Adult Rhabdomyosarcoma in the Nasal and Paranasal Sinuses Showing Complete Local Response to a Combination of Chemotherapy and Radiotherapy Using 3D-CRT and IMRT

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Case Report

Adult Rhabdomyosarcoma in the Nasal and Paranasal Sinuses
Showing Complete Local Response to a Combination of
Chemotherapy and Radiotherapy Using 3D-CRT and IMRT

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Abstract We report on a 69-year-old woman with rhabdomyosarcoma arising from the
nasal and paranasal sinuses. She was referred to our hospital with a reduced ability to
smell and impaired bilateral vision, narrowing of the visual field, and left facial pain.
Computed tomography (CT) revealed a large tumor in the nasal and left paranasal sinuses
invading the left orbital cavity and anterior skull base, and lymph node swellings in the
submental and left accessory nerve areas. A biopsy specimen from the nasal tumor was
diagnosed histologically as a rhabdomyosarcoma, alveolar type. Because the intra-
cranial direct invasion and distant metastases to the thoracic spine were suspected by
pretreatment examination, our case was determined to be inoperable by a head and neck
surgeon. Radiotherapy with a total dose of 60 Gy was carried out to control the primary
disease. The three-dimensional conformal radiotherapy (3D-CRT) and intensity-
modulated radiotherapy (IMRT) techniques were used in order to reduce the doses to risk
organs. Combined with radiotherapy, chemotherapy was also performed for the treat-
ment of lymph-node metastases and distant diseases. After the treatment was completed,
the primary tumor and lymph-node metastases disappeared completely; there was no
sign of re-growth during the follow-up period. Chemoradiotherapy may be an effective
treatment also for inoperable adult rhabdomyosarcoma in the head and neck region.
Furthermore, the 3D-CRT and IMRT techniques are both useful methods of radiotherapy
for this disease.

Introduction

Rhabdomyosarcoma (RMS) is a highly
malignant and not uncommon tumor that
accounts for 15-20% of all soft tissue sar-
comas. It occurs largely, but not exclusively,
in the pediatric population. The
intergroup Rhabdomyosarcoma Study
Group (IRSG) has recruited the majority of
children (defined by the IRSG as under 21
years old) with newly diagnosed RMS in the
United States into protocols designed to
investigate the biology of this disease and
therapies for it. Based on the results of
these studies, generally accepted treatment guidelines for pediatric RMS include gross total resection with preservation of function, systemic chemotherapy using combinations of vincristine (VCR), actinomycin-D (act-D), and cyclophosphamide (CPA), and radiation therapy for all but completely resected tumors of the embryonal subtype. As a result of this multimodal approach, the prognosis for children with RMS has improved dramatically, and more than 70% of children with localized RMS can be cured.

On the other hand, RMS in adults is rare; soft tissue sarcomas make up less than 1% of all adult malignancies, and RMS accounts for 3% of all soft tissue sarcomas. The standard treatment strategy for RMS in adults has not been established yet. Therefore, the prognosis of RMS is generally poorer in adults than in children. We describe here a case of adult RMS showing marked response to a combination of chemotherapy and radiotherapy using 3D-CRT and IMRT.

Case

A 69-year-old woman with a reduced ability to smell, impaired bilateral vision, narrowing of the visual field, and left facial pain was referred to our hospital. Computed tomography (CT) revealed a tumor in the nasal and left paranasal sinuses with destruction of bone and invasion into the orbital cavity and anterior skull base; in addition, the lymph nodes were swollen in the submental and left accessory nerve areas (Fig. 1). Bone scanning and magnetic resonance imaging (MRI) showed metastatic bone tumor in the fourth, tenth, and
eleventh thoracic vertebrae without any symptoms. A biopsy specimen from the nasal tumor was diagnosed histologically. On light microscopic examination, the tumor was composed of relatively small round cells with acidophilic cytoplasm and eccentric nuclei. The final pathological diagnosis was RMS, alveolar type (Fig. 2). Because the tumor invaded directly into the brain and because of the existence of bone metastases, a head and neck surgeon determined our case to be inoperable.
Initially, we considered radiation therapy in order to gain local control because of the severity of the symptoms, visual disturbance, facial pain, etc. However, our case also had lymph node metastases and bone metastases, so we decided to combine systemic chemotherapy with radiotherapy. Radiotherapy with a 6 MV X-ray was delivered to the primary tumor in the nasal and paranasal sinuses with three non-coplanar fields followed by an intensity-modulated radiotherapy (IMRT) boost with six coplanar fields. The total radiation dose was 60 Gy, 46 Gy with three non-coplanar fields to a wide region, and 14 Gy with the IMRT boost, with a fractionated dose of 2 Gy daily. The dose distribution and dose-volume histogram (DVH) in this case is shown in Fig. 3. By using the IMRT technique as a boost irradiation, we reduced the radiation dose to sensitive organs such as the right optic nerve and brain stem. Three cycles of combined chemotherapy (VAC regimen) including vincristine (VCR, 1.4 mg/m², day 1), actinomycin-D (act-D, 0.4 mg/m², day 1, 2), and cyclophosphamide (CPA, 600 mg/m², day 1) were performed concurrently with appropriate granulocyte colony-stimulating support. After chemoradiotherapy, the tumor disappeared completely from the nasal and paranasal sinuses (Fig. 4). Furthermore, the initial symptoms were improved except for the left visual loss. The only observed adverse effect related to the treatment was radiation-induced mucositis of less than grade 2 in the nasal cavity, paranasal sinus, and hard palate. Unfortunately, the bone metastases spread to multiple sites, including the spine, ribs, and femoral bone, and the patient died of this disease 12 months after completing the initial treatment. However, there were no signs of loco-regional recurrence before she died.

