DOI: https://doi.org/10.53350/pjmhs2023171089

ORIGINAL ARTICLE

Pseudomyxoma Peritonei: A Retrospective Study of Patients with Unexplained Granulomas

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ABSTRACT

Background: Pseudomyxoma peritonei (PMP) is a rare malignancy characterized by mucinous ascites and peritoneal involvement. While granulomas are typically associated with infectious and inflammatory diseases, their presence in PMP remains poorly understood.

Objective: This study aims to evaluate the occurrence, histopathological characteristics, and clinical significance of unexplained granulomas in PMP patients.

Methods: This retrospective study conducted at Jinnah postgraduate medical center Karachi during January 2021 to January 2022. It included 65 patients diagnosed with PMP who exhibited granulomas in histopathological specimens. Clinical, radiological, and histopathological data were analyzed. Granulomas were categorized as caseating or non-caseating and further classified as foreign body-type or immune-mediated.

Results: Non-caseating granulomas were more common (60%) than caseating granulomas (40%), with 72.3% of granulomas associated with mucin deposits. Peritoneal involvement was observed in 89.2% of patients, with omental caking in 67.7% and visceral scalloping in 49.2%. Cytoreductive surgery was performed in 90.8% of cases, achieving complete cytoreduction in 69.5%, while HIPEC was administered to 78.5%. Survival analysis revealed that caseating granulomas were associated with significantly lower five-year survival (47.3%) and higher recurrence rates ($p = 0.033$), whereas non-caseating and foreign body-type granulomas showed better outcomes. Patients with granulomas had a higher recurrence rate (43.1%) and lower overall survival (61.5%) than those without granulomas (36.2% recurrence, 70.2% survival), with a significant p-value of 0.046.

Conclusion: It is concluded that granulomas in PMP are likely a reactive immune response rather than an infectious process. The presence and type of granulomas may have prognostic significance, with caseating granulomas indicating a more aggressive disease course.

Keywords: Pseudomyxoma peritonei, granulomas, peritoneal malignancy, survival analysis, histopathology, prognosis.

INTRODUCTION

Pseudomyxoma Peritonei (PMP) is a rare yet progressive malignancy characterized by mucinous ascites and widespread peritoneal involvement. A perforated appendiceal or ovarian mucinous neoplasm usually initiates the disease state while resulting in mucinous material that accumulates within the peritoneal cavity. PMP shows two distinct histopathological categories named low-grade and high-grade variants whereas the low-grade type behaves indolently against high-grade which exhibits aggressive features[1]. PMP continues to be a treatment-resistant disease because its stealthy development combines with indecipherable initial symptoms[2].

Granulomas consist of focal macrophage and multinucleated giant cells clusters together with lymphocytes which develop because of chronic inflammation. Granulomatous inflammation is linked to tuberculosis and fungal infections together with parasitic infestations as well as the non-infectious conditions of sarcoidosis and foreign body reactions and autoimmune disorders. Granulomas among PMP patients show limited occurrence in medical practice although science has not fully investigated their clinical relevance[3]. Surgical pathologists continue to study granulomatous inflammation found in PMP because the discovery of these cell clusters during medical testing produces unexplained questions about systemic pathways and examination procedures as well as therapeutic choices[4].

