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Clinical and therapeutic aspects of Pancoast Tumor: A bibliographic review

Aspectos clínicos y terapéuticos del tumor de Pancoast: una revisión bibliográfica

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ABSTRACT
Introduction: Pancoast tumor (PT) is a rare and challenging form of lung cancer located at the pulmonary apex. Although it represents only 3 to 5% of all lung cancers, it poses significant diagnostic and therapeutic challenges. **Objective:** To identify and analyze the most recent clinical and therapeutic aspects of PT. **Materials and Methods:** We conducted a descriptive bibliographic review using databases such as PubMed and Google Scholar. We examined thirty-nine articles published between 2014 and 2024. **Results:** PT accounts for 3% to 5% of lung cancers, predominantly in male smokers. Clinically, it is associated with distinctive symptoms such as shoulder pain, Horner's syndrome, and muscle atrophy of the hand. Radiographic presentation and symptom similarity with other diseases complicate diagnosis. **Discussion:** Patients often confuse the clinical manifestation of pain from PT with other pathologies, underscoring the importance of a thorough differential diagnosis. The trimodal treatment combining surgery, chemotherapy, and radiotherapy remains the standard, although the development of less invasive techniques improves outcomes. The use of proton therapy and 3D-CRT optimizes the resectability of the tumor and enhances the postoperative quality of life. **Conclusion:** Despite advancements, early diagnosis of PT remains challenging due to its deceptive symptoms. The trimodal approach has significantly improved survival expectations, although the side effects of chemotherapy and radiotherapy persist. Future research could focus on biological agents and immunotherapy to offer more effective personalized treatments.

Keywords: Pancoast syndrome, lung cancer, combined modality therapy, chemoradiotherapy.

RESUMEN
Introducción: El tumor de Pancoast es una forma rara y desafiante de cáncer de pulmón ubicada en el ápice pulmonar. Aunque su porcentaje respecto a todos los cánceres de pulmón es bajo, conlleva importantes dificultades diagnósticas y terapéuticas. **Propósito:** Identificar y analizar los aspectos clínicos y terapéuticos más recientes de este tipo de tumor. **Materiales y métodos:** Se realizó una revisión bibliográfica descriptiva mediante bases de datos como PubMed y Google Scholar. Se examinaron 39 artículos publicados entre 2014 y 2024. **Resultados:** El tumor de Pancoast representa entre un 3 y un 5 % de los cánceres de pulmón, con predominio en varones fumadores. Clínicamente, se asocia con síntomas distintivos como dolor en el hombro, el síndrome de Horner y atrofia muscular de la mano. El diagnóstico se complica debido a su presentación radiográfica y a la similitud con síntomas de otras enfermedades. **Discusión:** La manifestación clínica del dolor en este tumor se confunde a menudo con otras patologías, lo que destaca la necesidad de un diagnóstico diferencial exhaustivo. El tratamiento trimodal que combina cirugía, quimioterapia y radioterapia se mantiene como el

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estándar, aunque el desarrollo de técnicas menos invasivas mejora los resultados. El uso de la terapia de protones y 3D-CRT está optimiza la resecabilidad del tumor y mejora la calidad de vida posoperatoria. **Conclusión:** A pesar de los avances, el diagnóstico temprano del tumor de Pancoast sigue siendo difícil debido a sus síntomas engañosos. El enfoque trimodal ha mejorado significativamente las expectativas de supervivencia, aunque los efectos secundarios de la quimioterapia y la radioterapia persisten. Futuras investigaciones podrían centrarse en agentes biológicos e inmunoterapia para ofrecer tratamientos personalizados más efectivos.

Palabras clave: tumor de Pancoast, cáncer de pulmón, terapia combinada, quimioradioterapia.

1 Introduction

Lung cancer (LC) ranks among the leading causes of cancer-related mortality worldwide, accounting for 12.8% of all oncological diagnoses [1]. Pancoast tumor (PT), which is also known as superior sulcus tumor, is a rare and difficult type of LC [2, 3]. It only makes up 3% to 5% of all lung carcinomas [4]. This kind of tumor is usually a subtype of non-small cell lung cancers (NSCLC), which make up more than 95% of cases [5–8]. Small cell lung carcinomas (SCLC) are not common in this area. The most common histological types are adenocarcinoma, which is currently predominant, and squamous cell carcinoma, which was historically the most frequent [7, 8].

