



Adult rhabdomyosarcoma combined with acute myeloid leukemia: A case report

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Abstract

BACKGROUND

Rhabdomyosarcoma is a tumor of mesenchymal origin. Secondary leukemia is a complication of previous transformation to other hematologic disorders or is a treatment-related acute myeloid leukemia secondary to cytotoxic chemotherapy or radiation therapy for other malignancies.

CASE SUMMARY

We present the case of a 36-year-old female patient who was diagnosed with rhabdomyosarcoma and acute myeloid leukemia. Further disease progression was observed after multiline chemotherapy. Eventually, the patient suffered cerebral hemorrhage, which resulted in death.

CONCLUSION

The incidence of rhabdomyosarcoma in adults is extremely low, and secondary leukemia caused by rhabdomyosarcoma is even rarer. Secondary leukemia has a very poor prognosis and a low overall survival rate.

Key Words: Rhabdomyosarcoma; Secondary acute myeloid leukocytes; Chemotherapeutics; Secondary leukemia; Case report

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Core Tip: This article reports on a patient with rhabdomyosarcoma who developed acute myeloid leukemia (AML-M5a) after 11 chemotherapy sessions. Eventually, the patient suffered cerebral hemorrhage, which resulted in death. The incidence of rhabdomyosarcoma in adults is extremely low, and secondary leukemia caused by rhabdomyosarcoma is even rarer. Secondary leukemia has a very poor prognosis and a low overall survival rate.

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INTRODUCTION

Rhabdomyosarcoma is a tumor of mesenchymal origin. It occurs most frequently in children and adolescents and has a very low incidence in adults[1]. The main treatments for rhabdomyosarcoma are surgery, chemotherapy and radiotherapy. Secondary leukemia is a complication of previous transformation to other hematologic disorders or treatment-related acute myeloid leukemia secondary to cytotoxic chemotherapy or radiation therapy for other malignancies[2,3]. With technological advances in chemotherapy and radiotherapy, the survival of oncology patients has increased, as has the probability of developing secondary leukemias. This article reports on a patient with rhabdomyosarcoma who developed acute myeloid leukemia (AML-M2) after 11 chemotherapy sessions.

CASE PRESENTATION

Chief complaints

A 36-year-old female patient visited our hospital on October 30, 2019, due to right cheek swelling for 1 month.

History of present illness

The patient was admitted with a mass on the left cheek. Physical examination revealed a mass approximately 3.4 cm in size on the right cheek. The peripheral blood and biochemical parameters (liver and renal function and serum lactate dehydrogenase level) were within normal limits. Pathology of the right buccal mass puncture showed spindle cell rhabdomyosarcoma. Immunohistochemistry (Figure 1) showed the following: ALK IA4 (portion+), Caldesmon (-), Desmin (+), H3K27ME3 (excalation), MyoD1 (+), Myogenin (+), S-100 (portion+), and SMA (-). She was diagnosed with spindle cell rhabdomyosarcoma. After the diagnosis, the patient underwent surgical treatment. The postoperative pathologic diagnosis was consistent with spindle cell rhabdomyosarcoma. The patient was subsequently given a 12-cycle VAC/IA regimen (VAC; Vinorelbine, 38 mg; cyclophosphamide, 1.4 mg; Epirus; IA: isocyclophosphamide 2.5 g 1-5 d, etoposide 0.1 g 1-5 d). Her disease went into remission after treatment. On April 28, 2021, the patient's repeat blood test showed a white blood cell count of $115.4 \times 10^9/L$, a hemoglobin level of 112 g/L, a blood platelet count of $144 \times 10^9/L$, and a primary cell count of 49%.

History of past illness

The patient had no family history or specific social history.

Personal and family history

No personal or family history was available.

Physical examination

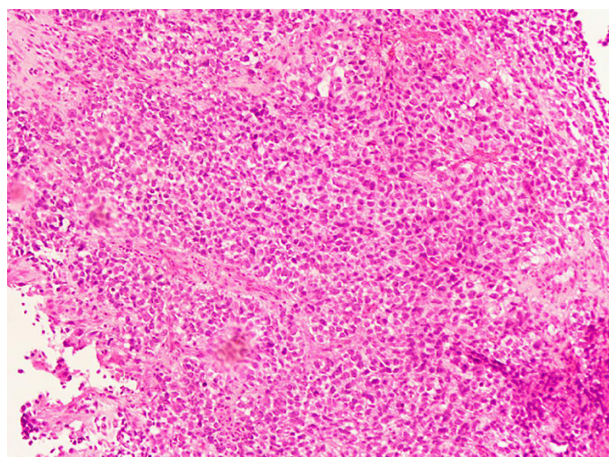
Physical examination revealed no palpable lymph nodes, organomegaly, or cutaneous lesions.