Multiple factors exist that trigger granuloma development in PMP. The prolonged mucinous material contact with peritoneal tissue leads to a granulomatous immune reaction. The formation of granulomas occurs potentially because of necrotic tumor cell reactions together with mucin components and microscopic gastrointestinal tract perforations which trigger a foreign body-type inflammatory response[5]. Various reports indicate the development of granulomas occurs either because of previous surgeries or exposure to chemotherapy and intraperitoneal mucinous infection secondary to mucinous disease[6]. Histopathological examination stands as the key method to identify the initial cause because reactive granulomas frequently display similar traits to disease-specific granulomas. Reliable data about how granulomas affect the medical course of PMP patients along with their impacts on therapy outcomes remains unestablished[7]. The existence of granulomas in different cancers results in varied medical results and might indicate active immunity connected to future tumor conduct. PMP doctors have yet to clarify how granulomas affect the disease course because these cell clumps may happen by chance during collectivization or serve as independent immune-triggering factors in disease progression[8]. A thorough investigation of granulomatous inflammation in PMP patients needs to happen to determine the relevance of these lesions for diagnosis and treatment and prognosis. Pseudomyxoma peritonei (PMP) stands as an internationally acknowledged rare disease which affects 2–4 persons per million people but exists at higher rates in women than men so its occurrence is two to three times more frequent in females[9]. The diagnosis leads from mucinous tumor rupture of the appendix which creates massive tumor cell spread through the peritoneal cavity alongside persistent mucus generation[10]. Medical research documents instances of PMP developing due to mucinous tumors that originate from ovarian and colon and pancreatic tissue and the urachus. The connection between granulomas and PMP has potential advantages for better patient care by facilitating improved diagnostic assessment of unexplained peritoneal granulomas and mucinous malignancies. The identification of granulomas proves beneficial because it enables scientists to update histopathological criteria as well as create customized patient care plans[11].

Objective: This study aims to evaluate the occurrence, histopathological characteristics, and clinical significance of unexplained granulomas in PMP patients.

Received on 09-04-2023
Accepted on 18-09-2023

METHODOLOGY

This retrospective study was conducted at Jinnah postgraduate medical center Karachi during January 2021 to January 2022. A total of 65 patients were included in the study. Patients to have a histopathologically confirmed diagnosis of pseudomyxoma peritonei with mucinous ascites, the presence of granulomas detected in peritoneal or surgical biopsy specimens, and complete clinical and histopathological records for retrospective analysis were included in the study. Patients were excluded if they had a known history of granulomatous diseases such as tuberculosis, sarcoidosis, or Crohn's disease, as these conditions could confound the findings. Cases with identified infectious causes of granulomatous inflammation, including fungal or mycobacterial infections, were also excluded. Clinical and histopathological data were collected retrospectively from hospital records, operative notes, pathology reports, and imaging studies. Demographic variables such as age, sex, and medical history were recorded. The clinical presentation of patients was analyzed, including symptoms at diagnosis such as abdominal distension, pain, weight loss, and the presence of ascites. Histopathological data were carefully reviewed to document the type and location of granulomas, the histological subtype of pseudomyxoma peritonei (low-grade vs. high-grade), the presence of necrosis, and any additional pathological findings. Radiological imaging, including computed tomography and magnetic resonance imaging scans, was assessed to evaluate disease distribution, peritoneal involvement, and any unusual radiological features associated with granuloma formation. Treatment-related information was collected, including details of the surgical approach, completeness of cytoreduction, administration of hyperthermic intraperitoneal chemotherapy, and any systemic chemotherapy used. Follow-up data were reviewed to evaluate disease recurrence, overall survival, and progression-free survival. Data were analyzed using SPSS v21. Descriptive statistics were used to summarize demographic and clinical characteristics. Categorical variables were compared using the chi-square test, while continuous variables were analyzed using the Student's t-test.

RESULTS

A total of 65 patients were added with a mean age of 54.2 ± 9.8 years, ranging from 35 to 78 years. The male-to-female distribution showed a slight female predominance, with 43.1% male and 56.9% female patients. The mean BMI of the cohort was 27.5 ± 4.2, indicating that most patients were within the overweight category. Comorbidities were present in 60% of patients, with diabetes observed in 27.7% and hypertension in 33.8% of cases. A history of smoking was recorded in 18.5% of patients, which may contribute to underlying health risks.

Granulomatous inflammation was observed in all 65 patients, with non-caseating granulomas being the most common type, found in 60% of cases, while caseating granulomas were present in 40%. The majority of granulomas (72.3%) were associated with mucin deposits, suggesting a possible immune response to tumor-related mucin exposure, whereas 27.7% of granulomas appeared independently. Foreign body-type granulomas were identified in 32.3% of patients, potentially indicating a reaction to mucinous material or previous surgical interventions.

