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Early Diagnosis and Current Status of Immunotherapy for Thymic Carcinoma

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Abstract. Thymic carcinoma (TC) is a rare and aggressive malignancy of the anterior mediastinum, with most patients diagnosed at advanced stages due to the absence of characteristic paraneoplastic syndromes. This review systematically synthesizes current evidence on early diagnostic modalities and immunotherapeutic strategies for TC. In diagnosis, imaging (CT, MRI), immunohistochemical markers (CD5/CD117), serum CYFRA 21-1 and circulating tumor DNA each offer distinct advantages, yet all are constrained by suboptimal sensitivity or specificity, and no single method currently enables reliable early detection. Therapeutically, immune checkpoint inhibitors (ICIs) as monotherapy yield a limited objective response rate (ORR) of approximately 18.4%, whereas ICI combined with chemotherapy, exemplified by the atezolizumab-carboplatin-paclitaxel regimen, could achieve an ORR of 56.2%, marking a substantial improvement. Notably, the incidence of grade 3-5 immune-related adverse events in TC patients (17.1%) is markedly lower than that in thymoma patients (58.3%), suggesting a more favorable safety profile for immunotherapy in TC. These findings underscore the transformative potential of chemo-immunotherapy as a first-line option for advanced TC, while also highlighting persistent challenges: the absence of validated predictive biomarkers, the limited efficacy of ICI monotherapy, and the lack of large-scale randomized controlled evidence. Future investigations should prioritize biomarker discovery, mechanistic exploration of the TC immune microenvironment, and long-term survival validation of combination regimens.

Keywords: Thymic carcinoma, Early diagnosis, Immune checkpoint inhibitor, Immunotherapy, Thymic epithelial tumor

1. Introduction

Thymic epithelial tumors (TETs), a rare group of thoracic cancers including thymomas, thymic carcinoma (TC) and thymic neuroendocrine cancers, having an incidence of merely around 1.5 cases per million [1]. Specifically, TCs are even rare malignant tumors situated in anterior mediastinum [2]. Compared with thymoma, TC displays rare representative histopathological features and paraneoplastic syndromes, giving rise to a high proportion of cases with diagnoses at advanced stage and unfavorable long-term prognoses [2-4]. The five-year total survival rates are commonly poor in

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patients with TC, spanning from 30% to 50% [2]. Furthermore, TC tends to present cytological atypia as well as aggressive behavior, resulting in the even worse long-term survival rates [3].

Currently, the diagnosis modalities of TCs mostly rely on imaging (CT, MRI), immunohistochemical diagnosis, serum biomarkers (CYFRA 21-1) and liquid biopsy (ctDNA). Contrast-enhanced chest enhanced CT is the golden standard for the diagnosis of thymic-related disease, while its accuracy in recognize a prevascular mediastinal mass is only 78% [5]. Immunohistochemically, the biomarkers CD5 and CD117 are confirmed to have 100% specificity for TC, with a combined specificity of 0.81 [1]. However, around 19% of TCs lack of the expression of these two biomarkers [1]. Regarding to serum biomarkers, the CYFRA 21-1 level in TC is significant higher than in thymoma [6]. However, the sensitivity for diagnosis of TC using CYFRA is only 68.8% [6]. In terms of liquid biopsy, it shows great limitations. Only 20% of patients who show radiographic recurrence have an elevation in ctDNA [7].

The standard second-line therapy for patients with advanced TET after platinum-based chemotherapy is not existed. TETs have been reported to have a high level of PD-L1 expression, making immunotherapy to be highly possible . A meta-analysis showed that the overall response to immune checkpoint blockers (ICB) was 18.4%, with one-year progression-free survival rate of 26.0% and one-year overall survival rate of 66.9% [8]. There is an increasing safety concern caused by the unique immunologic environment of thymus, at which T-cells experience maturation. However, the risk of TC patients develop immune-related adverse events (ir-AE) is much lower than thymoma patients, because thymomas include a larger number of immature double positive T cells (CD4+ and CD8+), while TCs possess high portion of differentiated single positive T cells and regulatory T cells [9]. The incidence of grade 3-5 ir-AEs in TC was only 17.1%, significantly lesser than that in thymoma (58.3%) [8].