Laboratory examinations

Her bone marrow morphology showed active cell hyperplasia, accounting for 77%. For these types of cells, the cytoplasm was 12-25 μm in size, the shape was round, oval or irregular, and the cytoplasmic volume was rich and colored dark blue. Part of the cell cytoplasm could be seen as tiny purplish-red particles, and the cytosolic nuclei were round and oval. The nuclear chromatin was meticulously granular, with 1 to several nucleoli that were not clear and seemed to be monophyletic. POX (+), butyric acid (+) and NaF (inhibition). The bone marrow picture was consistent with acute nonlymphocytic leukemia, with cytomorphology resembling M5. Immunohistochemistry revealed the following results: 87.57% of the primary cells predominantly expressed CD33, CD38, CD13, HLA-DR, CD11b, CD36, and CD64, while CD34, CD117, CD14, and cMPO were not expressed. The karyotype was 45, XX, -7. The leukemia genetic testing reported that the mutated genes are NRAS, CUX1, LIG4, MYH1, KMT2A, CTC1, ANKRD26, BCOR, KAT6A, GFI1 and MLLT3.

Imaging examinations

The patient did not have an imaging examination.



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Figure 1 Pathology of the right buccal mass puncture showed spindle cell rhabdomyosarcoma.

FINAL DIAGNOSIS

Based on the above findings, the final diagnosis was acute myeloid leukemia (AML-M5a).

TREATMENT

On May 5, 2021, the patient was treated with a VA program (venetoclax 400 mg for 28 d and azacitidine for 7 d). Repeat bone marrow cytology suggested a state of disease remission. On June 25, 2021, the patient relapsed with acute myeloid leukemia. Multiple but ineffective platelet transfusions were performed.

OUTCOME AND FOLLOW-UP

On July 10, 2021, the patient suffered cerebral hemorrhage, which resulted in death.

DISCUSSION

In 1992, fusiform rhabdomyosarcoma was first discovered by Cavazzana *et al*[4]. Rhabdomyosarcoma is a malignant tumor arising from embryonic mesenchymal tissue that occurs most commonly in children and adolescents and rarely in adults and accounts for 2%-5% of all tumors. When it is present in the head and neck, the prognosis is often poor, and the clinical manifestations are more malignant[5]. According to the WHO classification, rhabdomyosarcoma is divided into embryonal rhabdomyosarcoma, acinar rhabdomyosarcoma, polymorphic rhabdomyosarcoma and spindle cell/sclerosing rhabdomyosarcoma. Rhabdomyosarcoma has a very low incidence in adults, accounting for less than 1% of all adult malignancies and 3% of adult soft tissue sarcomas[6]. Rhabdomyosarcoma generally has a soft morphology, and its gross appearance is mainly a cauliflower-like or polypoid mass that can invade surrounding tissues, cause tissue adhesion, and subsequently invade bone[7]. Microscopically, the tumors were diverse and mainly composed of small round cells. After HE staining, the rhabdomyosarcoma cells showed small, elongated nuclei with frequent mitotic activity, a reddish cytoplasm, and a clear stroma. Immunohistochemistry revealed SMA (+), MyoD1 (+), myogenin (+), CD99 (+), and vimentin (+), with MyoD1 and vimentin being specific markers of striated muscle.

The immunophenotype of the patient in this case was MyoD1 (+) and Myogenin(+), which was consistent with the findings of other reports[8]. The optimal treatment method for rhabdomyosarcoma has not yet been determined, and there is no standardized systematic treatment method. Currently, local extensive resection combined with postoperative chemotherapy is the main treatment method.

