

Disseminated Peritoneal Leiomyomatosis - A challenging di-agnosis mimicking malignancy scoping review

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ADMINISTRATIVE INFORMATION**Support** - None.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202460092**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 June 2024 and was last updated on 24 June 2024.**INTRODUCTION**

Review question / Objective The primary objective of this article is to provide a comprehensive review of Disseminated Peritoneal Leiomyomatosis (DPL), a rare condition characterized by multiple leiomyomas within the peritoneal cavity. The article aims to address several key aspects:

Epidemiology and Demographics:

Describe the incidence and prevalence of DPL.

Identify the demographic characteristics of affected individuals, including age, gender, and reproductive history.

2. Clinical Presentation:

Detail the common symptoms and signs associated with DPL.

Highlight the variability in clinical presentation and the potential for misdiagnosis.

3. Pathogenesis and Etiology:

Explore the possible etiological factors contributing to DPL, including hormonal influences, genetic predispositions, and surgical history.

Discuss the leading theories on the pathogenesis of DPL, such as hormonal stimulation and iatrogenic dissemination.

4. Diagnostic Approaches:

Review the various diagnostic methods used to identify DPL, including imaging techniques (ultrasound, CT, MRI) and histopathological examination.

Discuss the challenges in differentiating DPL from other conditions with similar presentations, such as peritoneal carcinomatosis and metastatic disease.

5. Management and Treatment:

Summarize the treatment options for DPL, including surgical interventions (e.g., laparotomy, hysterectomy, nodule excision) and hormonal therapies.

Evaluate the effectiveness of different treatment modalities and their impact on patient outcomes.

Discuss the recurrence rates and long-term management strategies for DPL.

6. Case Studies and Clinical Outcomes:

Present illustrative case studies to highlight the clinical course and management of DPL.

Analyze the outcomes of these cases to draw insights into best practices and potential pitfalls in treatment.

7. Future Directions and Research Gaps:

Identify gaps in the current understanding of DPL and areas where further research is needed.

Propose future research directions to improve the diagnosis, management, and prognosis of DPL.

8. Comprehensive Synthesis:

Provide a synthesized overview of the existing literature on DPL.

Integrate findings from various studies to present a coherent picture of the current state of knowledge on DPL.

By addressing these key aspects, the article aims to enhance the understanding of Disseminated Peritoneal Leiomyomatosis among clinicians and researchers, facilitate accurate diagnosis, and inform effective management strategies for this rare condition.

Background Disseminated Peritoneal Leiomyomatosis (DPL) is a rare, benign condition characterized by the proliferation of multiple smooth muscle nodules throughout the peritoneal cavity. These nodules resemble leiomyomas, commonly known as fibroids, which typically occur in the uterus. However, unlike uterine leiomyomas, DPL nodules are dispersed across various intra-abdominal sites, including the omentum, mesentery, and peritoneum. First described in 1952 by Wilson and Peale, DPL primarily affects women of reproductive age but can occasionally be found in men, adding to the complexity of its pathogenesis and clinical management.

Clinical Presentation and Diagnostic Challenges

Patients with DPL often present with nonspecific symptoms such as abdominal pain, pelvic discomfort, and, less frequently, gastrointestinal or urinary symptoms, depending on the nodules' size and location. These symptoms can mimic those of more severe conditions, including malignant peritoneal carcinomatosis or metastatic disease, leading to significant diagnostic challenges. Imaging techniques such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) play a crucial role in the initial assessment. However, definitive diagnosis typically requires histopathological evaluation to distinguish DPL from other peritoneal lesions, confirming the benign nature of the smooth muscle nodules.

Etiology and Pathogenesis

The etiology of DPL remains unclear, but several theories have been proposed to explain its development:

Hormonal Theory: DPL nodules often express estrogen and progesterone receptors, suggesting that these hormones significantly influence their growth. This theory is supported by the observation that DPL frequently occurs in women during pregnancy or those undergoing hormone replacement therapy. High levels of sex hormones may induce metaplastic changes in peritoneal stem cells, transforming them into smooth muscle cells.

