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Contents

Monthly Volume 15 Number 6 June 24, 2024

EDITORIAL

667 Silica nanoparticle design for colorectal cancer treatment: Recent progress and clinical potential

Meng J, Wang ZG, Zhao X, Wang Y, Chen DY, Liu DL, Ji CC, Wang TF, Zhang LM, Bai HX, Li BY, Liu Y, Wang L, Yu WG, Yin ZT

674 An overview of the contemporary diagnosis and management approaches for anaplastic thyroid carcinoma

Zhou SY, Luo LX

677 Impact of sleep on gastrointestinal cancer

Lo J, Taweesedt PT, Kawai M

684 Current status of anaplastic thyroid carcinoma

Ocanto A, Torres L, Couñago F

687 New targets for cancer promotion and therapy in gliomas: Scinderin

Wang X, Luo LX

691 Vitamin D and prostate cancer prevention

Krumina E, Ocanto A, Couñago F

REVIEW

695 Gallbladder cancer: Progress in the Indian subcontinent

Kumar A, Sarangi Y, Gupta A, Sharma A

717 Overview of dyslipidemia and metabolic syndrome in myeloproliferative neoplasms

Găman MA, Srichawla BS, Chen YF, Roy P, Dhali A, Nahian A, Manan MR, Kipkorir V, Suteja RC, Simhachalam Kutikuppala LV, Găman AM, Diaconu CC

730 Systemic oncological therapy in breast cancer patients on dialysis

Khan S, Araji G, Yetiskul E, Keesari PR, Haddadin F, Khamis Z, Chowdhry V, Niazi M, Afif S, Dhar M, El-Sayegh S

ORIGINAL ARTICLE

Retrospective Study

745 Characteristics and distinct prognostic determinants of individuals with hepatosplenic T-cell lymphoma over the past two decades

Bangolo A, Fwelo P, Dey S, Sethi T, Sagireddy S, Chatta J, Goel A, Nagpaul S, Chen EPS, Saravanan C, Gangan S, Thomas J, Potiguara S, Nagesh VK, Elias D, Mansour C, Ratnaparkhi PH, Jain P, Mathew M, Porter T, Sultan S, Abbisetty S, Tran L, Chawla M, Lo A, Weissman S, Cho C

World Journal of Clinical Oncology

Monthly Volume 15 Number 6 June 24, 2024

Contents

Basic Study

755 Tankyrase 2 promotes lung cancer cell malignancy

Wang Y, Zhang YJ

SCIENTOMETRICS

765 What enlightenment has the development of lung cancer bone metastasis brought in the last 22 years

Chen Y, Chen XS, He RQ, Huang ZG, Lu HP, Huang H, Yang DP, Tang ZQ, Yang X, Zhang HJ, Qv N, Kong JL, Chen G

LETTER TO THE EDITOR

783 Predicting liver function after hemihepatectomy in patients with hepatocellular carcinoma using different modalities

Taherifard E, Saeed A

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Monthly Volume 15 Number 6 June 24, 2024

Contents

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EDITORIAL

Current status of anaplastic thyroid carcinoma

Abrahams Ocanto, Lisselott Torres, Felipe Couñago

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Abstract

In this editorial we comment on the article by Pavlidis *et al*, published in the recent issue of the *World Journal of Oncology*. We focus on the recent contributions in the management of anaplastic thyroid carcinoma, highlighting the importance of surgery and radiotherapy as first line therapies in its management and the introduction of new systemic therapies beyond chemotherapy, focused on molecular alterations, an essential step in the diagnosis and included in clinical guidelines for the selection of the ideal treatment. In contrast to other neoplasms, immunotherapy, is still beginning in studies of this pathology with encouraging results. Therefore, multimodal management of the pathology together with new drugs seems to be the logical step to increase the survival of this neoplasm.

Key Words: Anaplastic carcinoma; Thyroid diseases; Surgery; Radiotherapy; Immunotherapy

Core Tip: Anaplastic thyroid carcinoma is an entity with high mortality despite the combination of treatments, today molecular analysis opens the door to new drugs that impact survival in a positive way when used in a multimodal form.