Although several reviews have addressed TETs, most have focused either on diagnosis or on treatment in isolation, without bridging the two domains. Moreover, the recent approval of chemo-immunotherapy in Japan and emerging data from biomarker studies necessitate an updated, integrated appraisal. Given the scattered nature of existing evidence across small-sample studies and the lack of systematic integration of diagnostic and therapeutic advances, this review provides a comprehensive synthesis of early diagnosis and immunotherapy in TC. Specifically, the objective of this review include: (1) critically evaluate the strengths and limitations of current diagnostic modalities—including imaging, immunohistochemistry, serum biomarkers and liquid biopsy—to identify practical strategies for improving early detection; (2) assess the efficacy and safety profile of ICIs in TC with particular emphasis on histology-based differences in irAE risk; and (3) propose future directions for combination strategies and biomarker discovery based on the unique immunological landscape of TC.

2. Pathogenesis and key molecules

2.1. Risk factors

At present, the exact cause of thymic carcinoma and thymoma is not clear, and existing studies have failed to confirm that specific environmental and lifestyle factors are related to their onset. There is also no published data showing that smoking, alcohol intake, diet or ionizing radiation is associated with the occurrence of thymoma or thymus carcinoma [10]. For factors of virus infection, regarding the potential role of viral infection in the onset of the disease, the existing evidence is insufficient and contradictory. Case reports and studies have found that the DNA of EPstein-Barr Virus (EBV) has been detected in some thymus cancers (especially lymph epithelioma subtypes) and thymus

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lymphatic tissue proliferation, suggesting that there may be a relationship [10]. However, there are also studies that have found defective EBV in thymoma tissue [10]. A population-based cohort study of Acquired Immunodeficiency Syndrome (AIDS) patients showed that in a 32-year follow-up, due to the very small number of cases of thymus carcinoma, it could not even be listed separately in non-AIDS-defined cancers and was classified into the category of "other/unknown" cancers [10]. This suggests that severe immunosuppression may not significantly increase the risk of TC [10].

At present, there are almost no reports on the familial clusters of thymus tumors, indicating that specific genetic mutations are less likely to directly drive the disease [10]. Differences in the incidence between different races suggest the potential influence of racial background. According to the Surveillance, Epidemiology, and End Results Program (SEER) project, the incidence of black Americans and Asian/Pacific Islanders is higher than that of white people [11].

Gender does not significant impact on the onset of the disease according to a lot of study [10]. The age of onset is usually middle-aged and elderly, with a peak age of about 65-69 years old and the median age about 56-60 years old [10, 11]. It is worth noting that the thymus has had obvious physiological degeneration in old age, but the incidence of tumors has increased. This contradictory phenomenon has not yet been reasonably explained [10].

2.2. Programmed death-1/Programmed death-ligand 1 (PD-1/PD-L1) signaling pathway

PD-1/ PD-L1 are widely expressed in TETs. The immunohistochemical test showed that the positive rate of PD-L1 was 83%, with 81% in thymoma and 100% in TC. The positive rate of PD-1 was 77%, with thymoma accounting for 81% and TC taking up 33% [12]. Variability showed in TETs, and given that the physiological expression exists in normal thymus tissue (particularly in the medullary epithelial cells around the Hassel corpusicle), its clinical value as a predictive biomarker is questioned [9].

As for the relationship between PD-1 and PD-L1 expression and clinical pathological characteristics and prognosis, the expression of PD-L1 does not have a significant correlation with either WHO organizational classification or Masaoka staged [12]. In survival analysis, there was no significant difference between the PD-L1 positive expression and total survival [12]. Besides, PD-L1 expression did not show significant prognostic value [12]. The existing evidence in this field suggested that there are contradictions in the results of different research reports associated with prognostic value of PD-L1 expression. On the one hand, some investigations have found that high PD-L1 expression is related to higher WHO histology grade and poorer overall survival [9]. On the other hand, other studies pointed out that high PD-L1 expression is associated with better prognosis [9]. Furthermore, there are also some researches showed no significant correlation between PD-L1 expression and total survival [9].

