Efficacy of Vinblastine and Methotrexate in a Childhood Patient with Progressive Desmoid Fibromatosis of the Lower Jaw: A Case Report

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Desmoid fibromatosis (DF) is defined as a borderline tumor of the soft tissues with a low malignant potential. The most common tumor sites are the extremity, trunk, abdominal cavity, and head and neck. Surgical resection has been the standard treatment for DF. However, there are concerns regarding long-term cosmetic outcomes or functional morbidity associated with surgery particularly in the head and neck. Recently, the use of the front-line wait-and-see strategy and pharmacologic treatment such as chemotherapy for progression has been proposed as tumors can spontaneously stabilize and regress. Herein, we report the efficacy of vinblastine (VBL) and methotrexate (MTX) in a childhood patients with DF. A 21-month-old female patient with a 4-cm tumor at the left lower jaw was diagnosed with DF. She did not initially receive any therapies (wait-and-see) according to the recent treatment guidelines. However, the tumor gradually progressed, and the patient was managed with COX2 inhibitor. Since the tumor was not controlled with such a treatment and tracheal exclusion caused by the mass was a cause of concern, the patient was managed with chemotherapy with VBL and MTX. VBL and MTX were administered weekly for 26 weeks, every other week, and further for 26 weeks. The tumor size gradually decreased with VBL and MTX. Magnetic resonance imaging revealed no evidence of the disease at the end of chemotherapy. Good cosmetic outcomes were achieved, and recurrence was not observed after 24 months of follow-up.

Key words: desmoid fibromatosis, child, lower jaw, vinblastine and methotrexate

INTRODUCTION

Desmoid fibromatosis (DF) is an extremely rare condition and is referred to as a borderline tumor arising from the soft tissues [1]. It often develops in the extremity, trunk, abdominal cavity, and head and neck [2]. Head and neck DF accounts for 7%–15% of all cases [3]. Complete resection is an effective treatment in patients with DF. However, resection in the head and neck region is often challenging to perform because of neurovascular structures and cosmetic issues [4]. Recently, Kasper *et al*. reported that the wait-and-see (W&S) strategy is the primary choice of treatment for DF in all populations as the tumors can spontaneously stabilize and regress [5]. If the tumors progress during the monitoring period, several medical approaches such as surgery, radiation, and chemotherapy can be used [6]. Herein, we present the efficacy of vinblastine (VBL) and methotrexate (MTX) in a childhood patient with progressive DF of the lower jaw.

CASE

A 21-month-old female patient presented with a 2-week history of a rapidly growing, painless, left submandibular mass (Fig. 1). Upon examination, a firm and fixed mass was noted at the left submandibular area without nerve dysfunction. Ultrasonography revealed a 4.0 × 3.8 × 3.7-cm heterogeneous but solid-appearing mass with a high internal vascularity. Magnetic resonance imaging (MRI) showed a mass lesion at the left lower jaw with mandible destruction (Fig. 2). Biopsy was performed on the mass lesion.

Histopathological examination revealed a bland spindle-cell neoplasm. The specimen stained positive for β-catenin but negative for S-100, smooth muscle antibody, and desmin. Based on these results, the patient was diagnosed with DF. Whole-body computed tomography scan revealed no signs of other tumoral lesions. According to the recent W&S strategy, the patient was monitored without treatment. However, the tumor gradually grew within half a year. Therefore, oral COX2 inhibitors (Celecoxib) at a dose of 50 mg/day was initiated as the first-line treatment. After 4 weeks of treatment, the tumor continually grew causing challenges in opening the mouth. MRI showed a large mass, with a diameter of 10 cm, in the lower jaw that extended to the trachea (Fig. 3A).

Chemotherapy with VBL and MTX was initiated due to tracheal exclusion. VBL and MTX were administered via intravenous injection at a dosage of 5 and 30 mg/m^2, respectively. VBL and MTX was administered weekly for 26 weeks, every other week, and further for 26 weeks, with a total treatment sessions of 39. The mass size gradually decreased after chemotherapy initiation (Fig. 3B). The mass lesion had almost subsided after the end of chemotherapy (Fig. 3C). All

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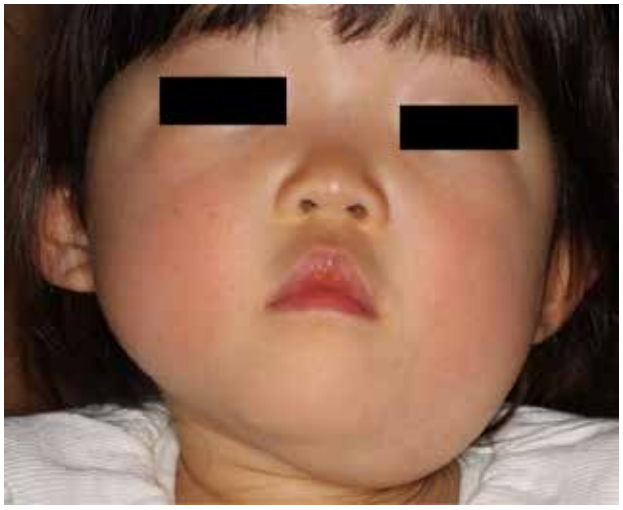

Fig. 1 Clinical appearance upon admission

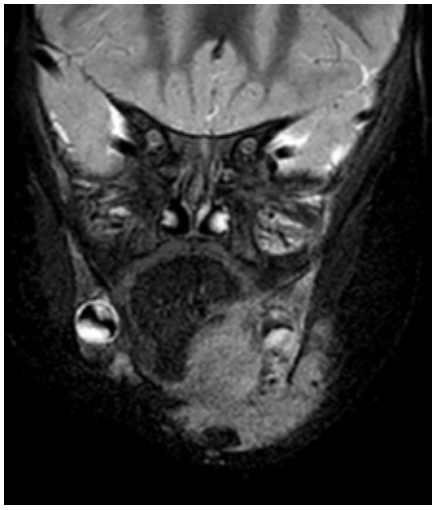

Fig. 2 Coronal magnetic resonance imaging (MRI) findings upon admission
MRI revealed a mass lesion at the left lower jaw with mandible destruction.

