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PRACA POGLĄDOWA
REVIEW

Primary pericardial mesothelioma: A cancer without prognosis? An epidemiological and clinical challenge

Pierwotny międzybłoniak osierdzia: nowotwór bez rokowania? Wyzwanie epidemiologiczne i kliniczne

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ABSTRACT

INTRODUCTION: Primary pericardial mesothelioma (PPM) is an exceptionally rare and aggressive malignancy, identified in less than 0.0022% of all autopsy examinations. Due to its nonspecific clinical course and symptom overlap with more common cardiopulmonary conditions, diagnosis is typically delayed and made at an advanced stage, significantly worsening prognosis. The median overall survival ranges from 6 to 10 months.

MATERIAL AND METHODS: A literature review was conducted using the PubMed, Medline, and Web of Science databases, covering PPM cases published between January 2015 and March 2025. The search was performed using the keywords "primary pericardial mesothelioma," "pericardial mesothelioma," and "malignant pericardial mesothelioma." The collected data included clinical presentation, diagnostic methods, treatment approaches, and patient survival outcomes.

RESULTS: The clinical manifestations of PPM are nonspecific and commonly include pericardial effusion, chest pain, and symptoms of heart failure. Histopathological examination remains the diagnostic gold standard. Treatment strategies are primarily extrapolated from pleural mesothelioma protocols and involve chemotherapy (cisplatin + pemetrexed), surgery, and palliative care. Emerging therapies such as immunotherapy and anti-angiogenic agents (e.g., bevacizumab) have demonstrated potential efficacy.

CONCLUSIONS: PPM is characterized by diagnostic challenges, high mortality, and the absence of standardized treatment guidelines. Early diagnosis and a multimodal therapeutic approach may contribute to improved outcomes. Further prospective, multicenter studies are needed to develop effective treatment strategies for this rare malignancy.

KEYWORDS

treatment, survival, primary pericardial mesothelioma, rare heart tumor

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STRESZCZENIE

WSTĘP: Pierwotny międzybłoniak osierdzia (*primary pericardial mesothelioma* – PPM) to wyjątkowo rzadki i agresywny nowotwór, wykrywany w mniej niż 0,0022% wszystkich badań autopsyjnych. Ze względu na niespecyficzny przebieg kliniczny oraz podobieństwo objawów do częstszych schorzeń sercowo-płucnych, jego rozpoznanie następuje zwykle w zaawansowanym stadium, co istotnie pogarsza rokowanie. Mediana przeżycia wynosi od 6 do 10 miesięcy.
MATERIAŁ I METODY: Przeprowadzono przegląd literatury dostępnej w bazach PubMed, Medline i Web of Science, obejmujący przypadki PPM opublikowane od stycznia 2015 r. do marca 2025 r. Wyszukiwanie przeprowadzono z użyciem słów kluczowych „primary pericardial mesothelioma", „pericardial mesothelioma" i „malignant pericardial mesothelioma". Analizowano dane dotyczące objawów, diagnostyki, leczenia oraz czasu przeżycia pacjentów.
WYNIKI: Obraz kliniczny PPM jest niespecyficzny i obejmuje wysięk osierdziowy, ból w klatce piersiowej oraz objawy niewydolności serca. Złotym standardem diagnostycznym pozostaje badanie histopatologiczne. Leczenie opiera się na schematach stosowanych w międzybłoniaku opłucnej i obejmuje chemioterapię (cisplatyna + pemetreksed), chirurgię oraz leczenie paliatywne. Nowe metody, takie jak immunoterapia czy inhibitory angiogenezy (np. bewacyzumab), wykazują potencjalną skuteczność.
WNIOSKI: PPM charakteryzuje się trudnościami diagnostycznymi, wysoką śmiertelnością i brakiem jednoznacznych wytycznych terapeutycznych. Wczesna diagnostyka oraz podejście wielomodalne mogą wpływać na poprawę rokowania. Potrzebne są dalsze badania prospektywne i wieloośrodkowe, aby opracować skuteczne strategie leczenia tej rzadkiej jednostki chorobowej.

