

Treatment of Triple Negative Breast Cancer

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Abstract

Triple negative breast cancer is highly malignant and heterogeneous. The treatment is difficult and the prognosis is poor. Endocrine and targeted therapy are not sensitive. At present, many medical experts have studied the treatment of triple negative breast cancer, and clinical trials have confirmed the effectiveness of some treatment methods. This paper mainly explores the treatment of triple negative breast cancer for clinical reference.

Keywords

Three Negative Breast Cancer; Heteromorphism; Treatment; Effectiveness.

1. Introduction

Three Negative Breast Cancer (TNBC) refers to breast cancer with negative estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2. TNBC has high mitosis and histological characteristics of infiltration and diffusion. The risk of early distant metastasis is very high, and it is easy to penetrate important organs such as lung, liver and brain. The overall survival of patients was low. If TNBC is treated locally, it is generally treated locally. The general surgical methods are modified radical surgery and breast conserving surgery. Neoadjuvant chemotherapy is the main systemic treatment for TNBC. Pathological complete remission is an important index to evaluate the sensitivity of neoadjuvant chemotherapy. Early neoadjuvant chemotherapy can improve the complete remission rate of pathology, improving the success rate of surgery, narrowing the scope and improving the long-term prognosis of the disease. With the deepening of molecular biology research, some important molecular characteristics of TNBC have been determined. Targeted therapy through some molecular pathways is expected to become a good alternative to systemic therapy.

2. Local Treatment of Early TNBC

Local treatment of breast cancer is a surgical treatment for all breast cancer subtypes. Surgical treatment of breast cancer includes radical resection, radical mastectomy, modified radical mastectomy and breast conserving surgery. With the rapid progress of comprehensive cancer treatment technology, the life expectancy of breast cancer patients has increased significantly. After breast cancer surgery, patients have a higher demand for breast morphology, and the scope of mastectomy will have a direct impact on the psychological state and social adaptability of patients. Therefore, breast conserving surgery combined with postoperative radiotherapy and chemotherapy may better meet the needs of patients. In traditional treatment, patients with early TNBC underwent mastectomy or breast conserving treatment, and there was no significant difference in survival rate between the two groups.

3. Neoadjuvant Chemotherapy for Early TNBC

3.1. Selection of Neoadjuvant Chemotherapy

TNBC has the characteristics of strong invasion and easy metastasis, and the prognosis of patients is often poor. Neoadjuvant chemotherapy is effective in patients with lymph node negative TNBC. In patients with early TNBC, the prevention rate of paclitaxel and anthracycline intelligent chemotherapy is 30% - 40%, while the cure rate of carboplatin and paclitaxel based intelligent chemotherapy is 45%. Sequential intensive doxorubicin, cyclophosphamide, paclitaxel and carboplatin can completely cure up to 50% of early TNBC patients. The total pathological remission rate of neoadjuvant chemotherapy with docetaxel combined with carboplatin was 55%. The addition of carboplatin to the standard chemotherapy regimen may lead to a higher pathological complete remission rate, but it will lead to more complex adverse reactions. At present, platinum based neoadjuvant chemotherapy is used in patients with early TNBC. There is no obvious advantage in clinical treatment.

3.2. Evaluation and Method of Curative Effect

Pathological complete remission is an important index to evaluate the efficacy of neoadjuvant therapy and predict the risk of recurrence. Studies have shown that pathological complete remission is significantly correlated with the long-term prognosis of early TNBC patients and the distant metastasis free survival rate of more than 90% of early TNBC patients. The evaluation of pathological complete remission should be completed by the pathologist, and the evaluation standard is:

In the surgical samples after neoadjuvant chemotherapy, there were no cancer cells in the cancer area, no lymph nodes or residual ductal carcinoma in situ, and no distant or other metastasis. After the improvement of neoadjuvant therapy, the pathological complete remission rate of TNBC patients was significantly improved, which was finally transformed into the survival benefit of patients. Although early TNBC responded well to neoadjuvant chemotherapy, the cytotoxic drugs used in chemotherapy had lower specificity and greater lethality to normal organs or tissues. Therefore, targeted individualized targeted therapy is effective for the treatment of early TNBC.

4. Surgical Treatment

At present, the optimal treatment for TNBC patients is still surgical treatment. For early TNBC patients, after breast conserving surgery combined with radiotherapy, modified surgery without radiotherapy and modified surgery with radiotherapy, the 5-year recurrence free survival rates were 94%, 85% and 87% respectively. This further confirmed the low-invasive breast conserving surgery combined with radiotherapy advocated by early TNBC, and the high-risk patients with positive margin or unknown supported radical breast cancer surgery. Relevant studies have shown that young TNBC patients with breast conserving therapy have a high local recurrence rate, but there is no significant difference in distant metastasis rate and overall survival status between young TNBC patients and non-TNBC patients, which indicates that young TNBC patients can be recommended for breast conserving therapy.

5. Classification of TNBC and Targeted Treatment of Early TNBC

5.1. TNBC Typing

TNBC has specific genetic and pathological characteristics, and its clinical feature is invasive ductal carcinoma. The classification of TNBC based on molecular biology provides a new driving force for its diagnosis and treatment through the in-depth study of gene expression profile system. Typical TNBC molecular subtypes include basal type 1, basal type 2,

immunosuppressive, mesenchymal and lumen androgen receptor types. Among them, the clinical symptoms of type I and type II basement are mostly invasive cancer, while the symptoms of immunosuppressive type are similar to those of moderately invasive cancer, indicating that TNBC is highly heterogeneous. Qualitatively, the disease is composed of populations with different biological characteristics. Therefore, targeted therapy based on different types of TNBC is a new direction of TNBC therapy.