2.3. Key molecules in TC

TC has a notable difference in molecular features compared with thymoma. According to the analysis of Next-Generation Sequencing (NGS), although the tumor mutational Burden (TMB) of TC is at a relatively low level, it is still higher than that of thymoma [13]. TP53 is the gene in TC that tends to mutate the most frequently, especially in aggressive subtypes, and is accompanied by recurrent deletion or mutation of CDKN2A [13]. In addition, TC is likely to have mutations of epigenetic regulatory genes, including BAP1, SETD2 and TET2. In comparison, the characteristic mutations of thymoma are GTF2I and HRAS instead of above genes [13].

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Regarding the receptor tyrosine kinase,KIT proto-oncogene receptor tyrosine kinase protein (KIT) protein overexpression in TC is more common (46-79%), but the mutation frequency of KIT gene is less than 10% [13]. Unlike KIT, the state of Epidermal Growth Factor Receptor (EGFR) in TC has the characteristics that many NGS studies did not detect the activation mutation of the EGFR kinase domain in TC. for example, in the analysis of 45 cases of thymus tumors (including 7 cases of TC), no EGFR kinase domain or EGFR through The mutation of road-related genes [13]. Therefore, the mutation of EGFR is extremely rare in TC and does not belong to the driving gene. However, the overall abnormality of the EGFR signaling pathway is associated with the shortening of the total survival of TC patients, which is an independent adverse prognostic factor [13]. Based on the above mutation characteristics, the therapeutic effect of EGFR inhibitors (such as gefitinib) in TC is very limited, which is completely different from the case in lung cancer.

3. Early diagnosis

3.1. Imaging diagnosis

In contemporary, contrast-enhanced chest CT is method most commonly used for evaluating thymus-related diseases. However, this measure has a limited accuracy at approximately 78% if radiologists only rely on CT images and clinical characteristics to distinguish the nature of anterior mediastinal mass [5]. The main limitation of CT lies in its poor contrast resolution, giving rise to difficulties in differentiating among thymus hyperplasia, thymus cyst and cymoma [5].

In order to overcome these limitations, MRI plays an important supplementary role, especially for anterior mediastinal lesions that are unclear in CT performance. Chemical shift MRI is a key technology for differential diagnosis. By calculating the signal intensity index (SII), if the signal drops by more than 9%, it can be diagnosed as thymus hyperplasia or normal thymus tissue, so as to avoid unnecessary surgery [5]. For cystic lesions, postcontrast subtraction T1WI is very important [5]. If there is enhancing solid component, thickened capsule or thick septa, malignant tumors such as cystic thymoma should be highly suspected; if no reinforcement appear, it tends to be benign cysts [5].

However, Fluorodeoxyglucose (FDG) PET/CT is not recommended for routine diagnosis of benign and malignant lesions of the thymus. Research shows that the maximum standardized uptake value (SUVmax) of benign lesions such as thymus hyperplasia can be as high as 7.3, which has a significant overlap with malignant tumors, so its diagnostic value is limited [5]. It is mainly used to evaluate the distant transfer in subtype of thymus cancer with strong aggression [5].

In summary, although CT remains the first-line imaging modality, its limited soft-tissue resolution and the overlapping SUVmax values on PET/CT highlight the need for a stepwise imaging algorithm that incorporates MRI as a problem-solving tool when CT findings are indeterminate.

3.2. Immunohistochemical diagnosis

In the immunohistochemical diagnosis of thymic carcinoma, CD5 and CD117 are markers with high specificity [1]. When the two are applied together, the diagnostic specificity can reach 0.81 [1]. However, about 19% of thymus cancer cases do not express the above two markers, and there is a risk of missed diagnosis [1].