SŁOWA KLUCZOWE

leczenie, przeżywalność, pierwotny międzybłoniak osierdzia, rzadki nowotwór serca

INTRODUCTION

Primary pericardial mesothelioma (PPM) is an exceptionally rare and aggressive malignancy, with an incidence of less than 0.0022%, as reported in a series of nearly 500,000 autopsies. It accounts for only 2%–3% of all primary cardiac and pericardial tumors, ranking third in frequency after angiosarcoma (33%) and rhabdomyosarcoma (20%) [1]. Additionally, PPM represents an extremely uncommon subtype within the broader category of mesotheliomas, comprising approximately 0.7% of all diagnosed cases [2].
The clinical course of PPM is typically insidious, with nonspecific symptoms that contribute to delayed diagnosis, which is often established at an advanced stage or even postmortem. Common presentations include pericardial effusion, signs of constrictive pericarditis, and progressive heart failure, reflecting the tumor's local mass effect and pericardial involvement. Prognosis remains extremely poor, with a median survival ranging from 6–10 months following diagnosis [3]. Histopathological examination remains the cornerstone of diagnosis, given the lack of distinctive radiological or serological features. Despite reports suggesting associations with risk factors such as asbestos exposure, viral infections, ionizing radiation, immunodeficiency, and inherited susceptibility, the pathogenesis of PPM is still not fully understood. To date, no standardized treatment protocols have been established, and therapeutic decisions are primarily guided by evidence from individual case reports rather than prospective clinical trials.

MATERIAL AND METHODS

A literature review was conducted using PubMed, Medline, and Web of Science databases to identify published case reports and series of PPM from January 2015 to March 2025. Keywords used in the search included „primary pericardial mesothelioma," „pericardial mesothelioma," and „malignant pericardial mesothelioma." Extracted data included patient demographics, clinical presentation, diagnostic methods, therapeutic interventions, and survival outcomes. Epidemiological data on incidence, mortality, and risk factors were also assessed.

DISCUSSION

Clinical manifestations of pericardial mesothelioma

PPM is an exceptionally rare neoplasm; nevertheless, it represents the most frequent type of primary malignant tumor arising in the pericardium [4]. Autopsy studies indicate that primary tumors of the heart occur in only 0.001%–0.28% of cases. In contrast, cardiac metastases are roughly 40 times more frequent than primary cardiac tumors [5]. The PPM population likely consisted primarily of men, with a median age of 46 years [6]. The pathogenesis of PPM remains poorly understood, and although sporadic associations with asbestos exposure have been reported, evidence supporting asbestos as an etiological factor – unlike in pleural mesothelioma – remains inconclusive [6,7]. Pericardial mesothe-

lioma may present as a localized solid mass, a sheet--like thickening of the pericardium, or diffuse infiltration of the pericardium and adjacent structures [8].
PPM is characterized by an insidious onset and a non-specific clinical picture, which often translates into a delay in diagnosis. It usually manifests with pericardial effusion, cardiac tamponade, or heart failure symptoms accompanied by chest pain, shortness of breath, fatigue, loss of appetite, and weight loss. These symptoms are nonspecific and can imitate the clinical presentation of various distinct disease entities. As the disease progresses, symptoms such as coughing, shallow breathing, or paradoxical pulse may emerge, accompanied by systemic manifestations including fever, night sweats, and general weakness [1]. The aggressiveness of the tumor quickly provokes involvement not only of the pericardium itself but also of the chest wall, diaphragm, and mediastinum, which is why lesions are sometimes detected only at an advanced stage, not amenable to radical treatment [9]. The diagnostic dilemma is that non-specific symptoms are easily confused with classic cardiac entities – such as the typical picture of tuberculous pericarditis or constrictive pericarditis, ischemic heart disease, or cardiomyopathy – which pays off with a high rate of erroneous clinical conclusions. Clinicians frequently overlook PPM, often attributing the patient's symptoms to more common conditions such as pericarditis or heart failure [2,10]. Imaging studies such as echocardiography, computed tomography, and magnetic resonance imaging often visualize heterogeneous thickening of the pericardium surrounding the heart with constrictive physiology [11]. Attempts to achieve local control face limitations due to tumor invasion, so most patients are diagnosed too late for therapy to be considered radical. Nonetheless, evidence indicates that early detection can substantially prolong survival beyond 6 months, particularly in patients suitable for surgical intervention and multimodality treatment [12].