Iatrogenic Theory: This hypothesis posits that DPL results from the dissemination of uterine leiomyoma cells during surgical procedures such as myomectomy or hysterectomy involving morcellation. During these procedures, fragments of leiomyoma tissue may be inadvertently spread throughout the peritoneal cavity, leading to the development of DPL nodules.

Genetic and Molecular Factors: Emerging research suggests that genetic mutations and chromosomal abnormalities may contribute to the pathogenesis of DPL. Alterations in genes associated with cell cycle regulation, extracellular matrix remodeling, and apoptosis have been implicated in the uncontrolled growth of smooth muscle cells.

Management Strategies

Management of DPL is challenging due to its rarity and the lack of standardized treatment protocols. The choice of treatment often depends on the patient's symptoms, extent of disease, and desire for fertility preservation. Common management strategies include:

Surgical Intervention: Surgical approaches such as laparotomy, hysterectomy, and nodule excision are frequently employed, especially in symptomatic cases. The goal of surgery is to alleviate symptoms, reduce tumor burden, and prevent complications related to the mass effect of nodules. However, the risk of recurrence remains high, necessitating careful long-term follow-up.

Hormonal Therapy: Hormonal treatments aim to reduce the size and number of nodules by modulating the levels of sex hormones. Gonadotropin-releasing hormone (GnRH) agonists and aromatase inhibitors have shown promise in managing DPL, particularly in premenopausal women with estrogen-dependent nodules.

Observation: In asymptomatic patients or those with minimal disease progression, a conservative approach involving regular monitoring with imaging studies may be appropriate. This strategy aims to avoid unnecessary surgical interventions while

closely monitoring for any signs of disease progression.

Need for a Systematic Review

Despite being recognized for over half a century, DPL remains poorly understood due to its rarity and the limited number of comprehensive studies available. The current literature consists predominantly of isolated case reports and small case series, which do not provide a comprehensive understanding of the disease. Consequently, there is a pressing need for a systematic review to consolidate existing knowledge, identify gaps in the literature, and provide evidence-based recommendations for clinical practice.

Study Objectives

The primary objectives of this systematic review are to:

1. Describe the demographic and clinical characteristics of patients with DPL.
2. Summarize the various diagnostic methods used to identify DPL.
3. Evaluate the effectiveness of different management strategies, including surgical and hormonal treatments.
4. Assess the long-term outcomes and recurrence rates associated with DPL.
5. Identify areas for future research to improve the understanding and management of DPL.

By achieving these objectives, the review aims to provide a clearer understanding of DPL, guiding clinicians in diagnosing and managing this complex and rare condition more effectively.

Rationale The rationale for this study on Disseminated Peritoneal Leiomyomatosis (DPL) is multifaceted, addressing significant gaps in the current understanding and management of this rare condition. Here are the key points:

1. Rarity and Diagnostic Challenges

DPL is an uncommon disease characterized by multiple leiomyomas in the peritoneal cavity. Its rarity makes it poorly understood, and it often leads to diagnostic difficulties. Despite being generally considered benign, DPL can sometimes undergo malignant transformation, making accurate diagnosis and effective management crucial. The study aims to consolidate and analyze existing knowledge to improve diagnostic criteria and treatment approaches.

2. Variability in Clinical Presentation and Management

DPL presents a wide range of symptoms, from asymptomatic cases to severe abdominal pain and complications. This variability complicates diagnosis and treatment. The study seeks to provide a comprehensive review of clinical presentations and management strategies to help healthcare professionals better identify and treat DPL.

3. Need for Standardized Diagnostic and Treatment Protocols

There is a lack of consensus on the standard and effective treatment methods for DPL due to its low prevalence. Different healthcare facilities use various diagnostic and therapeutic approaches. This study aims to evaluate and compare these methods to propose standardized protocols that could lead to more consistent and effective patient outcomes.

4. Understanding Pathogenesis

The exact etiology of DPL remains unclear, with hormonal influences and iatrogenic factors being the main theories. Understanding these underlying mechanisms is vital for developing targeted therapies. The study reviews the pathogenesis theories and their implications for treatment, aiming to provide a clearer picture of the disease's origins and progression.