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INTRODUCTION

Anaplastic thyroid cancer (ATC) is a clinical entity with a high mortality and a 5-year survival of less than 0.2%. Pavlidis *et al*[1] have performed a review of ATC, emphasizing the importance of early diagnosis and multimodal therapy to achieve the highest survival in this group of patients.

DIAGNOSIS

The initial diagnosis is the clinical presentation: Neck mass, cough, hemoptysis and dyspnea (more frequently), hoarseness and dysphagia if tracheal involvement, physical examination and ultrasound, preferably high resolution, followed by core needle biopsy; which should be prioritized over fine needle aspiration to obtain a representative sample for histopathological, genetic and molecular analysis. For both locoregional and distant staging, computed tomography angiography is preferable to magnetic resonance image. Positron emission tomography is the best option for finding occult tumor deposits. Liquid biopsy can detect malignant cells and it could contribute to diagnosis, prognosis and follow-up[1].

American thyroid association (ATA) recently integrated molecular testing in this type of tumors into its clinical guidelines, highlighting the analysis of a series of mutations involved in the aggressive evolution of these tumors and increased mortality[2], highlighting the mutation in the *RAS* gene, however, there are no approved targeted therapies that can improve the evolution of this disease. Other genes such as *BRAF*, *MET*, *NTRK* have first-line targeted therapies. With regard to the field of immunotherapy, PD-L1 expression is high in the samples analyzed, which may improve the response according to data recently published[1].

The early diagnosis in young patients (< 65 years) as well as the absence of lymph node involvement and metastasis at diagnosis, tumor size < 5 cm, are the most important prognostic factors and those that allow us to select the best treatment combination[1].

TREATMENT AND NOVEL THERAPIES

Surgery and radiotherapy have so far been shown independently to be associated with increased survival, being the corner stone, however the combination of treatments is the key, even with the advent of targeted therapies, new chemotherapy drugs and immunotherapy. Surgery according to National Comprehensive Cancer Network[2] and ATA[3] guidelines is indicated in localized cases: Lobectomy +/- thyroidectomy and lymphadenectomy. Palliative "debulky" surgery is indicated in large tumor masses and clinically significant, accompanied by adjuvant radiotherapy, chemotherapy and/or targeted therapy.

Chemotherapy, in this type of tumor there is talk of "chemoresistance", even so with the introduction of taxanes combined with platinum or anthracyclines. The combination of dabrafenib and trametinib, in *BRAF* and *MEK* gene mutation, helps to overcome this "resistance". For non-mutated gene cases, immunotherapy (anti-PD-1 and anti-PD-L1) is a new option with promising results[4].

Recently, anlotinib (tyrosine kinase inhibitor) was approved for use in combination with chemotherapy as a first-line treatment for ATC[5]. Lenvatinib, another tyrosine kinase inhibitor is used in ATC as an alternative to radioiodine and in unresectable patients as neoadjuvant therapy with increased survival. The best data continues to be provided by the combination of Dabrafenib-Trametinib when indicated. However, 5-year survival rates remain poor, immunotherapy has so far demonstrated 1-year survival rates of around 40%, and results are awaited from new treatments including oncolytic viruses, epigenetic modulators, apoptosis-inducing agents, multikinase and aurora inhibitors[1].

CONCLUSION

The management of ATC must be multimodal. The new targeted therapies as well as timing represent the change in the management of the pathology where neoadjuvant or adjuvant therapy are the novelty, however the surgery continues to be the best therapy in the initial stages of the disease. More studies and especially clinical trials directed to multimodal molecular therapy with surgery and radiotherapy are needed to optimize the results of this group of patients.

FOOTNOTES

Author contributions: Ocanto A, Torres L and Couñago F contributed to this paper; Ocanto A, Torres L and Couñago F designed the overall concept and outline of the manuscript; Couñago F contributed to the discussion and design of the manuscript; Ocanto A, Torres L and Couñago F contributed to the writing, and editing the manuscript and review of literature.

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