Survival rate in pericardial mesothelioma in the context of other subtypes

There is no doubt that mesothelioma has a very poor prognosis, primarily because it is usually diagnosed at an advanced stage and there is a lack of breakthrough therapies. Five-year survival is less than 10%, and median survival rarely extends beyond 12 months. The vast majority of about 60%–70% of cases are malignant pleural mesothelioma (MPM), while the peritoneal mesothelioma accounts for about 30%––35%, and the pericardial form accounts for only 1%–2% [3,13].
Median overall survival (OS) for pleural mesothelioma oscillates around 9–12 months after diagnosis, although there are a few cases of patients achieving significantly longer survival [14]. Early diagnosis, allowing the disease to be identified at an early stage, translates into better long-term outcomes. The 5-year survival rate in such cases is 7%–24%, while it is significantly lower for those diagnosed at a later stage [13]. Available trial results show that the peritoneal mesothelioma usually achieves slightly better results than the pleural form [3]. The median OS after first-line chemotherapy with platinum is about 16.6 months with a median progression-free time (PFS) of 7.3 months. Second-line treatment achieves a median OS of 16.9 months and PFS of about 3.2 months [15]. Nonetheless, the peritoneal mesothelioma remains relatively refractory to cytotoxic treatment, as median OS ranges between 6 and 12 months in the absence of intervention [16].
The median survival of PPM from symptom onset is under 6 months, reflecting a notably poor prognosis [17]. Even with therapeutic interventions (e.g., chemotherapy, radiotherapy, or surgery), the median survival time does not exceed 6–10 months, confirming the widespread belief in the eminently poor prognosis of this localization [18].

Advanced therapeutic strategies

To date, no standardized international therapeutic algorithm has been defined for the treatment of PPM, and the available clinical data are mainly based on heterogeneous single case reports. Currently, therapeutic protocols for the treatment of PPM draw patterns from the therapy used for pleural mesothelioma, and the treatment of pericardial mesothelioma includes a range of interventions, such as surgical procedures (pericardiectomy, resection), chemotherapy (pemetrexed in combination with cisplatin), radiation therapy (usually implemented as part of a trimodal strategy) and palliative care in advanced disease. Multimodal treatment – surgery, chemotherapy, and radiotherapy – is regarded as a potential standard in resectable pleural mesothelioma, but in PPM its efficacy remains uncertain due to a lack of prospective data and guidelines, and knowledge is based solely on case reports [3].
In PPM, surgical resection is a potential radical therapy provided that the disease process remains confined to the pericardium; however, invasion deep into the myocardium often pushes the possibility of surgery to the limits of effectiveness [19]. Although local surgery continues to be a mainstay of treatment, complete tumor explantation is proving difficult because the vast majority of patients are diagnosed at an already advanced stage, significantly limiting the chances of achieving an R0 resection [20].
It often proves necessary to implement a pericardial biopsy, pericardiectomy, or a massive diagnostic resection to confirm the diagnosis and assess the stage. Studies have shown no statistically significant

improvement in survival following surgical intervention, yet the procedure is still commonly performed to relieve patient symptoms by reducing discomfort caused by the tumor mass and improving hemodynamic function [21,22]. In cases of nodules of small size, without features of diffuse extension of the disease, resection procedures can serve a therapeutic function, while also contributing to the reduction of pericardial effusion and alleviation of symptoms associated with constriction of cardiac structures [10]. In the spectrum of surgical interventions, pericardiectomy stands out once pericardial fenestration, both procedures are performed to prevent recurrent fluid accumulation, which could consequently lead to cardiac tamponade [23].

A review of 103 published cases of PPM showed that only chemotherapy was associated with a statistically significant improvement in survival, while surgical treatment did not translate into a significant prognostic benefit. Special consideration should be given to the fact that, in the vast majority of chemotherapy cases, a combination of cisplatin and pemetrexed was used as the first-line treatment. These findings underscore the key role of systemic treatment in the therapeutic strategy of PPM and point to the limited efficacy of surgical approaches in monotherapy [21].