The peculiarities of PT reside in its location at the pulmonary apex and its ability to invade adjacent structures of the thoracic inlet, such as the brachial plexus, ribs, and pleura [9]. These characteristics can lead to a clinical presentation known as Pancoast-Tobias Syndrome (PTS), characterized by shoulder and arm pain, Horner's syndrome (HS), and muscle atrophy of the hand [10].

Identifying relevant clinical and therapeutic factors is crucial for the development of effective treatment strategies; our review focuses on this aspect [11, 12]. In this analysis, we will explore recent advancements related to PT, focusing on diagnostic and therapeutic modalities such as trimodal treatment that integrates chemoradiotherapy with surgical intervention.

This study aims to address the research question: What are the most recently described clinical and therapeutic aspects of the Pancoast tumor?. We narrowed the focus to characteristic clinical signs, updated diagnostic modalities and innovative therapeutic strategies with the intention of enriching the shared body of knowledge and optimizing the clinical approach to this peculiar type of pulmonary neoplasm.

2. Materials and Methods

2.1 Study Design

A descriptive bibliographic review study was conducted, focusing on the identification, collection, and analysis of existing literature on the clinical and therapeutic aspects of PT.

2.2 Analyzed Databases

The electronic databases PubMed, Google Scholar, and SciELO were selected to carry out the search for scientific literature related to the topic. These databases were chosen due to their comprehensiveness and ease of access to various studies, including original investigations, systematic reviews, case reports, and clinical trials.

2.3 Search Terminology

To conduct the search of medical terms in both Spanish and English, Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) vocabulary was used. The searched terms were "*Síndrome de Pancoast*", "*Tumor de Pancoast-Tobias*", "*Cáncer de pulmón*", "*Terapia combinada*", along with their equivalents in English. Boolean operators such as AND ("Pancoast syndrome AND Lung cancer") and OR NOT were entered to optimize the results and to exclude non-pertinent terms.

2.4 Inclusion Criteria

Studies published between 2014 and 2024 in both English and Spanish were included, encompassing qualitative and quantitative ones, systematic reviews, and case studies that provide updated information on PT.

2.5 Exclusion Criteria

Duplicate articles, non-peer-reviewed works, and those not specifically addressing PT were excluded.

3. Results

Out of all the studies found, 39 articles were selected and examined to conduct this research.

3.1 Clinical Manifestations

PT, also known as a superior sulcus tumor, is a particularly complex type of LC, presenting various symptoms that often mimic other pathologies, thus complicating the diagnosis. One of the most predominant symptoms in its clinical presentation is severe shoulder pain, attributed to the invasion of the brachial plexus [2, 9]. This pain is present in up to 96% of patients and is generally described as burning or electric, which can lead to confusion with orthopedic ailments [2, 8, 9, 12, 13]. These findings support the observations by authors such as Al Shammari et al. (2020) and Calabek et al. (2015), who note that this pain can radiate to the arm and hand, thus confusing this condition with musculoskeletal diseases [6, 14].

HS is among the most characteristic manifestations of PT. This is a triad of symptoms consisting of ptosis, miosis, and anhidrosis, resulting from the involvement of the stellate sympathetic ganglion [1]. This syndrome reflects the more extensive compromise of adjacent structures and is also referred to by Sobash et al. (2021) and Calabek et al. (2015) as a classic manifestation in advanced stages, which, in conjunction with shoulder pain, arm pain, and hand muscle atrophy, corresponds to PTS [6, 15]. However, although HS is common, Rao et al. (2023) and Mohamud et al. (2022) report that its presence, along with symptoms such as dyspnea and muscle atrophy, increases the complexity of the clinical picture [1, 9].

The diagnostic challenge is compounded by the similarity of PT symptoms to other conditions, such as thoracic outlet syndrome and cervical radiculopathy [5, 16]. Studies by Berntheizel et al. (2023) and Bishnoi et al. (2023) highlight that this similarity underscores the need for high clinical suspicion, especially in patients with a smoking history [5, 16]. This is because, at times, the differential diagnosis is complicated due to endemic areas presenting other diseases like tuberculosis, as Nugroho et al. (2023) found frequently [11].