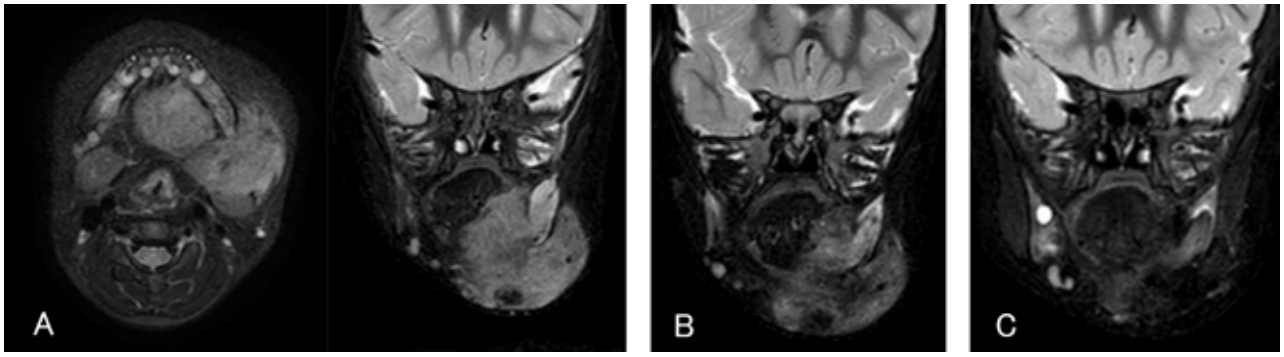

Fig. 3 Magnetic resonance imaging (MRI) findings before and after chemotherapy with vinblastine and methotrexate
A. MRI revealed a large mass in the lower jaw that extended to the trachea before chemotherapy.
B. The mass size gradually decreased at 13 weeks after chemotherapy initiation.
C. The mass had almost subsided after the end of chemotherapy.

chemotherapeutic courses could be completed without any severe side effects. Treatment was postponed for only 1 week due to neutropenia, and any associated infections were not observed. The patient remained in complete remission at 24 months after therapy.

DISCUSSION

DF is classified by the World Health Organization as borderline grade because of its propensity for locally invasive growth and the absence of metastatic potential [1].

Furthermore, DF has extreme features indicating the potential for spontaneous regression or progression [5]. Approximately 7%–15% of DF develops in the head and neck [3]. In pediatric DF of the head and neck, the tumors commonly arise from the mandible and submandibular area (40%) [7]. Surgical resection is the primary treatment for DF. However, it may be challenging to perform due to neurovascular structures and cosmetic issues particularly in the head and neck [4, 8]. More than 50% of patients have a slow growing or potentially regressive disease, with treatment reserved to progressing cases. Thus, recently, a stepwise approach including the front-line W&S strategy has been proposed for DF [5, 6, 9]. Based on these strategies, the only caveat is that tumors located at critical sites such as the head and neck, pelvis, and intra-abdominal cavity must be cautiously followed-up. This is because regional growth can be an issue or even life-threatening in exceptional cases. Further, patients with important symptoms may occasionally skip the initial observation. The W&S strategy was first selected in this case since the patient did not have any symptoms at diagnosis. However, the tumor size gradually increased during observation. COX2 inhibitors or antihormonal agents such as tamoxifen should be recommended as the initial pharmacological treatment [10, 11] if substantial progression occurs during the initial observation period. The side effects of antihormonal agents that interfere with physiological hormone expression are evident in young female patients. Rather than antihormonal agents, COX2 inhibitor was used as the initial pharmacological treatment in our patient. This is because the patient's tumor size gradually decreased and the side effects of tamoxifen had been a cause of concern.

However, COX2 inhibitor was not effective, and the tumor grew further. Low-dose chemotherapy with VBL and MTX is recommended in case of failed hormonal/COX2 inhibitor therapy [12, 13]. Skapec *et al.* performed a prospective phase 2 trial using VBL and MTX for childhood DF [13]. Based on this trial, 62% of patients completed chemotherapy without disease progression. However, 50% of patients have experienced disease progression after chemotherapy discontinuation. Neutropenia (79%) was the most common toxicity. Further, 18% of patients presented with grade 4 neutropenia. The patients' absolute neutrophil count increased to $>500/\mu l$ within 1 week. In our case, according to the phase 2 regimen, chemotherapy with VBL and MTX was initiated since the tumor grew toward the trachea and tracheal exclusion had been a cause of concern. The tumor stopped growing after chemotherapy initiation. The tumor size gradually decreased and almost completely subsided after the end of chemotherapy.

Although the treatment was postponed for 1 week due to neutropenia, other severe side effects were not observed. Therefore, the 52-week treatment could be completed.

CONCLUSION

DF is an extremely rare disease with unpredictable behavior and heretical characteristics. A treatment algorithm including the W&S strategy has recently been established. Although the W&S strategy is recommended as appropriate, therapeutic intervention is required in case of progression. Surgical resection for DF of the head and neck is challenging to perform due to the involvement of major neurovascular structures. Nevertheless, combination chemotherapy with VBL and MTX might be effective against progressive DF.

DECLARATION OF CONFLICTING INTERESTS

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

ETHICAL APPROVAL

Our institution does not require ethical approval for reporting individual cases or case series.

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INFORMED CONSENT

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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