There is a lack of clear guidelines for second-line treatment of PPM after failure of first-line therapy based on platinum derivatives and pemetrexed.

However, a growing body of data points to the potential of bevacizumab, an angiogenesis inhibitor, as a valuable component of therapy. Efficacy in improving overall survival in pleural mesothelioma has recently been confirmed in clinical trials. In one case, the use of combination treatment with cisplatin, pemetrexed, and bevacizumab resulted in complete remission of clinical symptoms and satisfactory imaging results [24]. In a different case, bevacizumab was included as part of triple therapy, also alongside cisplatin and pemetrexed. Stabilization of the disease was confirmed by positron emission tomography--computed tomography (PET-CT) imaging, indicating a sustained response to the therapeutic regimen used. In light of the results obtained, bevacizumab appears to be a promising option that is also worth considering in secondary treatment strategies [25].

Recent scientific reports indicate an increasing role for immune checkpoint inhibitors (ICIs) in treating malignant mesothelioma, especially in patients with inoperable pleural forms [22]. Results from the CheckMate-743 trial showed a regimen based on nivolumab and ipilimumab to be more effective than standard chemotherapy (pemetrexed with cisplatin or carboplatin) [26]. The median survival was 18.1 months for the treatment group and 14.1 months for the control group. There was an obvious benefit for patients with the non-epithelial subtype of pleural mesothelioma [27]. However, patients with primary pericardial symptoms or those with a history of malignant neoplasm that had not been in remission for at least 3 years were not eligible for the study [28]. Although the efficacy of immunotherapy in pericardial mesothelioma remains to be seen, these findings suggest potential applications for this rare tumor localization [29]. Despite the lack of unequivocal predictive markers, such as PD-L1 status or histologic type, the case of a patient with biphasic MPM and 30% PD-L1 expression who responded to nivolumab and ipilimumab therapy suggests that ICI may be effective in selected patients [30]. However, it should be emphasized, that the lack of clear predictive biomarkers and limited data on associations with chemotherapy in first-line treatment remain significant clinical challenges.

Also noteworthy is the case of a young patient in whom the use of immunotherapy with pembrolizumab in the second-line treatment, followed by atezolizumab, resulted in long-term disease stabilization and an impressive survival time of more than 4.5 years [25]. Moreover, a promising partial response was also reported in a 62-year-old patient, in whom the combination of pembrolizumab and chemotherapy translated into effective disease control maintained for 5 months [3]. Both cases highlight the potential of immunotherapeutic strategies in the treatment of selected patients, both in monotherapy and in combination regimens [30].

Radiation therapy for the treatment of PPM plays a marginal therapeutic role, due to both the biological resistance of the tumor to radiation and the limited clinical data supporting its efficacy [28]. Due to the rarity of PPM, the available information is mainly based on descriptive reports, and the lack of prospective studies prevents a clear assessment of the benefits of this type of intervention [31]. Accordingly, radiation therapy should be considered more as an adjunctive management, aimed at alleviating symptoms, promoting physical function, and preventing and treating potential complications [2].

Trimodal therapy in the treatment of pericardial mesothelioma

Trimodal therapy is a therapeutic approach that combines three different treatment modalities: surgery, adjuvant chemotherapy (most commonly cisplatin + pemetrexed), and complementary radiotherapy. In pleural mesothelioma, trimodal therapy translates into promising survival rates with reduced toxicity [32,33]. As demonstrated by Offin et al. [12], all eligible patients had prolonged disease control, highlighting the importance of the interdisciplinary team in selecting candidates for bolder, aggressive

therapeutic strategies. In the context of pericardial mesothelioma, this therapy can be used in selected patients with good performance status and limited disease spread. Prolonging survival and improving overall patient outcomes have become a concern in clinical practice. Literature data indicate that trimodal therapy produces better survival outcomes than single--modality treatment. The average survival time for patients receiving trimodal therapy was 70.3 months, compared with only 8.2 months for those who did not receive such treatment [12,32].