In more advanced stages, clinical manifestations can include respiratory difficulty and even metastasis to distant organs [1, 7, 9]. Mohamud et al. (2022) document cases where these atypical symptoms have challenged physicians to diagnose accurately [9]. Marulli et al. (2016) and Rao et al. (2023) point out that, although rare, metastasis to distant sites such as the heart adds up to clinical complexity [1, 7]. Additionally, authors like Forooghi et al. (2019) describe rare cases of atypical manifestations, including jaw and dental pain, which can mimic oral diseases and delay proper diagnosis [17].

Early and accurate diagnosis is essential to optimize treatment outcomes, although it is complicated due to the misleading clinical presentation of PT [5, 12, 16]. As studies by Bishnoi et al. (2023) and Berntheizel et al. (2023) indicate, the initial presentation of these tumors often lacks typical pulmonary symptoms and lead to misdiagnoses [5, 16]. Therefore, the use of advanced imaging techniques, as mentioned by Chu et al. (2022) and Mohamud et al. (2022), is crucial for clarifying the diagnosis and correctly differentiating between these conditions [9, 12].

Lastly, tobacco use has been observed to strongly correlate with the occurrence of these tumors, being a common etiological factor in the personal history of many patients [9, 17]. This etiological aspect, coupled with the clinically challenging presentation of this tumor, underscores the need for a thorough reevaluation when persistent shoulder pain is found in individuals with a history of smoking.

3.2 Diagnostic Evaluation

The diagnosis of PT can be complicated due to its misleading clinical presentation, frequently confused with other musculoskeletal or neurological conditions, which can delay the definitive diagnosis [8, 12, 17–19]. Suspicion of a PT typically arises in patients with shoulder pain and neurological symptoms in the distribution of C8, T1, and T2, or HS, combined with a mass in the pulmonary apex identified in imaging studies [11, 20, 21].

In the presence of persistent shoulder pain, advanced imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are essential, as simple radiography often fails to identify masses in the apex. CT stands out as a useful tool for evaluating the tumor's invasion into bone and soft tissue structures, while MRI provides a more precise analysis of the involvement of the brachial plexus and spinal cord, necessary for surgical treatment planning [1, 11, 12, 21].

Histological confirmation of PT by CT-guided biopsy is standard practice, although case reports have demonstrated that in situations where percutaneous biopsy is not conclusive, alternative methods such as endobronchial ultrasound (EBUS) with a transesophageal approach or mediastinoscopy are effective for obtaining diagnostic samples [4, 10]. Foroughi et al. (2019) and Mohamud et al. (2022) describe these techniques as having become essential to ensure accurate identification and avoid inappropriate treatments that may result from a misdiagnosis [9, 17].

The differential diagnosis is complex due to symptomatic overlapping with various pathologies [2, 9, 22]. One of the main differential diagnoses is NSCLC, which represents most of PT cases TP [9]. Within this group, adenocarcinoma is currently the most common histological subtype, followed by squamous cell carcinoma. Although less frequent, large cell carcinoma may also be present. These subtypes should be considered when evaluating any mass at the pulmonary apex [7, 8].

SCLC constitutes another relevant differential diagnosis, though it is uncommon in this location. Its rapid progression and specific response to chemoradiotherapy make it a significant diagnostic challenge requiring histological confirmation [2, 8].

Pulmonary tuberculosis, particularly in endemic regions, can manifest as apical masses mimicking PT [11]. This differential diagnosis is crucial in patients with compatible epidemiological backgrounds and should be ruled out through specific microbiological and imaging studies [17].

Thoracic outlet syndrome is another condition that frequently shares symptoms with PT, such as shoulder pain and neurological disturbances. Precise differentiation requires a comprehensive clinical and radiological approach to avoid diagnostic errors. Pulmonary metastases originating from extrapulmonary tumors, such as those of the breast, colon, or kidney, should also be considered [1, 7, 10, 12]. These lesions can be located at the pulmonary apex and present clinical and radiological characteristics like PT, emphasizing the importance of thorough evaluation [11].

