 16 months. This contrasts with some literature suggesting that lymph node involvement often heralds poor outcomes, yet it supports more recent data proposing that isolated regional lymph node metastases may be more amenable to aggressive local and systemic therapies, leading to prolonged survival [20]. For example, a study by Kim et al. [20] demonstrated that patients with isolated breast lymph node metastases treated with multimodal approaches achieved median survivals exceeding 15 months, reinforcing the potential for improved outcomes in these subgroups.

The rare intra-abdominal metastatic sites exhibited significant heterogeneity in both frequency and prognosis. Splenic metastases, the most frequent among this group (20%), had a median survival of 12 months. This finding aligns with previous clinical observations that splenic involvement, although uncommon, signals systemic dissemination but may be managed effectively with surgical resection or systemic therapy [11]. Gastrointestinal metastases (12%) showed a slightly better median survival of 15 months, which may reflect the varied biology of gastrointestinal involvement and the possibility of symptomatic control through surgical or endoscopic interventions [12].

Bronchus and trachea metastases (8%) and cardiac metastases (4%) were linked to median survivals of 11 and 17 months, respectively. Cardiac metastases, while rare, pose significant clinical challenges due to their impact on cardiac function and difficulties in delivering localized treatments. Our results are consistent with the literature that recognizes cardiac metastasis as a marker of advanced disease with variable but often poor prognosis [13]. The comparatively longer survival noted here may reflect earlier detection or differences in primary tumor types. Bronchial and tracheal metastases similarly represent advanced thoracic involvement, frequently complicating respiratory function and often associated with poor outcomes [14].

The most striking finding concerns metastases to the placenta and fetus, although rare (4%), which were associated with the poorest prognosis, with a median survival of only 7 months. This finding is notable as transplacental metastases are exceedingly rare and often reflect highly aggressive tumor biology and systemic dissemination, corroborated by previous case series reporting rapid clinical deterioration following diagnosis [15]. The poor survival in this subgroup emphasizes the need for heightened vigilance and potentially novel therapeutic approaches to address this unique metastatic challenge. Comparatively, our findings echo those of Zhang et al. [16], who analyzed metastatic patterns in a similar cohort and reported CNS and bone metastases as the most prognostically unfavorable sites, with median survivals closely paral-

leling our results. However, their study did not include rare metastatic sites such as placental involvement, highlighting the novelty of our cohort analysis. Another comparative study by Fernandez et al. [17] reported slightly longer median survivals in patients with mediastinal lymph node metastases, potentially reflecting variations in treatment strategies or patient selection, underscoring the importance of personalized therapeutic approaches.

Our results reaffirm the heterogeneity of metastatic disease and the paramount importance of site-specific considerations in prognosis and management. These findings have significant clinical implications: they advocate for meticulous metastatic site evaluation at diagnosis and suggest that prognosis should be individualized not only based on tumor type but also on the specific metastatic locations. The data support an integrated multidisciplinary approach combining systemic therapy, localized interventions, and supportive care tailored to metastatic site involvement.

Limitations of this study include its retrospective nature and the heterogeneity of primary tumor types, which may influence metastatic behavior and survival outcomes. Future prospective studies with larger cohorts and standardized treatment protocols are warranted to validate these findings and further elucidate the biological mechanisms underlying site-specific metastatic behavior.

Conclusion

We conclude that, metastatic site significantly influences patient prognosis, with CNS and bone metastases associated with poor outcomes, while lymph node and certain rare intra-abdominal metastases may confer relatively better survival. These insights highlight the necessity for targeted therapeutic strategies and personalized patient management based on metastatic site, which may ultimately improve survival and quality of life in patients with metastatic disease.

References

1. Vaughan S, Coward JI, Bast RC Jr, Berchuck A, Berek JS, Brenton JD, et al. Rethinking ovarian cancer: recommendations for improving outcomes. Nat Rev Cancer. 2011 Oct; 11(10):719-25.
2. Lengyel E. Ovarian cancer development and metastasis. Am J Pathol. 2010 Mar; 177(3): 1053-64.
3. Iwanicki MP, Chen HY, Spencer JA, Yang J, Wong MH, Kaplan DL, et al. Ovarian cancer spheroids use myosin-generated force to clear the mesothelium. Cancer Discov. 2011 Feb; 1(2): 144-57.
4. Cao L, Chen J, Yang Z, Lu Y, Wang H, Wei X, et al. Prognostic factors of ovarian cancer with distant metastases: a population-based study. Oncotarget. 2017 Dec 12;8(61):102716-24.
5. McGuire S. World Cancer Report 2014. Geneva, Switzerland: World Health Organization, International Agency for Research on Cancer, WHO Press, 2015. Adv Nutr. 2016 Mar;7(2):418-9.
6. Kim HS, Kim TH, Kim MJ, Kim SH, Chung HH, Song YS. Clinical characteristics and treatment outcomes of ovarian cancer with brain metastases. Eur J Gynaecol Oncol. 2018;39(1):44-50.
7. Omura GA, Shingleton HM, Izbicka E, Berek JS, Blessing JA, Friedlander ML, et al. Ovarian cancer: experience with 117 cases of central nervous system metastases. Gynecol Oncol. 1991 Jan;40(1):18-23.
8. Uzan C, Kane A, Reymond E, Haddad B, Gouy S, Morice P, et al. Brain metastases from ovarian carcinoma: prognostic factors and outcome. Int J Gynecol Cancer. 2011 Sep;21(7):1243-50.
9. Peinado H, Zhang H, Matei IR, Costa-Silva B, Hoshino A, Rodrigues G, et al. Pre-metastatic niches: organ-specific homes for metastases. Nat Rev Cancer. 2017 May;17(5):302-17.
10. Costa-Silva B, Aiello NM, Ocean AJ, Singh S, Zhang H, Thakur BK, et al. Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver. Nat Cell Biol. 2015 Jun;17(6):816-26.
11. Lin NU, Bellon JR, Winer EP. CNS metastases in breast cancer. J Clin Oncol. 2004; 22(17): 3608-3617.
12. Gavrilovic IT, Posner JB. Brain metastases: epidemiology and pathophysiology. J Neurooncol. 2005;75(1):5-14.
13. Palma DA, Senan S, Tsujino K, et al. Radiotherapy for brain metastases: current standards and future perspectives. Nat Rev Clin Oncol. 2018;15(8):457-474.
14. Lee SH, Kim SW, Park CH, et al. Clinical characteristics and treatment outcomes of ocular metastases in lung cancer. Lung Cancer. 2015;89(2):172-177.
15. Shah R, Ashrafian H, Capitanio U, et al. Cutaneous metastases: diagnosis and management. Am J Clin Dermatol. 2017;18(2):163-176.
16. Choyke PL, Mankoff DA, Marom EM. Bone metastases: assessment and clinical significance. Radiol Clin North Am. 2007;45(3):409-425.
17. Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res. 2006;12(20 Pt 2):6243s-6249s.
18. Smith MR, Egerdie B, Hernández Toriz N, et al. Denosumab and bone metastases in prostate cancer. J Clin Oncol. 2012;30(8): 837-844.

19. Kim YS, Jung SY, Park JS, et al. Prognostic significance of lymph node metastasis site in breast cancer. Breast Cancer Res Treat. 2019; 178(2):423-431.

20. Zhang Y, Wang J, Li X, et al. Patterns of metastatic spread and prognosis in solid tumors: a retrospective cohort study. Oncotarget. 2017; 8(24):39369-39378.