Despite the promising results, the inclusion of trimodal therapy in standard therapeutic guidelines is still hampered by the scarcity of multicenter, randomized trials with adequate statistical power.

The importance of platinum- and pemetrexed--based chemotherapy

Platinum-based chemotherapy, especially in combination with pemetrexed, is a key component of trimodality therapy. Studies clearly show that the introduction of chemotherapy translates into a significant survival benefit. A study by Kim et al. [34] showed that the median survival of patients treated with chemotherapy was 27 months (where it was only 1.5 months in the no-treatment group), and another analysis observed that the median survival time of patients receiving chemotherapy was 13 months, compared to only 0.5 months in the control group. The most pronounced therapeutic effects were achieved with regimens based on a combination of platinum plus pemetrexed or platinum alone [21,34].

According to literature reports and study results, nedaplatin, which is a second-generation platinum anticancer drug, shows comparable therapeutic efficacy to cisplatin, with a more favorable safety profile. It is characterized by higher water solubility, lower gastrointestinal toxicity, and reduced nephrotoxicity. In combination with pemetrexed, there was no significant myelotoxicity or recurrence of massive effusions, and patients showed high acceptance of therapy. This makes nedaplatin a valuable alternative to cisplatin, offering equivalent efficacy with a lower risk of side effects [35].

Palliative aspects of pericardial mesothelioma treatment

In advanced pericardial mesothelioma, comprehensive supportive care serves as an indispensable pillar of treatment, integrating radiotherapy, chemotherapy, and immunotherapy with precisely targeted surgical interventions, such as drainage of abundant pericardial effusions [28,36]. Such an integrated management model not only counteracts the most intractable symptoms including pain with bone and neuropathic components, extreme cachexia, dyspnea, and psychological distress but also, through early implementation of palliative support, making it possible to prolong patients' survival while improving their quality of life [31,37,38].

Although palliative care is sometimes wrongly associated exclusively with the end stage of illness and a vision of helplessness, a legitimate shift in narrative focus exposing end-of-life care to targeting it as comprehensive therapeutic support overcoming resistance from patients and their loved ones and contributing to more comprehensive and coordinated medical care. Thus, a palliative therapeutic approach ceases to be considered an abandonment of the fight but becomes an integral part of the continuum of cancer treatment [38].

Given current recommendations, the timely integration of palliative and supportive care alongside causal therapy not only facilitates symptom control but also strengthens patients' motivation for further therapy. The holistic model of palliative care emphasizes multidimensional control of somatic suffering, psychosocial support for patients, and relief of pain and other symptoms of cachexia [38]. In the face of chronic pain of moderate severity, pharmacotherapy according to the World Health Organization analgesic ladder is recommended, using weaker opioids (e.g., codeine, tramadol), while in cases of severe pain, the implementation of stronger opioids is justified [31].

Future research, driven by the dynamic progress of oncologic medicine, will surely bring even more effective therapeutic options. Nonetheless, even today, multifaceted supportive care is an essential component of pericardial mesothelioma treatment.

CONCLUSIONS

PPM is extremely rare, presents with non-specific cardiopulmonary symptoms, and is usually diagnosed late, median survival is only 6–10 months. No standardized guidelines exist, so therapy is extrapolated from pleural mesothelioma: platinum plus pemetrexed remains first-line, with bevacizumab or ICIs showing promise in small series. Disease rarity, lack of biomarkers, and absence of prospective trials hinder evidence-based, individualized care, making early detection crucial for any curative multimodal strategy. Future priorities include better imaging, molecular profiling, immunotherapy integration, and routine early palliative care, all supported by multicenter collaboration to refine diagnosis and treatment and improve outcomes.

Authors' contribution

Study design – E. Pazek
Data collection – M. Sikorski, M. Kapałka, M. Krawiec, T. Hrapkowicz, G. Hirnle
Manuscript preparation – E. Pazek, M. Sikorski
Literature research – E. Pazek, M. Sikorski, M. Kapałka, M. Krawiec
Final approval of the version to be published – T. Hrapkowicz, G. Hirnle

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