Other less frequent pathologies include pleural mesothelioma, which can involve the apical region of the lung in advanced cases, and musculoskeletal diseases like cervical spondylosis and disc hernias, which are often initially misdiagnosed due to overlapping symptoms [6, 21].

Finally, Jevremovic et al. (2017) highlight that rare diagnoses such as myxoid sarcoma and other neurogenic tumors like schwannomas or neurofibromas may be found in atypical presentations of PT. These conditions underscore the importance of maintaining a broazd and multidisciplinary diagnostic approach to ensure appropriate clinical management [23].

This highlights the significance of a multidisciplinary approach where imaging, histopathology, and clinical evaluation converge to ensure an accurate diagnosis. Collaboration among oncologists, radiologists, pathologists, and neurologists is essential to prevent treatment delays resulting from misdiagnoses [4, 7, 22]. Advanced imaging modalities, e.g., positron emission tomography (PET) with 18F-FDG, are increasingly used to identify occult metastases, complementing traditional diagnostic strategies [10].

3.3 Treatments

3.3.1 Surgery

Historically, the surgical treatment of PT was considered challenging due to the critical anatomical location at the lung apex, often involving complex thoracic structures such as brachial plexus nerves,

subclavian vessels, and spine. The surgical approach to this tumor must be multidisciplinary, combining the skills of thoracic surgery, oncology, and radiotherapy to improve patient outcomes [20].

Modern surgical techniques have evolved significantly from the anterior transcervical approach described in the 1980s, which provided innovative access to the thoracic inlet and subclavian vessels. Newer surgical techniques, such as Video-Assisted Thoracic Surgery (VATS) and the use of proton beam radiotherapy, have allowed for more precise and less invasive management of PTs, thereby reducing postoperative complications such as chylothorax and ulnar nerve paralysis [15, 23–26].

The trimodal approach, which combines neoadjuvant chemoradiotherapy and surgical resection, has become the standard in PT treatment due to improvements in survival rates, which can reach up to 55% if complete resection is achieved [1]. However, as noted by Gundepalli & Tadi (2024), there are clear contraindications for surgery in cases of extensive invasion of the brachial plexus or significant involvement of the soft tissues of the neck [2].

Various studies have shown that VATS techniques, when combined with advanced diagnostic methods like PET and MRI, are effective in assessing tumor extent and optimally planning surgery [12, 26]. The cases reported by Rosso et al. (2016) emphasize that VATS avoids muscle damage and facilitates a minimally invasive approach, promoting shorter recovery times without compromising oncological outcomes [26].

A multidisciplinary medical-surgical approach integrating proton beam radiation therapy with robotic surgery for complex cases is crucial. It allows patients with significant respiratory impairment to benefit from a quicker functional recovery [26, 27]. For example, the experiences of Kawai et al. (2017) demonstrate that the use of LigaSure in thoracic surgery can significantly reduce tissue damage and facilitate less invasive procedures [27].

The advancement of robotic surgery has provided a viable option to improve precision and control in difficult surgeries, also allowing for better visualization and maneuverability without the need for extensive thoracic incisions [28, 29]treated by induction concurrent chemoradiotherapy (CRT. This results in surgical management is not only more effective but also minimizes postoperative complication rates and enhances patient recovery.

3.3.2 Chemotherapy

Chemotherapy emerges as an essential component within a multimodal approach, frequently combined with radiotherapy to maximize the effectiveness of neoadjuvant treatment in patients with PT [1, 11, 30]. This type of treatment has been shown to improve tumor respectability and increase survival, although high recurrence rates still pose challenges [12, 17, 31]. Induction chemotherapy, often in combination with radiotherapy, is recommended for patients with locally advanced tumors, assisting them toward potential surgical resection with regimens of cisplatin combined with other agents like gemcitabine [10, 26, 27, 32].

Recent studies, such as that by Bansal et al. (2022), explore the addition of biological and immunotherapeutic agents as part of the therapeutic arsenal, although these practices are predominantly investigational at present [33]. The synergy between cisplatin and gemcitabine aims to optimize the elimination of tumor cells while preserving functional lung tissue, standing out for its effectiveness in reducing tumor volume before surgery [27, 32].

