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Case Report

Chemotherapy Regimen for Ovarian Juvenile Granulosa Cell Tumor in a Pediatric Patient: Case Report and Literature Review

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Abstract

Introduction: Juvenile granulosa cell tumor is a rare sex cord stromal tumor. Due to the low incidence rate of juvenile granulosa cell tumor, there is no consensus on the best treatment, especially for the choice of chemotherapy regimen.

Case report: We present the case of a 9-year-old girl with juvenile granulosa cell tumor, the current tumor stage is IC stage. Paclitaxel combined with carboplatin regimen chemotherapy have undergone once, but now because of allergy to paclitaxel, a new chemotherapy regimen was required.

Management and outcome: According to the relevant clinical practice guidelines and literature, clinicians and pharmacists discussed the following treatment regimens: bleomycin 15 U/m2 on day 1, etoposide 100 mg/m2 and cisplatin 25 mg/m2 every 21 days on days 1-3. The dosage and duration of treatment were within the recommended range of the relevant guidelines. The clinical pharmacist monitored adverse effects during chemotherapy and the process went smooth.

Discussion: The value of chemotherapy in patients with stage IC is still unknown, and there is no uniform standard for BEP regimens in pediatric patients. So, clinicians need to consider it comprehensively and individualize treatment.

Keywords: Juvenile granulosa cell tumor; Chemotherapy; Paclitaxel

Abbreviations: GCT: Granulosa cell tumor; JGCT: Juvenile granulosa cell tumor; TC: Paclitaxel + Carboplatin; BEP: Bleomycin + Etoposide + Cisplatin

Introduction

Granulosa cell tumor (GCT) of ovary is a non-epithelial ovarian tumor, with an incidence of 2-5% of ovarian tumors, and the overall incidence is (0.6-1.7)/100000 per year [1]. According to the clinical and pathological features, it can be divided into two types: adult granulosa cell tumor and juvenile granulosa cell tumor (JGCT), of which JGCT accounts for only 5% of GCT [2]. It is a relatively rare

tumor, and patients often present because of an abdominal mass on physical examination or lower abdominal discomfort caused by mass compression [3].

Currently guidelines recommend TC (paclitaxel + carboplatin) as the preferred chemotherapy regimen for ovarian granulosa cell tumors, and BEP (bleomycin + etoposide + cisplatin) as a second-line option, but the guidelines do not include information for pediatric patients [4]. Although there are relevant guidelines for the diagnosis and treatment of JGCT in children at home and abroad, there are still controversies in the selection of adjuvant chemotherapy regimens and doses for JGCT in children. The timing and dose of chemotherapy vary from guideline to guideline. The article analyzes a pediatric JGCT patient in which clinical pharmacists are involved in the treatment process, summarizes the clinical treatment experience with adjuvant chemotherapy for JGCT children, and provides further guidance for treating pediatric JGCT in chemotherapy.

Case Report

A 9-year-old girl underwent a "transabdominal left ovarian tumor removal" for a "pelvic mass" and postoperative pathology revealed a "juvenile granulosa cell tumor". The patient was treated once with TC chemotherapy. The chemotherapy went smoothly. However, there was a generalized scattered rash with itching in the form of wheals eight days after chemotherapy, which gradually improved after two days of loratadine.

MRI examination of the patient's pelvic showed that there was a possibility of residual disease after surgery, TC chemotherapy was continued, and the appropriate pretreatment was given before chemotherapy. When the patient started 25-minute paclitaxel infusions, he had itching and unbearable feeling all over the body, chest tightness, obvious nausea and vomiting, and incontinence once.

The patient was allergic to paclitaxel and wanted to switch chemotherapy to BEP. The physician consulted with the clinical pharmacist about the appropriate subsequent dose of chemotherapy for the patient.

Analysis and Discussion

Adjustment of Chemotherapy regimen

The 2023 NCCN guidelines for ovarian cancer recommend postoperative observation or consideration of platinum-based chemotherapy for patients with high-risk stage I tumors (tumor rupture, stage 1C, poorly differentiated tumors, tumor size > 10-15cm) [4]. The Guidelines of the Chinese anti-cancer association recommend chemotherapy for juvenile granulosa cell tumors from stage IA [5]. A Study has shown that tumor size > 13cm, tumor rupture, and tumor removal are closely related to the patient's recurrence. The recurrence rate and duration are higher and shorter for IC than IA [6].