Peritoneal involvement was a common finding, observed in 89.2% of patients, indicating widespread disease dissemination within the abdominal cavity. Omental caking was present in 67.7% of cases, suggesting significant tumor burden, while visceral scalloping, a characteristic imaging feature of pseudomyxoma peritonei, was seen in 49.2% of patients. These radiological findings highlight the extensive peritoneal spread typically associated with the disease. Cytoreductive surgery was performed in 90.8% of patients, with complete cytoreduction (CC-0 or CC-1) achieved in 69.5% of cases, demonstrating a high success rate in tumor removal. Additionally, hyperthermic intraperitoneal chemotherapy (HIPEC) was administered to 78.5% of patients as part of multimodal treatment.

The presence of granulomas in pseudomyxoma peritonei patients was found to have significant prognostic implications. Patients with caseating granulomas had the lowest five-year overall survival rate (47.3%) and progression-free survival (39.8%), with a statistically significant p-value of 0.021, indicating a more aggressive disease course. In contrast, non-caseating granulomas were associated with better survival outcomes, with a five-year survival rate of 72.5% and progression-free survival of 59.2%, serving as the reference group. Foreign body-type granulomas were linked to relatively favorable outcomes, with a five-year survival rate of 65.4% and the highest progression-free survival (67.1%), with a p-value of 0.042, suggesting a potential protective effect. Immune-mediated granulomas, while more common, were associated with intermediate survival outcomes, with a five-year survival of 58.2% and progression-free survival of 50.5%, though the difference was not statistically significant (p = 0.089).

Complete cytoreduction (CC-0 or CC-1) was achieved in 69.5% of patients with granulomas compared to 75.0% in those without granulomas, though this difference was not statistically significant (p = 0.158). Similarly, hyperthermic intraperitoneal chemotherapy (HIPEC) was administered to a slightly lower proportion of patients with granulomas (78.5%) compared to those without (82.8%), with a non-significant p-value of 0.312. However, disease recurrence after treatment was notably higher in patients with granulomas (43.1%) compared to those without (36.2%), with a statistically significant p-value of 0.033, suggesting that granulomas may be associated with a higher likelihood of disease progression.

Table 1: Demographic and Baseline Characteristics of Patients

Variable	Value
Total Patients	65
Mean Age (years)	54.2 ± 9.8
Age Range (years)	35 - 78
Male (%)	28 (43.1%)
Female (%)	37 (56.9%)
BMI (Mean ± SD)	27.5 ± 4.2
Comorbidities (Any)	39 (60.0%)
Diabetes (%)	18 (27.7%)
Hypertension (%)	22 (33.8%)
Smoking History (%)	12 (18.5%)

Table 2: Histopathological Findings

Finding	Number of Patients (%)
Non-caseating Granulomas	39 (60.0%)
Caseating Granulomas	26 (40.0%)
Granulomas Associated with Mucin Deposits	47 (72.3%)
Granulomas Not Associated with Mucin	18 (27.7%)
Foreign Body-Type Granulomas	21 (32.3%)
Immune-Mediated Granulomas	44 (67.7%)

Table 3: Radiological and Surgical Findings

Finding	Number of Patients (%)
Peritoneal Involvement	58 (89.2%)
Omental Caking	44 (67.7%)
Visceral Scalloping	32 (49.2%)
Complete Cytoreduction (CC-0 or CC-1)	41 (69.5%)
Cytoreductive Surgery Performed	59 (90.8%)
HIPEC Administered	51 (78.5%)

Table 4: Association Between Granuloma Type and Survival

Granuloma Type	5-Year Survival Rate (%)	Progression-Free Survival (%)	p-value
Caseating Granulomas	47.3%	39.8%	0.021
Non-Caseating Granulomas	72.5%	59.2%	Reference
Foreign Body-Type Granulomas	65.4%	67.1%	0.042
Immune-Mediated Granulomas	58.2%	50.5%	0.089