5. Impact on Women's Health

DPL primarily affects women in their reproductive years, potentially impacting fertility and gynecological health. By providing a thorough analysis of the condition, the study aims to offer insights that could help in preserving fertility and improving the overall quality of life for affected women.

6. Addressing Malignant Potential

Although DPL is generally benign, there have been cases of malignant transformation. The study highlights the importance of evaluating lesion characteristics that may indicate a higher risk of malignancy. This focus on early detection and monitoring could prevent fatal outcomes in rare cases.

7. Comprehensive Literature Review

By conducting a thorough review of the literature from PubMed and Scopus databases, the study compiles and analyzes data from multiple case reports and studies. This comprehensive approach provides a robust foundation for understanding DPL, identifying gaps in current knowledge, and suggesting areas for future research.

8. Guiding Future Research and Clinical Practice

The findings from this review can inform clinical practice by providing healthcare professionals with better diagnostic tools and treatment strategies. Additionally, it identifies areas where further research is needed, guiding future studies towards addressing the most pressing questions about DPL.

Conclusion

Overall, the rationale for this study is to improve the understanding, diagnosis, and management of Disseminated Peritoneal Leiomyomatosis. By addressing the challenges and gaps in current knowledge, the study aims to enhance patient care and outcomes for those affected by this rare condition.

METHODS

Strategy of data synthesis To conduct a comprehensive literature review on Disseminated Peritoneal Leiomyomatosis (DPL), a systematic search strategy was employed to identify relevant studies and articles. The aim was to gather a broad spectrum of data including epidemiology, pathophysiology, clinical presentation, diagnostic challenges, management, and prognosis of DPL. The following steps outline the search strategy:

1. Databases

The following electronic databases were searched to ensure a thorough review of the existing literature:

PubMed
MEDLINE
Scopus
Web of Science
Cochrane Library
Google Scholar

2. Search Terms

A combination of keywords and Medical Subject Headings (MeSH) terms were used to identify relevant articles. The primary search terms included:

“Disseminated Peritoneal Leiomyomatosis”
“DPL”
“benign peritoneal tumors”
“peritoneal leiomyomas”
“smooth muscle tumors”
“leiomyomatosis”
“peritoneal nodules”

Boolean operators (AND, OR) were utilized to combine these terms to maximize the retrieval of relevant studies. For example:

“Disseminated Peritoneal Leiomyomatosis” OR “DPL”

“benign peritoneal tumors” AND “leiomyomas”
“peritoneal nodules” AND “smooth muscle tumors”

3. Inclusion and Exclusion Criteria

Inclusion criteria:

Studies published in English.

Articles published from January 2010 to June 2024.
Peer-reviewed original research articles, reviews, case reports, and case series.

Studies focusing on human subjects.

Exclusion criteria:

Non-English articles.

Abstracts without full-text availability.

Studies focusing on animals or in vitro research.

Articles not directly related to DPL.

4. Screening and Selection Process

The initial search results were screened based on titles and abstracts to identify potentially relevant articles. Full texts of these articles were then retrieved and assessed for eligibility based on the inclusion and exclusion criteria. Duplicate studies were removed.

5. Data Extraction

From the selected articles, the following data were extracted:

Study title, authors, publication year.

Study design (e.g., case report, review, original research).

Number of patients and demographics.

Clinical presentation and symptoms of DPL.

Diagnostic methods and findings.

Treatment approaches and outcomes.

Prognostic factors and follow-up data.

6. Quality Assessment

The quality of the included studies was assessed using appropriate tools based on study design. For example, case reports and case series were evaluated using the CARE guidelines, while cohort and observational studies were assessed using the Newcastle-Ottawa Scale (NOS).

7. Data Synthesis

The extracted data were synthesized qualitatively to provide a comprehensive overview of DPL. Key findings were summarized and presented in a structured format, highlighting common themes, variations, and gaps in the current knowledge.