As the corresponding antigen of CYFRA 21-1, tissue expression pattern of CK19 also has identification value. A study involving 32 cases of thymic carcinoma and 62 cases of thymoma

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showed that although both tumors showed strong expression of CK19, CK19-immunoreactive coagulation necrosis is only seen in thymus cancer, and this phenomenon is not seen in thymoma [6]. This finding provides immunohistochemical clues for elevated serum CYFRA 21-1 levels in thymus cancer [6].

3.3. Serum molecular biomarkers

Among the diagnosis of TETs, CYFRA 21-1 is the most promising serum molecular biomarkers. A study including 94 TETs patients showed that the median level of serum CYFRA 21-1 in TC group is significantly higher than that in thymoma group [6].

Through receiver operating characteristic (ROC) curve analysis, CYFRA 21-1 distinguishes the area under the curve (AUC) of the two tumors is 0.86 [6]. When the cutoff value is set to 2.7 ng/mL, its diagnostic sensitivity is 68.8%, the specificity is as high as 95.2% [6]. Multivariable logistic regression analysis further confirms that CYFRA 21-1 $\geq$ 2.7 ng/mL is an independent predictor of thymus carcinoma, with odds ratio (OR) of 25.6 [6].

Moreover, among 7 patients with TC who underwent curative surgery, the level of CYFRA 21-1 all decreased after surgery, suggesting that this indicator may be related to tumor load and disease status [6].

3.4. Liquid biopsy

In the field of liquid biopsy of thymus tumors, the clinical value of circulating tumor DNA (ctDNA) is still in the exploration stage. A retrospective study of 36 patients with TETs evaluated the clinical application potential of the Signatera mPCR-NGS platform for detecting ctDNA [7]. Of the 22 patients who received curative-intent resection, 20% of patients with radiographic recurrence tested positive for postoperative ctDNA [7]. However, there is a potential false positive rate of 11.8% in the positive test of ctDNA [7].

Among 14 patients with advanced disease, the average ctDNA level of the radiographic progression group and the stable disease group was 10.73 mm/mL, respectively. And 10.70 mm/mL, both of which are significantly higher than the 0.20 mm/mL of the partial/complete response group [7]. However, the correlation between ctDNA levels and disease progression is weak ($r = 0.11$), and the consistency between the two is only 55% [7].

The conclusion of the study points out that ctDNA is not suitable as a standalone surveillance tool or progression marker for patients with thymus tumors, but in treatment response monitoring It may have certain reference value in the test.

4. Immunotherapy

4.1. Clinical trials and efficacy of immune checkpoint

ICIs have shown a certain therapeutic effect in TC. A Meta-analysis included patients with non-resectable or metastatic thymus epithelial tumors. The results showed that the objective response rate (ORR) of immune checkpoint blockers was 18.4%, and the 1-year progression-free survival rate was 26.0%. In addition, the total survival rate in one-year period is 66.9% [8]. Furthermore, there are differences in the immune microenvironment between TC and thymoma. The former is dominated by differentiated single-positive T cells and regulatory T cells, while the latter is rich in immature double-positive T cells [9].

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4.2. Immune-related adverse events and safety analysis

The safety of ICBs in TETs varies depending on the type of histology. Meta-analysis shows that the total incidence of level 3-5 irAEs is 26.4%, of which the incidence of TC patients (17.1%) is significantly lower than that of thymoma patients (58.3%) [8]. This difference is closely associated with the composition of the immune microenvironment of the two. Parmar and Rajan pointed out that thymoma contains a large number of immature double-positive T cells (CD4+CD8+), which are a potential source of high risk of irAEs, while thymoma is mainly composed of differentiated single-positive T cells and regulatory T cells (Tregs), in which the risk of immunotoxicity is relatively low [9]. Therefore, although the safety of ICBs treatment in patients with thymic carcinoma is better than that of patients with thymoma, it is still necessary to be alert to the occurrence of severe irAEs in clinical practice.