After the patient is hospitalized, the possibility of residual postoperative is considered based on imaging. Because of the patient's young age, a history of surgery in the past month, a significant risk of reoperation trauma, and the patient's current stage of tumor stage is IC stage, chemotherapy is recommended.

A Cochrane Review from 2014 provisionally compared TC and BEP regimens in malignant ovarian disease. The review compared the efficacy of the two therapies and found that TC has a lower recurrence rate [7]. A randomized phase 2 trial is currently underway to compare the efficacy of TC with BEP in treating patients with malignant ovarian germ cell tumors directly. Primary completion results will be expected in 2025, and clinical pharmacists will continue to monitor the progress of this trial [8]. It has also been reported that the incidence of bleomycin-associated pneumonia during chemotherapy is 7.7 percent, and the mortality rate is 1.8 percent [9]. In terms of side effects, clinical pharmacists believe that TC regimens have fewer side effects than BEP. Given the patient's young age and poor tolerance to chemotherapy, the physician decided to treat her with a TC regimen.

However, severe allergic reactions occur in patients treated with paclitaxel, and clinicians wish to use BEP regimens. However, there is no uniform standard for BEP regimens in pediatric patients, and several guidelines reduce the toxicity of chemotherapy by optimizing BEP regimens in adults, lowering the dose of bleomycin, and reducing the number of days of chemotherapy.

Dosage of BEP regimen

The NCCN and FIGO guidelines for ovarian cancer do not specifically address treatment options for children. The American Children's Oncology Group has suggested two regimens: bleomycin 15 U/m^2 on day 1, etoposide 100 mg/m^2, and cisplatin 20 mg/m^2 on days 1 to 5 or bleomycin 15 U/m^2 on day 1 and etoposide 167 mg/m^2 and cisplatin 33 mg/m^2 on days 1 to 3 [10]. The Italian study group recommended etoposide 100 mg/m^2, cisplatin 25 mg/m^2 on days 1 to 4, and bleomycin 15 U/m^2 on day 2. In addition, the Indian consensus document for the treatment of pediatric malignant germ cell neoplasms recommends bleomycin 15 U/m^2 on day 1, etoposide 120 mg/m^2 and cisplatin 35 mg/m^2 on days 1 to 3 [11]. Based on the above literature, the guidelines for BEP regimens in pediatric patients recommend a dose of bleomycin of 15 U/m^2 for only one day, with differences in the duration and dose of etoposide and cisplatin.

As JGCT is mostly early-stage and chemotherapy are controversial, there are no prospective comparative studies between the different therapies, so no differentiated studies compare the therapies. However, in a study of 299 pediatric patients, including 74 with ovarian-related tumors, in which the standard dose of cisplatin was increased from 20 mg/m^2 to 40 mg/m^2 cisplatin to increase response rates, the increase in cisplatin dose resulted in higher event-free survival with no difference in overall survival [12]. In the high-dose group, magnesium and potassium losses, reduced creatinine clearance, nausea and vomiting, and thrombocytopenia occurred more frequently. However, severe infections led to the death of 7 people, 6 of whom were in the high-dose group; Hearing loss (grade 3/4 toxicity according to the National Cancer Institute

criteria) was observed in 14% of patients in the high-dose group, while no ototoxicity was observed in the standard group. 67% of patients in the high-dose group required a hearing aid. Therefore, pharmacists believe that when the cisplatin dose is increased to 40 mg/m^2 in BEP pediatric treatment, the associated adverse effects increase, and there is no benefit to patient survival. In conjunction with the relevant clinical practice guidelines and literature, clinicians and pharmacists discussed the following regimens: bleomycin 15 U/m^2 on day 1, etoposide 100 mg/m^2 and cisplatin 25 mg/m^2 every 21 days on days 1-3. The dosage and duration of the treatment were within the recommended range of the relevant guidelines.

The literature reports that 10-20% of children with pediatric germ cell tumors treated with standard doses of BEP (bleomycin 15 U/m^2 on day 1, etoposide 100 mg/m^2, and cisplatin 20 mg/m^2 on days 1 to 5) have permanent bilateral high-frequency hearing loss, which can affect education, social-emotional development, and quality of life [12]. Due to concerns regarding nephrotoxicity and ototoxicity of BEP therapies, clinical pharmacists have continued to search the literature. The UK Childhood Cancer Research Group included 23 pediatric patients treated at least four times with etoposide 150 mg/m^2 on days 1 to 3, carboplatin 600 mg/m^2 on day 2, and bleomycin 10 mg/m^2 on day 3 after a preliminary lung, kidney, and ear evaluation. All patients achieved a complete or partial response. The median follow-up time was 58 months, with an overall survival rate of 91% and an event-free survival rate of 87% [13]. The patients were well tolerated, and nephrotoxicity and ototoxicity occurred rarely or to a minor extent in the patients studied.