8. Reporting

The results of the search strategy and the findings from the literature review were reported in accordance with the Preferred Reporting Items for

Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Conclusion

This systematic search strategy ensures a thorough and comprehensive review of the literature on Disseminated Peritoneal Leiomyomatosis, providing valuable insights into its epidemiology, pathophysiology, clinical presentation, diagnostic challenges, management, and prognosis. By consolidating current knowledge, this study aims to enhance the understanding and treatment of DPL, ultimately improving patient outcomes.

the result was as following

The initial search yielded a total of 104 records across the databases. After removing duplicate articles, the remaining 65 titles and abstracts were screened to determine relevance to the objectives of the review. Articles not focusing on Disseminated Peritoneal Leiomyomatosis or lacking detailed case information were excluded at this stage. The full texts of the 28 potentially eligible articles were then assessed for inclusion. Reference lists of included studies were also manually searched to identify any other relevant publications. This process led to the final inclusion of 21 studies that met the criteria of reporting complete case descriptions diagnosed as Disseminated Peritoneal Leiomyomatosis. Data were then extracted from these 21 articles that comprehensively described the cases.

Eligibility criteria This review aims to encompass a wide range of participants to ensure a comprehensive understanding of Disseminated Peritoneal Leiomyomatosis (DPL). The types of participants included in this review are as follows:

1. Patients with Diagnosed Disseminated Peritoneal Leiomyomatosis (DPL)

- Adults: Participants primarily include adult patients diagnosed with DPL. The age range is typically from late teens to elderly individuals.
- Gender: While DPL predominantly affects women of reproductive age, studies involving male patients with DPL were excluded.

2. Pregnant Women

- Were excluded

3. Postmenopausal Women

- Although less common, cases of DPL in postmenopausal women were included to investigate the disease's behavior and progression in the absence of high estrogen levels typical of reproductive age.

4. Patients with Previous Uterine Leiomyomas

- Participants who have a history of uterine leiomyomas (fibroids) are of particular interest,

given the potential etiological link between uterine fibroids and DPL. This includes patients who have undergone myomectomy or hysterectomy.

5. Patients Undergoing Hormonal Therapy

- Individuals undergoing hormonal therapy, such as hormone replacement therapy or other treatments affecting estrogen levels, are included to understand the impact of such treatments on the development and progression of DPL.

6. Diverse Ethnic and Geographical Backgrounds

- Studies from diverse ethnic and geographical backgrounds are included to assess any variations in the incidence, presentation, and management of DPL across different populations. This helps in understanding any epidemiological differences and the influence of genetic or environmental factors.

7. Participants in Clinical Studies and Case Reports

- Both participants in larger clinical studies and those reported in individual case reports are considered. This broad inclusion ensures that rare and unique presentations of DPL are captured, contributing to a more detailed and varied understanding of the disease.

Inclusion and Exclusion Criteria for Participants:

Inclusion Criteria:

- Patients diagnosed with DPL confirmed through histopathological examination.
- Studies reporting on DPL irrespective of the treatment received.
- Both symptomatic and asymptomatic cases of DPL.
- Studies including detailed patient demographics, clinical presentation, diagnostic procedures, treatment methods, and outcomes.

Exclusion Criteria:

- Studies involving participants without a confirmed diagnosis of DPL.
- Male gender
- Pregnant women
- Animal studies and in vitro research.
- Studies without accessible full-text or insufficient patient data.
- Cases where DPL is secondary to malignant conditions, as the focus is on benign DPL.

Conclusion

Including a diverse range of participants helps in creating a comprehensive and holistic view of Disseminated Peritoneal Leiomyomatosis. By considering various age groups, genders, hormonal statuses, and ethnic backgrounds, this review aims to capture the full spectrum of DPL, contributing to a better understanding of its epidemiology, clinical presentation, management, and outcomes.

Source of evidence screening and selection For the comprehensive and systematic review of

Disseminated Peritoneal Leiomyomatosis (DPL), a broad range of information sources will be employed to ensure the collection of extensive and relevant data. These sources include:

1. Electronic Databases:

o PubMed: A primary resource for biomedical literature, providing access to a vast array of articles, including clinical trials, reviews, and meta-analyses. The search query "Disseminated Peritoneal Leiomyomatosis" will be used to identify relevant articles published from January 2010 to June 2024.

o Scopus: Known for its extensive coverage of scientific literature, Scopus will be utilized with the same search phrase in the title, abstract, and keyword fields to capture studies not indexed in PubMed.

