Brain metastases from endometrial carcinoma: Tumor genetic alterations in a case series and meta-analysis

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INTRODUCTION

- Endometrial carcinoma (EC) is the most common gynecologic malignancy in the world.
- While most patients (80%) can be cured with a hysterectomy, the remaining 20% patients who are diagnosed with advanced or recurrent disease have worse survival rates and limited adjuvant treatment options.
- Discovery of novel target(s)/pathway(s) is needed for better understanding of the pathogenesis and treatment development for this disease.

OBJECTIVES

The aim of this study is to review clinical characteristics and genetic signatures of histologically proven EC brain metastasis (BM).

METHODS

For the period 2000-2019 the medical records of patients with histological diagnosis of EC BM at our institution were reviewed. Data were collected and analyzed for age, time interval between EC and EC BM diagnoses, tumor molecular and genetic signatures, and outcome. Immunohistochemistry and genomic sequencing were performed as published. A meta-analysis was also performed for the same time period. Data presented as mean±SD and analyzed by t-test and Chi square.

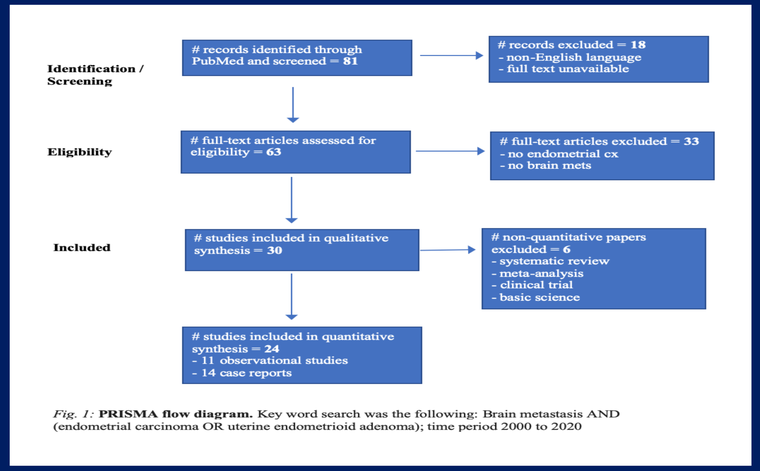

Fig. 1: **PRISMA flow diagram.** Key word search was the following: Brain metastasis AND (endometrial carcinoma OR uterine endometrioid adenoma); time period 2000 to 2020

Variable	Cohort	Literature	p
Age, years (mean ± SD)	57.6 ± 11.7	60.7 ± 10.0	0.59
Age range (years)	39-69	42-82	
Metachronous (%)	100%	67%	
Time from primary diagnosis to BM (months; mean ± SD, range)	36 ± 30 (8 - 69)	19.4 ± 27.8	<0.05
FIGO (%)	I=60% III=40%	I=20% II=6% III=42% IV=32%	
Chemotherapy at the time of BM diagnosis (%)	0%	20%	

Table 1: Demographics of patients in our cohort and those published in the literature.

Variable	Cohort	Literature	p
SRS (%)	0%	34%	
Surgery (%)	100%	19%	
SRS after surgery (%)	40%	66%	
WBXRT (%)	60%	81%	
Chemotherapy after BM diagnosis (%)	0%	20%	
Survival from BM diagnosis, months (mean ± SD)	24 ± 25	12 ± 23	0.1
Survivors (%)	40%	19%	

Table 2: Treatment(s) and outcome of patients in our cohort and those published in the literature.

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RESULTS

- **Figure 1** shows the PRISMA diagram of our literature review yielding 24 peer-reviewed papers included in the quantitative analysis
- A total of 123 EC BM cases were found in the literature. We report 6 additional EC BM in 5 patients in our cohort
- **Table 1** summarizes demographics of patients in our cohort and those reported in the literature
- **Table 2** summarizes treatment and outcome of patients in our cohort and of those reported in the literature
- In our cohort **immunohistochemistry** showed positivity for epithelial membrane antigen (EMA) and keratins AE1/AE3 consistent with reported data
- **Genomic sequencing of DNA mismatch repair (MMR)** genes showed intact MSH2 and MSH6 genes, and mutated MLH1 and PMS2 genes. The latter encode the MLH1-PMS2 heterodimeric protein complex (mutSα) which is involved in the initial identification of mismatched bases, and initiates DNA repair
- PD-L1 expression was low at <5%
- EC BM genomic reports were not found in the reviewed literature

CONCLUSIONS

- Our genetic sequencing supports previous data in EC about the prognostic value of MMR.
- Additional contributions from genomic sequencing will allow implementation of information-driven patient-centered therapeutic approaches for EC patients with BM.