In addition, the Indian consensus document on the treatment of pediatric germ cell neoplasms recommends that JEP (etoposide 120 mg/m^2 on days 1 to 3; carboplatin 600 mg/m^2 on day 2; bleomycin 10 mg/m^2 on day 3) can be used as an alternative to BEP in patients with renal insufficiency [11]. Carboplatin can successfully replace with cisplatin in the treatment of pediatric germ cell tumors without compromising response or survival.

Summary and Experience

This case report summarizes the chemotherapy regimen and drug dose selection in a pediatric patient with JGCT. The clinical pharmacist is actively involved in the formulation of chemotherapy regimens, drug dosage selection, and monitoring of side effects. BEP may be used as an alternative in children with JGCT if paclitaxel is not tolerated, but there is no uniform standard of care for BEP in pediatric patients. The clinical pharmacist has actively engaged with the literature and collaborated with the physician to formulate the specific dose of BEP treatment regimen for the patient.

Based on the existing guidelines and literature, the clinical pharmacist fully considers the patient's factors, actively participates in formulating individualized medication regimens for the patients and assists the physicians in closely monitoring the patients' side effects by providing ideas and experiences for the treatment of JGCT.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Makhija A, Patel BM, Kenkre MA, Desai AD, Patel SM, et al. (2020) Retrospective Analysis of 32 Cases of Ovarian Granulosa Cell Tumours. J Obstet Gynaecol India 70(1): 50-56.
2. Dridi M, Chraiet N, Batti R, Ayadi M, Mokrani A, et al. (2018) Granulosa Cell Tumor of the Ovary: A Retrospective Study of 31 Cases and a Review of the Literature. Int J Surg Oncol 2018: 4547892.
3. Ray-Coquard I, Morice P, Lorusso D, Prat J, Oaknin A, et al. (2018) Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 29(Suppl 4):iv1-iv18.
4. (2023) NCCN Clinical Practice Guidelines in Oncology. NCCN Clinical Practice Guidelines in Oncology.
5. (2018) The Guidelines for the Diagnosis and Treatment of Ovarian Malignancies (4th edn), Gynecologic oncology of the Chinese Anti-Cancer Association 34(7): 739-749.
6. Wilson MK, Fong P, Mesnage S, Chrystal K, Shelling A, et al. (2015) Stage I granulosa cell tumours: A management conundrum? Results of long-term follow up. Gynecol Oncol 138(2): 285-291.
7. Gurumurthy M, Bryant A, Shanbhag S (2014) Effectiveness of different treatment modalities for the management of adult-onset granulosa cell tumours of the ovary (primary and recurrent). Cochrane Database Syst Rev 2014(4): CD006912.
8. https://www.clinicaltrials.gov/study/NCT02429687?intr=BEP&term=TC&rank=1#publications
9. Delanoy N, Pécuchet N, Fabre E, Combe P, Juvin K, et al. (2015) Bleomycin-Induced Pneumonitis in the Treatment of Ovarian Sex Cord-Stromal Tumors: A Systematic Review and Meta-analysis. Int J Gynecol Cancer 25(9): 1593-1598.
10. Schneider DT, Orbach D, Ben-Ami T, Bien E, Bisogno G, et al. (2021) Consensus recommendations from the EXPeRT/PARTNER groups for the diagnosis and therapy of sex cord stromal tumors in children and adolescents. Pediatr Blood Cancer 68 Suppl 4: e29017.
11. Agarwala S, Mitra A, Bansal D, Kapoor G, Vora T, et al. (2017) Management of Pediatric Malignant Germ Cell Tumors: ICMR Consensus Document. Indian J Pediatr 84(6): 465-472.
12. Shaikh F, Nathan PC, Hale J, Uleryk E, Frazier L (2013) Is there a role for carboplatin in the treatment of malignant germ cell tumors? A systematic review of adult and pediatric trials. Pediatr Blood Cancer 60(4): 587-592.
13. Stern JW, Bunin N (2002) Prospective study of carboplatin-based chemotherapy for pediatric germ cell tumors. Med Pediatr Oncol 39(3): 163-167.