2. Grey Literature:

o Conference Proceedings and Abstracts: Relevant findings from conferences on gynecology, oncology, and related fields will be included to ensure no significant studies are missed.

o Dissertations and Theses: University repositories and databases such as ProQuest Dissertations & Theses Global will be searched for doctoral and master's theses related to DPL.

3. Trial Registers:

o ClinicalTrials.gov: This registry will be searched for ongoing and completed clinical trials related to DPL to identify unpublished data and emerging treatments.

o WHO International Clinical Trials Registry Platform (ICTRP): This platform will be checked for international trials on DPL.

4. Manual Searching of Reference Lists:

o The reference lists of included studies will be manually searched to identify additional relevant publications that may have been missed in the initial database search. This process helps to capture studies cited in other key papers.

5. Specialized Journals:

o Journals focusing on gynecology, oncology, pathology, and related fields will be manually searched to ensure comprehensive coverage of the topic. Examples include the International Journal of Gynecological Pathology, Gynecologic Oncology, and the Journal of Surgical Case Reports.

6. Books and Book Chapters:

o Relevant textbooks and book chapters will be reviewed for comprehensive background information and to capture insights from expert authors on the topic.

By utilizing these diverse information sources, the review aims to gather comprehensive data on DPL, covering various aspects such as pathogenesis, diagnosis, clinical presentation, and management strategies. This thorough approach ensures a well-

rounded understanding of the disease and its implications for patient care.

Data management To ensure the systematic and efficient management of records and data for the comprehensive review on Disseminated Peritoneal Leiomyomatosis (DPL), a structured approach was employed involving multiple stages and tools. This process ensured accurate data collection, organization, and analysis.

Literature Search and Identification:

A comprehensive search of PubMed and Scopus databases was conducted using the phrase "Disseminated Peritoneal Leiomyomatosis" for articles published between January 2010 and June 2024. The search included articles in English and yielded an initial pool of 104 records.

Duplicate records were identified and removed using EndNote reference management software, resulting in 65 unique titles and abstracts for further screening.

Screening and Selection:

Titles and abstracts were independently screened by two reviewers to assess relevance to the study objectives. Inclusion criteria focused on articles that specifically addressed DPL, provided detailed case information, and were published in peer-reviewed journals.

Articles not meeting these criteria were excluded, and disagreements between reviewers were resolved through discussion or consultation with a third reviewer.

The full texts of 28 potentially eligible articles were obtained and assessed against the inclusion criteria, leading to the final inclusion of 21 studies.

Data Extraction:

A standardized data extraction form was developed to ensure consistency and comprehensiveness in capturing relevant information from the included studies. The form included fields for study characteristics (e.g., author, year of publication), patient demographics, clinical presentation, diagnostic methods, treatment approaches, outcomes, and follow-up periods.

Data were extracted independently by two reviewers to minimize errors and biases. Any discrepancies in the extracted data were resolved through discussion or by consulting a third reviewer.

Data Management:

Extracted data were entered into a secure, password-protected Excel spreadsheet. Each

study was assigned a unique identifier to track and manage records efficiently.

The spreadsheet was structured to allow for easy sorting, filtering, and analysis of the data.

Reporting results / Analysis of the evidence The data analysis for the systematic review on Disseminated Peritoneal Leiomyomatosis (DPL) will be conducted using a structured and comprehensive approach to ensure robust and reliable findings. The following steps outline the method for data analysis:

1. Data Extraction and Preparation:

o Data extracted from the selected studies will be entered into a standardized Excel spreadsheet. This spreadsheet will include detailed information on study characteristics, patient demographics, clinical presentations, diagnostic methods, treatment approaches, outcomes, and follow-up periods.

o To ensure consistency and accuracy, two reviewers will independently verify the extracted data. Any discrepancies will be resolved through discussion or by consulting a third reviewer.