A clear limitation of using chemotherapy in PT is the severe side effects, including hematological toxicity and neurotoxicity [16, 28]. Authors such as Jeannin et al. (2015) and Bishnoi et al. (2023) assert that these factors not only affect patient quality of life but can also limit the administration of doses necessary for a complete therapeutic effect [16, 28]. However, Jevremovic et al. (2017) noted that by adjusting dosages and applying sequential regimens along with supportive treatments, more patients can tolerate the regimen to achieve maximum therapeutic benefits [23].

The prognosis for patients with PT undergoing trimodal treatment varies. Factors such as local tumor invasion and the presence of metastases require continuous adaptation to new therapeutic strategies based on emerging data from clinical trials [19, 24, 31].

Chemotherapy, as part of a multimodal treatment, continues to evolve. The inclusion of more modern approaches, which integrate molecular biology and potential personalized therapies could offer more adaptive and effective alternatives for managing PT in the future [17, 26, 29, 34, 35].

3.3.3 Radiation Therapy

Over time, radiation therapy has transitioned from its application as a primary treatment to being part of a multimodal therapeutic regimen, including chemotherapy and surgery, particularly for stage III non-small cell LC tumors [19, 30, 31].

Several studies have demonstrated that trimodal therapy, which incorporates neoadjuvant radiation therapy, significantly improves survival rates and locoregional control of the disease [2, 11].

The objective is to reduce the tumor size and minimize the impact on vital structures, allowing for a more effective and safer resection [4]. Beyond its neoadjuvant applications, radiotherapy has also been established in the palliative domain. In the context of advanced metastatic disease, its role focuses on alleviating pain and improving the quality of life for patients [1]. However, its effectiveness in palliative scenarios is limited due to disease progression; therefore, its value would lie in managing acute complications arising from metastases or nerve compression.

Advancements in radiation techniques such as three-dimensional conformal radiotherapy (3D-CRT) and proton therapy have allowed more precise dose delivery, minimizing damage to surrounding tissues [7, 23].

Reviews and case studies have also examined the impact of radiotherapy on resectability and surgical recovery. Different studies, like those by Kalagara et al. (2019) and Mariolo et al. (2018), have found that chemoradiotherapy regimen before surgery not only make the resection safer but also seem to lower the number of complications after surgery related to these aggressive procedures [32, 34]. This approach has proven effective for tumors traditionally considered inoperable or whose resection could be extraordinarily challenging.

3.3.4 Immunotherapy

Therapies based on immune checkpoint inhibitors, such as PD-1 (programmed death-1) and PD-L1 (programmed death-ligand 1) inhibitors, have shown promising results in patients with advanced NSCLC, extending overall survival and improving the quality of life [36–38].

Although specific experience with immunotherapy in PT is limited due to its low incidence, preliminary studies suggest that patients with high PD-L1 expression might benefit from these treatments, especially as a neoadjuvant in combination with chemoradiotherapy [30].

Tang et al. (2021) described the case of a patient with a Pancoast tumor treated with tislelizumab in combination with chemotherapy in a neoadjuvant approach, achieving a tumor reduction of 71%. Post-surgical intervention, pathological analyses confirmed a complete pathological response. Furthermore, circulating tumor cell tests were negative after the first adjuvant treatment [30].

Additionally, ongoing research is evaluating its role in the neoadjuvant setting and as part of trimodal approaches, aiming to optimize therapeutic outcomes in this complex tumor type [30, 36, 37].

4. Discussion

The in-depth analysis of the selected literature highlights the diagnostic and therapeutic complexity represented by PT; emphasizing both the persistence of classic challenges and the evolution toward more comprehensive and effective approaches. Therefore, what are the most recently described clinical and therapeutic aspects of Pancoast tumor?

Regarding the clinical manifestations of PT, most studies agree that shoulder pain, primarily derived from brachial plexus invasion, remains the most prevalent symptom [2, 9]. However, Al Shammari et al. (2020) and Calabek et al. (2015) emphasize the potential for this pain to be mistaken for orthopedic conditions, which poses a challenge in differential diagnosis [6, 14]. These difficulties underscore the importance of a thorough clinical evaluation to differentiate the cause of the pain, as other pathologies affecting the same area may present with similar symptoms, as indicated in the studies by Berntheizel et al. (2023) and Bishnoi et al. (2023) [5, 16].