5.2. Early TNBC Targeted Therapy

5.2.1. Poly Adenosine Diphosphate Ribose Polymerase Inhibitor

Adenosine polyphosphate ribose polymerase inhibitor is the first drug approved for targeted therapy. They have anti-inflammatory and anti apoptotic properties and can be used as chemotherapeutic agents. All genes related to class I reproduction, such as highly expressed cell cycle, DNA repair pathway and TNBC basis, are highly sensitive to platinum, drugs and polyadenylribose polymerase inhibitors. Therefore, the use of poly ADP ribose polymerase inhibitor alone or in combination with platinum drugs is expected to provide a new targeted treatment for patients with early TNBC. Relevant studies have shown that the proportion of patients with early TNBC treated with ribose polymerase combined with carboplatin and paclitaxel is 51%, and the overall proportion of patients treated with paclitaxel alone is 26%. This proves that the clinical efficacy of adenosine polyphosphate ribose polymerase inhibitor combined with carboplatin is significant.

5.2.2. Epidermal Growth Factor Receptor Inhibitor

Epidermal growth factor receptor is a transmembrane tyrosine kinase receptor located on the cell surface, which can inhibit cell proliferation, angiogenesis and apoptosis. In type 2, such as TNBC basal, the high expression of epidermal growth factor receptor and epidermal growth factor receptor related genes makes epidermal growth factor receptor inhibitors the target of early TNBC receptor targets. Phase II clinical trial confirmed that panimab combined with docetaxel was effective in the treatment of early TNBC, and the side effects were controllable. The clinical trial in the second stage confirmed that CNBC patients who received cetuximab combined with docetaxel in the early stage could obtain a higher pathological complete remission rate than docetaxel, and the clinical efficacy and toxicity were lower.

At present, the target of epidermal growth factor receptor inhibitors is unselected TNBC patients who have been pretreated for many times, suggesting that patients with earlier detection of epidermal growth factor receptor expression may improve the prognosis. When treating epidermal growth factor with anticoagulants, it is particularly important to follow effective combination therapy in patients with early TNBC to prevent drug resistance. Relevant studies have found that afatinib combined with dasatinib has a positive clinical effect on patients with early TNBC, but further preclinical studies are needed to confirm this.

5.2.3. Androgen Receptor Inhibitor

About 50% of TNBC patients express androgen receptor, which is related to disease-free survival, overall survival and relapse free survival. The lumen androgen receptor of TNBC highly expresses androgen receptor and lumen cytokeratin. Studies have shown that androgen also plays an important role in basal like type 1, basal like type 2 and immunomodulatory type. Therefore, androgen receptor inhibitors are expected to provide a new alternative to the targeted therapy of TNBC. Relevant studies have confirmed that bilirubin and abiraterone have positive clinical effects on TNBC patients with high expression of androgen receptor. Enzalutamide has significant clinical efficacy and high safety in patients with advanced androgen receptor positive TNBC, but 84% of the enrolled patients received rapid chemotherapy in the early stage, which will have a certain impact on the efficacy. Clinical trials

are needed to evaluate the efficacy of androgen receptor inhibitors only in patients with TNBC and the prognosis of early TNBC patients using androgen receptor inhibitors.

5.2.4. Immune Checkpoint Inhibitor Therapy

Immunosuppressants are widely used in the clinical treatment of cancer. As a special subspecies of breast cancer, TNBC has potential targets for immunotherapy. The research of programmed cell death protein-1 and programmed cell death protein ligand-1 has effectively promoted the development of TNBC targeted therapy. At present, there are five types of immune checkpoint inhibitor drugs: pabrolizumab against programmed cell death protein-1, navuzumab, atzumab against programmed cell death protein ligand-1, avilumab and duvumab. Relevant studies have shown that in patients with early TNBC, the incidence of pathological complete remission in pabrolizumab combined with neoadjuvant chemotherapy group is significantly higher than that in placebo combined with neoadjuvant chemotherapy group. Treatment with atzumab combined with albumin paclitaxel can achieve significant survival benefits in TNBC patients with positive expression of programmed ligand 1 protein. However, it should be noted that the subjects we studied are mainly patients with locally advanced or metastatic TNBC, so the results may be abnormal depending on the stage of the disease. Therefore, the application of early TNBC needs further clinical trials to prove it.

6. Conclusion

In conclusion, individualized treatment is particularly important for breast cancer patients. Making different treatment plans for different patients is an urgent problem for clinicians to bring maximum benefits and best prognosis to patients. The clinical treatment of TNBC has made rapid progress. The treatment mode has developed from a single mode to a specific precise individual treatment. Neoadjuvant chemotherapy is the main treatment for patients with TNBC, especially for patients with early TNBC. However, cytotoxic drugs also kill normal cells and tissues, so they have some limitations.

TNBC molecular targeted therapy is a new direction of TNBC in-depth pathogen research and precision medicine. Targeted therapy can destroy cancer cells with low resistance to adverse reactions. Therefore, the development of targeted treatment strategies for specific populations provides a new impetus for the early treatment of TNBC. However, due to the high heterogeneity, different biological characteristics and typing methods and large number of TNBC, the process of finding reliable biomarkers for each subtype is complex and expensive, and it is difficult to achieve clinical transformation. In the future, TNBC classification needs to be further simplified to provide feasible and specific targeted treatment for patients.

References

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