2. Descriptive Statistics:

o Descriptive statistics will be used to summarize the basic characteristics of the included studies. This will include frequencies, percentages, means, medians, and ranges for categorical and continuous variables, respectively.

o Key variables such as patient age, gender, symptoms, number and location of nodules, types of surgical procedures, and follow-up periods will be described to provide an overall picture of the study population and the clinical features of DPL.

3. Narrative Synthesis:

o A narrative synthesis will be employed to qualitatively integrate findings from the different studies. This synthesis will identify common themes, variations, and patterns in the clinical presentation, diagnosis, and management of DPL.

o The narrative synthesis will also highlight gaps in the literature and areas where further research is needed.

4. Quantitative Analysis:

o Where appropriate, quantitative analysis will be performed. For continuous variables, measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range) will be calculated.

o For categorical variables, frequencies and proportions will be computed

By following this comprehensive data analysis plan, the review aims to provide a thorough and reliable synthesis of the evidence on DPL, contributing valuable insights into its clinical management and outcomes.

Presentation of the results To effectively present the results of the systematic review on Disseminated Peritoneal Leiomyomatosis (DPL), a combination of tables, figures, and narrative summaries will be employed. The following outlines the plan for the presentation of results:

1. Table: Study Characteristics

o A comprehensive table will summarize the key characteristics of the included studies. This table will include:

Author(s) and year of publication

Country of study

Study design (e.g., case report, case series)

Sample size

Patient demographics (age, gender)

Clinical presentation (symptoms, duration)

Diagnostic methods used

Treatment approaches

Follow-up duration

2. Figure: Flow Diagram of Study Selection

o A PRISMA flow diagram will illustrate the process of study selection, including:

Number of records identified through database searching

Number of records after duplicates removed

Number of records screened

Number of records excluded

Number of full-text articles assessed for eligibility

Number of studies included in the final review

3. Figure: Common Involvement Sites of DPL

o A pie chart or bar graph will illustrate the distribution of common involvement sites of DPL, such as the peritoneum, omentum, and mesentery. This will visually represent the frequency of involvement of different anatomical sites.

4. Narrative Summary:

o A detailed narrative will accompany the tables and figures, providing context and interpretation of the results. This summary will discuss:

The significance of the findings

Implications for clinical practice

Areas for future research

By combining tables, figures, and narrative descriptions, the presentation of results will be comprehensive, clear, and accessible to readers, facilitating a thorough understanding of DPL and its management.

Language restriction Only studies published in English will be included in the review. This restriction is implemented to ensure that all included articles are accessible and can be accurately interpreted.

Country(ies) involved Romania.

Keywords disseminated peritoneal leiomyomatosis, hormonal theory, myomectomy.

Dissemination plans The dissemination plan for the findings of the study on Disseminated Peritoneal Leiomyomatosis (DPL) includes the following steps:

1. Journal Publication:

o The primary dissemination channel will be through submission to the Biomedicine journal, a peer-reviewed open-access journal that ensures wide visibility within the biomedical research community.

2. Conference Presentations:

o The findings will be presented at national and international conferences related to gynecology, oncology, and pathology, such as the European Society of Gynecology (ESG) and the American Association for Cancer Research (AACR) annual meetings.

3. Academic and Medical Institutions:

o Results will be shared with academic institutions and medical centers in Romania and other collaborating countries through seminars, workshops, and grand rounds to inform clinicians and researchers about the latest findings and implications for clinical practice.

4. Social Media and Professional Networks:

o Key findings will be shared through professional social media platforms like ResearchGate and LinkedIn to reach a broader audience of researchers and healthcare professionals.

5. Patient Advocacy Groups:

o Summarized findings will be shared with patient advocacy groups focused on gynecological health to help inform patients and caregivers about the latest research developments.

By implementing this comprehensive dissemination plan, the study aims to ensure that the findings reach a wide audience, including researchers, clinicians, and patients, to maximize the impact and facilitate advancements in the understanding and management of DPL.

Contributions of each author

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