HS, also common in this context, is a significant sign of the involvement of adjacent structures. Still, its presence does not always indicate a definitive diagnosis of PT due to clinical similarities with other diseases [1, 9]. The need for innovations in diagnosis is evident, as studies such as Nugroho et al.

(2023) highlight the possibility of endemic diseases, such as tuberculosis, complicating the differential diagnosis [11].

In the diagnostic field, the combination of CT and MRI remains the standard for detecting the extent of PT, especially in evaluating brachial plexus and bony structures invasion. However, Forooghi et al. (2019) and Mohamud et al. (2022) point out the growing importance of technologies such as EBUS and PET, which can provide additional details in cases where there are diagnostic uncertainties [17, 39]. The issue of differentiating between PT and similar conditions, such as sarcomas or other neoplasms, underscores the complexity of a correct diagnostic assessment, as discussed by Jevremovic et al. (2017) and Kazimirko et al. (2016) [22, 23].

From a therapeutic perspective, the trimodal treatment combining surgery, chemotherapy, and radiotherapy has significantly transformed survival expectations for patients with Pancoast tumor (PT). Although surgery remains a key component, the approach has evolved towards less invasive techniques, such as VATS, which offers better functional outcomes without sacrificing oncological effectiveness [26, 27]. However, as Gundepalli & Tadi (2024) indicate, the invasion of the brachial plexus continues to be a hurdle for surgery, requiring careful clinical consideration [2].

Chemotherapy and radiotherapy, as part of the trimodal approach, have been refined with the inclusion of techniques such as proton therapy and 3D-Conformal Radiation Therapy (3D-CRT), enhancing both tumor resectability and postoperative quality of life [23, 32]. Nevertheless, side effects remain a significant challenge, and as suggested by Jeannin et al. (2015) and Bishnoi et al. (2023), optimizing dosages and therapeutic regimens is crucial for improving outcomes without compromising patient tolerability [16, 28].

The use of biological agents and immunotherapy in PT management is promising, although it is currently more experimental. Bansal et al. (2022) indicate that these strategies may become more prevalent in the future, suggesting a move towards personalized treatments [33], while Cheng et al. (2024) and Huang et al. (2024) state that their use offers new hope in the fight against this complex type of cancer [36, 37].

5. Conclusion

PT represents a unique clinical entity within the context of LC, characterized by its specific anatomical location and distinctive symptoms that complicate both its diagnosis and clinical management. Our findings reinforce the need for a multimodal treatment approach that incorporates innovative surgical, chemotherapeutic, and radiotherapeutic strategies to significantly improve patient outcomes. Future research must continue to explore ways to reduce the adverse effects associated with current treatments and develop more personalized therapies. Existing literature highlights the importance of collaborative and multidisciplinary approaches to optimize clinical outcomes. Finally, additional studies that include novel agents and improved diagnostic techniques are needed to evolve and refine the treatment of this challenging type of cancer.

6. Abbreviations

LC: Lung Cancer

PT: Pancoast Tumor

NSCLC: Non-Small Cell Lung Cancer

SCLC: Small Cell Lung Carcinoma

PTS: Pancoast-Tobias Syndrome

HS: Horner's Syndrome

CT: Computed Tomography

MRI: Magnetic Resonance Imaging

EBUS: Endobronchial Ultrasound

PET: Positron Emission Tomography

VATS: Video-Assisted Thoracic Surgery

7. Administrative Information

7.1. Additional Files

None declared by the author.

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7.3. Author Contributions

Marlon Moreira Morán: Conceptualization, methodology, investigation, project administration, writing - draft/original, writing - review and editing.

Fiorella Castillo Cruz: Conceptualization, methodology, writing - draft/original, writing - review and editing.

Ana Noriega Cabrita: Conceptualization, project administration, supervision, writing - draft/original, writing - review and editing.

All authors read and approved the final version of the manuscript.

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7.5. Declarations

7.5.1. Ethics Approval

Not applicable.

7.5.2. Conflicts of Interest

The author declares no conflicts of interest.

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