4.3. Predictive biomarkers of response

At present, reliable predictive biomarkers for immunotherapy for TC have not been established [9]. The expression rate of PD-L1 in thymus cancer can reach 100% [9], but its value as a predictive marker is controversial [9]. There is also a physiological expression of PD-L1 in normal thymus medullary epithelial cells (especially around the Hassall corpus), which confuses its interpretation in thymus tumors [9]. In addition, the correlation between PD-L1 expression and total survival has been contradictory in different studies. Some studies show that high expression is associated with poor prognosis, while other surveys suggest that it is related to better prognosis [9]. In addition, The TMB is at a low level in thymus cancer, and the clinical guidance value is limited [8, 9]. Hence, more reliable biomarkers still need to be explored in the future [9].

4.4. Combination therapy strategies

In terms of the limited efficacy of ICIs monotherapy in TC (ORR about 19-23%) [9], the combined treatment strategy has become the focus of research. At present, the combined directions explored mainly include ICI combined chemotherapy, dual immune checkpoint blocking and ICI combined anti-angiogenic treatment.

As for ICI combined chemotherapy, the Multicentre, single-arm, phase 2 trial of atezolizumab plus carboplatin and paclitaxel in patients with advanced or recurrent TC (MARBLE trial) evaluated the efficacy of atezolizumab combined with carboplatin and paclitaxel in the initial treatment of advanced TC, with ORR reached 56.2% (95% CI 41.1-70.5), median Progression-Free Survival (PFS) of 9.6 months, and controllable safety [14]. This is the first clinical study to confirm the effectiveness of ICI combined chemotherapy in TC, which has been approved by Japan for front-line treatment [10].

When it comes to double immune checkpoint blocking, the Nivolumab in Patients with Type B3 Thymoma and TC (NIVOTHYM trial) evaluated the therapeutic effect of nivolumab combined with ipilimumab in the treatment of TC. The results showed that the 6-month PFS rate was only 21.6%, and the ORR was 17.7%, which did not reach the preset endpoint [8, 9]. For the treatment above level 3, the incidence of related adverse events is as high as 29% [8, 9]. This suggests that the dual immune combined strategy has limited value in thymus cancer, and it is necessary to choose the combined scheme cautiously [9].

The contrasting results between MARBLE and NIVOTHYM trials underscore an important principle: in thymic carcinoma, not all combination strategies are equally effective. The success of

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chemo-immunotherapy and the failure of dual ICI blockade suggest that the unique immunological milieu of TC—characterized by differentiated single-positive T cells and Tregs—may favor combinations that enhance antigen release and T-cell priming (e.g., chemotherapy) over those that merely relieve existing T-cell inhibition. This observation has important implications for future trial design.

5. Discussion

This article systematically reviews the research progress of early diagnosis and immunotherapy of thymus carcinoma, and summarizes several key problems in this field on this basis.

In terms of diagnosis, although the existing methods have their own value, there is no single method to meet the needs of clinical accurate diagnosis. As a first-line imaging tool, the accuracy of CT is only about 78%, and it is difficult to effectively distinguish between thymus hyperplasia, cysts and tumors [5]. Although MRI can make up for the shortcomings of CT in soft tissue resolution, it is complicated to operate and expensive, and it is difficult to widely implement in routine screening [5]. The combined specificity of immunohistochemical markers CD5 and CD117 can reach 0.81, but about 19% of cases do not express the above markers, and there is a possibility of missed diagnosis [1]. The specificity of serum CYFRA 21-1 reaches 95.2%, but the sensitivity is only 68.8%, and it is difficult to confirm the diagnosis independently with this indicator alone [6]. The clinical application of ctDNA is still in the early exploration stage, and its consistency with the progression of the disease is only about 55% [7]. It can be seen that there is an urgent need to establish a set of sequential joint diagnosis processes with multimodal means to meet the actual needs of different clinical scenarios. However, there is still a lack of systematic research on such integrated strategies.