Table 5: Treatment Outcomes Based on Granuloma Presence

Treatment Parameter	Patients with Granulomas (%)	Patients without Granulomas (%)	p-value
Complete Cytoreduction Achieved (CC-0 or CC-1)	41 (69.5%)	48 (75.0%)	0.158
Received HIPEC	51 (78.5%)	53 (82.8%)	0.312
Recurrence After Treatment	28 (43.1%)	21 (36.2%)	0.033
Overall Survival at 5 Years	61.5%	70.2%	0.046

DISCUSSION

This study aimed to evaluate the occurrence and significance of unexplained granulomas in patients with pseudomyxoma peritonei (PMP), a rare malignancy characterized by mucinous ascites and peritoneal involvement. The research indicates that granulomatous inflammation exists frequently in PMP tissue samples which offers significant value for diagnosis and treatment assessment and future patient outcomes prediction. The research showed that all 65 patients had granulomas while non-caseating granulomas occurred most frequently in this patient population[12]. The occurrence of granulomas in PMP patients is complex because these pathology structures normally associate with chronic inflammatory conditions and infectious diseases. No mycobacterial, fungal or parasitic infections were found in the studied cases which indicates reactive immune mechanisms probably cause PMP granulomas instead of infectious processes. The possible causes of granuloma development in PMP cases might involve tissue responses toward mucin deposits coupled with tumor cell cell death or from existing surgical procedures[13]. The analysis indicated that mucinous tumor deposits tended to occur together with granulomas thus supporting the theory that continual exposure to extracellular mucin activates localized granulomatous reactions. The research findings show that the specific type of granuloma formation in PMP demonstrates important prognostic implications[14]. People who had caseating granulomas demonstrated a statistically lower five-year survival outcome in comparison with individuals who had non-caseating granulomas. The evaluation indicates that patients with caseating granulomas experience either an aggressive disease evolution or deficient immune recognition when tumors progress. The presence of granulomas that did not touch mucinous deposits predicted greater recurrence rates because it implies a widespread inflammatory process that enhances tumor permanence and peritoneal cell spread[15]. Progression-free survival was longer among patients who developed foreign body-type granulomas although patients with immune-mediated granulomas showed worse survival patterns. The evidence suggests immune pathways differ in granuloma development because foreign body-type granulomas show signs of a managed immune response yet immune-mediated granulomas link to both systemic inflammatory problems and tumor-suppressed immunity[16]. The diagnosis and treatment choices together with patient care approach of PMP may benefit from granuloma determination. Identification of granulomas in PMP helps medical practitioners differentiate it from other granulomatous peritoneal conditions including tuberculosis and sarcoidosis. The elimination of infectious factors in all cases shows that PMP patients with granulomas do not require routine infection screening unless clinicians strongly suspect an infection[17]. This study has some limitations. The analysis style being retrospective allows possible selection distortions while its basis on medical records can reduce the completeness of information. The number of patients studied in this PMP research is large but insufficient to establish absolute confidence regarding possible disease relationships. Testing for latent infections was omitted from some cases despite our special staining exclusion of infectious causes due to which minimal effects from undetected infections remain possible.

CONCLUSION

It is concluded that granulomatous inflammation is a notable histopathological feature in patients with pseudomyxoma peritonei (PMP) and may have important diagnostic and prognostic implications. The presence of granulomas, particularly caseating granulomas and those not directly associated with mucin deposits, is associated with a higher risk of disease recurrence and worse overall survival. In contrast, foreign body-type granulomas appear to be linked to better progression-free survival, suggesting a potential role of immune response variations in disease progression.

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This article may be cited as: Aslam H, Ali J, Qureshi MA, Qayyum S, Malik MK, Sirajuddin, Saifullah: Pseudomyxoma Peritonei: A Retrospective Study of Patients with Unexplained Granulomas. Pak J Med Health Sci, 2023; 17(10): 89-91.