The causes of secondary leukemia include chemotherapy, radiotherapy, genetics, and other factors, and secondary leukemia caused by chemotherapy drugs ranks first. The main chemical drugs that can cause secondary leukemia are alkylating agents (such as cyclophosphamide, mefalam, nitrogen mustard, *etc.*), topoisomerase II inhibitors (etoposide, doxorubicin, mitoxantrone, *etc.*), dioxypyrazine drugs, *etc.* The disease progression of leukemia caused by alkylating agents is gradual and is usually accompanied by myelodysplastic syndrome, with a median latency of 5 yr (range 1-14 yr) [9]. The median latency of leukemia caused by topoisomerase II inhibitors was 1.5 yr[9]. The patient in this case had a history of rhabdomyosarcoma and was cured after multiple rounds of chemotherapy. Multiple chemotherapy cycles may also cause secondary leukemia, and the duration from chemotherapy to secondary leukemia was 1.5 yr. Studies have

shown that the incidence of secondary leukemia increases 7-fold when etoposide and/or cyclophosphamide are used[10].

Compared with those of primary leukemia, secondary leukemia often has worse clinical outcomes, including a significantly worse complete remission (CR) rate, relapse-free survival rate and overall survival rate[11]. This may be related to the older age and worse organ function of patients with secondary leukemia. In addition, these patients may have persistent malignant disease or experience recurrence of primary malignancies. Previous chemotherapy or radiotherapy leads to hematopoietic failure and prolongs bone marrow suppression after treatment for acute myeloid leukemia, which can easily cause more serious treatment-related complications.

The median survival time of patients with secondary leukemia is 6-12 mo, and the main cause of death is the tumor itself[12]. Molecular mutations and cytogenetic abnormalities, such as TP53 mutations, may be more common in patients with secondary leukemia and are associated with resistance to conventional chemotherapy[13]. The median survival time of patients with secondary leukemia is 6-12 mo, and the main cause of death is the tumor itself[12]. However, molecular mutations and cytogenetic abnormalities, such as TP53 mutations, which are associated with resistance to conventional chemotherapy[13], may be more common in patients with secondary leukemia.

With the progress of medical technology, there have been obvious breakthroughs in understanding the etiology and pathogenesis of secondary leukemia and in its treatment. At present, the best method for treating secondary leukemia is still unclear, and intensive chemical treatment is still one of the main methods for treating secondary leukemia. Godley *et al*[12] conducted a study on 32 patients with secondary leukemia. After treatment with high-dose cytarabine + mitoxantrone, the complete response rate was 66%, the partial response rate was 16%, and the overall response rate was 82%. The mortality rate after treatment on the 30th day was 9%. At present, a variety of small molecule inhibitors targeting Bcl-2 have been marketed, among which venetoclax has been widely used. Venetoclax is an oral, potent, selective Bcl-2 inhibitor. Several studies have reported clinical trials of venetoclax in elderly AML patients who cannot tolerate chemotherapy. The results showed that the median CR rate was 62%, the median response time was 1 mo, the median survival time was 18.4 mo, and the 1-yr OS was 70.4%[14]. Venetoclax in combination with the hypomethylating agents azacitidine and decitabine is a new treatment for refractory relapsed leukemia. At present, venetoclax is mainly used in elderly patients with acute leukemia and recurrent/refractory acute leukemia, and it is still rarely used for the treatment of primary drug-related secondary leukemia.

In this case, the patient had received multiple rounds of chemotherapy for the treatment of spindle rhabdomyosarcoma and was physiologically resistant to chemotherapy. Therefore, she first received 100 mg azacitidine on days 1 to 7 and 400 mg venetoclax once daily for 28 d. She achieved CR, but the remission time was not long. Finally, the complications of cerebral hemorrhage led to death. It was also suggested that the prognosis of secondary leukemia patients was very poor, which was basically consistent with reports in the literature. In this case, the patient had received multiple rounds of chemotherapy for the treatment of spindle rhabdomyosarcoma and was physiologically resistant to chemotherapy. Therefore, she first received 100 mg azacitidine for days 1 to 7 and 400 mg venetoclax once daily for days. She achieved CR, but the remission time was not long. Ultimately, cerebral hemorrhage complications led to death. These findings also suggest that the prognosis of secondary leukemia patients is extremely poor, which is basically consistent with reports in the literature.

CONCLUSION

In summary, the incidence of rhabdomyosarcoma in adults is extremely low, and secondary leukemia caused by rhabdomyosarcoma is even rarer. Secondary leukemia has a very poor prognosis and a low overall survival rate. Despite the development of various new treatment technologies in recent years, we still need to continue to explore treatment options.

FOOTNOTES

Author contributions: Zheng L designed the report and wrote the paper; Zhang FJ revised the paper; all the authors have read and approved the final version of this manuscript.

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