Discussion

Rhabdomyosarcoma (RMS) is the most common sarcoma in the pediatric population. RMS is classified into three histological subtypes: embryonal, alveolar, and pleomorphic.8-11) Embryonal RMS is the most common in childhood, and more than 70% of children with localized RMS can be cured with multidisciplinary treatment protocols that include chemotherapy.7 In contrast, RMS in adults is rare. In adults, pleomorphic RMS is the most common subtype, and this subtype is refrac-
Embryonal RMS is reported to have a relatively good response to multidisciplinary treatment protocols, including radiotherapy and chemotherapy, in adults as well as in children. On the other hand, there has not been a sufficient evaluation of therapies for the alveolar type of RMS. In our present case, the tumor, which was alveolar, showed good local response to radiotherapy and chemotherapy. Ng et al. reported that alveolar-type RMS in the uterine cervix also responded well to chemotherapy or radiation therapy. Radiotherapy combined with chemotherapy may also be effective for alveolar-type RMS in adults.

To obtain local control of RMS in children, a total dose ranging from 35 to 66 Gy is required in radiotherapy. In adult RMS, a radiation dose of more than 50-60 Gy has been reported to be necessary to gain local control. In our case, the tumor invaded important at-risk organs such as bilateral optic nerve, optic chiasm, and brain stem. Therefore, it was difficult to deliver radiation doses sufficient for local control of the primary tumor using the conventional technique. As a result, we used 3D-CRT plus IMRT in this case and delivered a total dose of 60 Gy to the primary tumors without overdosage to sensitive organs such as the right optic nerve, brain stem, and temporal lobe. Radiation therapy with 3D-CRT and/or IMRT is considered very useful for the treatment of invasive tumors of the head and neck, because it applies an effective dose to the tumor while minimizing radiation to sensitive organs.

Pediatric RMS has a standard chemotherapy regimen: a combination of VCR, act-D, and CPA (VAC). For adult RMS, there is no standard regimen of chemotherapy. It has been reported that the pediatric protocols for chemotherapy were not effective for prostatic RMS in adults. In contrast, Takahashi et al. have reported a patient with embryonal RMS in axilla, who was successfully treated by radiotherapy combined with chemotherapy using the VAC regimen. In our case, chemotherapy with the VAC regimen was combined with radiotherapy concurrently. This combined method was well tolerable and very effective for our patient. Considering that the metastatic cervical lymph node that were not irradiated also disappeared after treatment, it is considered that the tumors in this case were sensitive to the VAC regimen.

Our case, with alveolar-type RMS, was treated with radiotherapy using 3D-CRT plus IMRT and systemic chemotherapy with a VAC regimen. Although adult RMS is generally reported not to be radiosensitive or chemosensitive compared to RMS in children, we were able to control loco-regional disease and relieve the symptoms by this combined treatment. Chemoradiotherapy may be an effective treatment option also for inoperable adult RMS in the head and neck region. Furthermore, the 3D-CRT and IMRT techniques are both useful radiotherapeutic methods for this entity. However, further efforts to develop more effective chemotherapy regimens to control systemic diseases are necessary to improve survival in adult RMS.

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Chemoradiotherapy for Adult Rhabdomyosarcoma

(和文抄録)

3D-CRT・IMRT を用いた放射線治療と化学療法の併用にて
局所制御が得られた鼻腔・副鼻腔原発横紋筋肉腫の 1 例

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症例は 69 歳、女性、鼻腔および副鼻腔原発横紋筋肉腫で、両側視力低下、視野狭窄および嗅覚異常にて九大病院に紹介受診。CT 上、腫瘤は鼻腔および副鼻腔を充満し、左眼窩内および頭蓋底部への浸潤を認めた。また、オトガイ下および左副神経領域にリンパ節転移を考えられるリンパ節腫大を認めた。鼻腔腫瘤からの生検にて、横紋筋肉腫・胞巣型と診断された。頭蓋底部への浸潤および胸椎転移を認め、手術適応なしと判断された。治療として、原発巣への放射線治療 60Gy / 30 分割および化学療法 (VAC 療法) 3 サイクルを行った。放射線治療には、局所線量増加と周囲リスク脳器線量低減目的にて、3 次元原体照射 (3D-CRT) および強度変調放射線治療 (IMRT) を用いた。治療後、原発腫瘍およびリンパ節転移は消失した。症例は、12 ケ月後に骨転移の増悪にて死亡したが局所領域の再発は見られなかった。化学療法および放射線治療の併用は成人の横紋筋肉腫においても有効であり、3D-CRT や IMRT を用いた放射線治療は局所制御および副作用低減において有用と考えられた。