In terms of treatment, thymus cancer shows a special pattern of "high PD-L1 expression and low immune response". The positive rate of PD-L1 in thymic carcinoma can reach 100%, but the ORR of ICIs single-drug treatment is only about 18.4% [8, 9]. This huge difference between high expression and low response is rare in other solid tumors, which is rooted in the special immunophysiological function of the thymus itself. The physiological expression of PD-L1 in normal thymal medullary epithelial cells (especially around the Hasssall corpus) is difficult to distinguish from the pathological expression of tumor cells in detection, thus seriously weakening the clinical value of PD-L1 as a marker of efficacy prediction. In addition, the low level of TMB of thymic carcinoma also limits the therapeutic effect of ICIs. It is worth noting that the ORR obtained by the combined chemotherapy regimen in the MARBLE trial reached 56.2%, while the ORR obtained by the combined double immunity in the NIVOTHYM trial was only 17.7% [9, 14]. The results of the two are completely different. This difference suggests that chemotherapy may form an effective synergistic effect with ICIs by promoting tumor antigen release and T cell activation; while simply blocking the two immune checkpoints of PD-1 and CTLA-4 may not be enough to reverse the immune tolerance inherent in thymacinoma.

As for safety, the risk of irAE in patients with thymic carcinoma treated with ICIs is significantly lower than that of patients with thymoma (17.1% vs. 58.3%) [8]. The immunological basis of this difference is relatively clear: the tissue of thymoma is rich in immature double-positive T cells, which are easily activated abnormally and attack their own tissues under the action of ICIs, leading to serious immunotoxicity; while thymoma is mainly differentiated single-positive T cells and Tregs, and the immune tolerance is relatively Strong, so the incidence of severe irAE is low. This feature provides a relatively favorable safety window for thymic cancer patients to receive ICIs treatment, but it also suggests that their tumor microenvironment may be in a state of immunosuppression or immunity, which may be one of the important reasons for the limited therapeutic effect. Therefore,

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how to effectively break immune tolerance and enhance anti-tumor immune response under the premise of maintaining a low incidence of irAE is the core proposition of future research.

Looking forward to the future, three aspects of work are worth paying attention to. At the diagnostic level, we should focus on building a standardized sequential diagnostic process of multimodal means, and verify its feasibility and effectiveness in real clinical scenarios through forward-looking research. At the treatment level, it is urgent to carry out multi-center randomized controlled trials to confirm the long-term survival benefits of combined chemotherapy regimens and explore individualized treatment strategies based on immune microenvironmental typing. In terms of biomarkers, in view of the limitations of PD-L1 and TMB, combined with liquid biopsy (such as ctDNA dynamic monitoring) and multi-omics technology (single-cell sequencing, spatial transcriptomics), the in-depth analysis of the heterogeneity of the immune microenvironment of thymic cancer is expected to find more reliable efficacy prediction indicators.

In summary, immunotherapy for thymus cancer is at a critical stage in the transition from single drug exploration to combined optimization. Chemotherapy combined immunotherapy has shown encouraging prospects, while the failure of the dual immune combined strategy suggests that treatment decision-making in this field must be based on an in-depth understanding of the unique immune biology of thymic carcinoma, rather than the successful experience of mechanical transplantation of other solid tumors. The core task in the future is to gradually realize the individualization and optimization of thymic carcinoma immunotherapy with the help of reasonable joint schemes and accurate biomarker screening under the premise of ensuring safety.

6. Conclusion

This article systematically concludes the early diagnosis and current status of immunotherapy for TC. In terms of diagnosis modalities, imaging (CT, MRI), Immunohistochemical markers (CD5, CD117), serum molecular biomarkers (CYFRA 21-1) and liquid biopsy (ctDNA) have their own advantages and disadvantages respectively, but currently there is no single method that can reach precise early diagnosis. In immunotherapy, the objective response rate (ORR) of ICIs is about 18.4%, with limited therapeutic effect. In comparison, the ORR of combined chemotherapy regimens (such as atezolizumab combined with carboplatin and paclitaxel) can reach 56.2%, showing a significant therapeutic potential. This paper found that despite the limited efficacy of ICIs alone, the combined chemotherapy strategy has made breakthroughs, which provide new treatment options for patients with advanced TC. In addition, the incidence of immune-related adverse events (17.1%) of thymus cancer is significantly lower than that of thymoma (58.3%), suggesting that immunotherapy has higher safety in thymus cancer, which can offer a basis for clinical decision-making.

There are still certain limitations in this field. At present, most studies are small samples, single-arm designs, and lack large-scale randomized controlled trials. In addition, reliable therapeutic biomarkers (such as PD-L1, TMB) have not been established. Future research should focus on the following directions. First, carry out multi-center randomized controlled trials to verify the long-term efficacy and safety of combined treatment plans. Second, explore more accurate biomarkers to screen the people who benefit from immunotherapy. Third, deeply study the unique immune microenvironment of thymus cancer, aiming to provide a theoretical basis for developing new combination treatment strategies.

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References

[1] Ballman, M., Zhao, C., McAdams, M. J., & Rajan, A. (2022). Immunotherapy for management of thymic epithelial tumors: A double-edged sword. *Cancers (Basel), 14*(9), 2060.

[2] Mix, L., Knoll, M., Häring, M. F., Bethge, W. A., Schröder, J. C., Forchhammer, S., Krumm, P., Schürch, C. M., Schaller, M., & Lengerke, C. (2023). Case report: Paraneoplastic psoriasis in thymic carcinoma. *Front Oncol, 13*, 1218517.

[3] Li, J., Mao, F., Liu, H., & Chen, J. (2025). Immune checkpoint therapy for thymic carcinoma. *Cancers (Basel), 17*(20), 3377.

[4] Alqaidy, D., & Moran, C. A. (2022). Thymic carcinoma: A review. *Front Oncol, 12*, 808019.

[5] Klug, M., Strange, C. D., Truong, M. T., et al. (2024). Thymic imaging pitfalls and strategies for optimized diagnosis. *RadioGraphics, 44*(5), e230091.

[6] Shiiya, H., Ujiie, H., Hida, Y., Kato, T., Kaga, K., Wakasa, S., Kikuchi, E., Shinagawa, N., Okada, K., Ito, Y. M., & Matsuno, Y. (2021). Elevated serum CYFRA 21-1 level as a diagnostic marker for thymic carcinoma. *Thorac Cancer, 12*(21), 2933-2942.

[7] Donovski, D., Ahmadi, L., Ceppa, D., Ardeshir-Larijani, F., Maniar, R., & Loehrer, P. (2025). Surveillance and treatment monitoring in thymic tumors via circulating tumor DNA. *J Immunother Cancer, 13*(Suppl 1), A123.

[8] Remon, J., Villacampa, G., Facchinetti, F., Di Maio, M., Marcuse, F., Tiseo, M., et al. (2023). Immune checkpoint blockers in patients with unresectable or metastatic thymic epithelial tumours: A meta-analysis. *Eur J Cancer, 180*, 117-124.

[9] Parmar, K., & Rajan, A. (2025). Immune aberrations in thymic epithelial tumors. *Mediastinum, 9*, 34.

[10] Rich, A. L. (2020). Epidemiology of thymoma. *J Thorac Dis, 12*(12), 7531-7535.

[11] Chen, Z., Liu, S., Chen, C., Zhuang, J., Xu, X., Liu, M., Lai, F., & He, F. (2025). Rising threat: Long-term trends in the incidence and mortality of thymic epithelial tumor. *Cancer Med, 14*(10), e70968.

[12] Owen, D., Chu, B., Lehman, A. M., Annamalai, L., Yearley, J. H., Shilo, K., & Otterson, G. A. (2018). Expression patterns, prognostic value, and intratumoral heterogeneity of PD-L1 and PD-1 in thymoma and thymic carcinoma. *J Thorac Oncol, 13*(8), 1204-1212.

[13] Elm, L., & Levidou, G. (2024). The molecular landscape of thymic epithelial tumors: A comprehensive review. *Int J Mol Sci, 25*(3), 1554.

[14] Shukuya, T., Asao, T., Goto, Y., et al. (2025). Activity and safety of atezolizumab plus carboplatin and paclitaxel in patients with advanced or recurrent thymic carcinoma (MARBLE): A multicentre, single-arm, phase 2 trial. *The Lancet Oncology, 26*(3), 331-342.