Radiotherapy for recurrent juvenile nasopharyngeal angiofibroma

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SUMMARY

Juvenile nasopharyngeal angiofibroma (JNA) is a rare paediatric tumour known for its local destructiveness and high recurrence rate. Surgery is the primary treatment modality for JNA, though other options, such as hormonal therapy, embolisation and radiotherapy, exist for inoperable cases. The location of the tumour makes surgical intervention challenging. A 14-year-old male presented with epistaxis and headaches as the chief complaints and was diagnosed with nasopharynx angiofibroma by computed tomography (CT) scan in 2018. Pre-operative embolisation was performed and followed by surgical removal of a 4 cm tumour in January 2019. Pathological examination revealed CD34 positivity, S100 negativity and Ki-67 positivity (5 to 10%), confirming angiofibroma. In October 2019, a 3.6 cm recurrent tumour was treated with embolisation and a second surgery. Pathological findings again confirmed JNA. The patient underwent four surgeries in total, but epistaxis persisted. In 2021, local radiotherapy was administered using intensity-modulated radiation therapy (IMRT) at a dose of 60 Gy in 25 fractions. Serial magnetic resonance imaging (MRI) post-radiotherapy showed a decreasing tumour size, with no further epistaxis and no observed radiation side effects 2 years post-treatment. Radiation therapy remains a strong alternative for managing recurrent JNA.

INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is a rare tumour of the nasopharynx, around less than 1% of all head and neck cancers, and typically affects young males between the ages of 14 to 25 years.[1,2] It originates from vascular endothelial cells or fibroblasts and has a vasoproliferative nature, resulting vascular and stromal components appearance in pathological findings.[3,4] The primary clinical manifestation of JNA is unilateral nasal obstruction accompanied by epistaxis.

Definitive diagnosis is achieved through angiography, which can also serve as an embolisation therapy.[2] Surgical treatment aims to remove the tumour, but JNA often presents with tumours at the base of the skull, where resection is difficult. This can also interfere with natural facial growth in adolescent patients and lead to higher morbidity rates. Endoscopic JNA could be an alternative to avoid craniofacial alterations. On the other hand, radiotherapy remains an effective primary treatment and adjuvant post-surgery option with residual cases.[5] Therefore, despite being histologically benign, JNA is locally invasive and associated with a high rate of persistence and recurrence, primarily due to incomplete surgical resection. The aim of this report is to highlight the use of a slightly hypofractionated radiation dose of 60 Gy in 25 fractions in a highly recurrent case of JNA.

CASE PRESENTATION

A 14-year-old male came with epistaxis and headaches as a chief complaint, the first computed tomography (CT) scan in 2018 showed nasopharynx angiofibroma, Andrews staging type 2 with destruction at the nasal cavity and left ethmoid (Figure 1).

Preoperative embolisation was performed, followed by surgery to remove a 4 cm tumour in January 2019. The margins were not entirely clear, with some evidence of residual tumour. Pathological findings with CD34 positive, CD31 positive, S100 negative and Ki-67 5 to 10% positive suggested angiofibroma.

In October 2019, 3.6 cm tumour recurred with epistaxis, and another embolisation followed by surgery was performed for a second time (Figure 2).

Pathological findings also suggested juvenile angiofibroma. Residual disease persisted, and a total of four surgeries were performed. Despite these efforts, epistaxis continued to occur, necessitating several blood transfusions. Local radiotherapy was performed using IMRT dose 60 Gy in 25 fractions in 2021.

The target for radiotherapy was the local tumour fuse with Magnetic resonance imaging (MRI) as gross tumour volume (GTV) with a 5 mm margin as planning target volume (PTV) and was performed using IMRT (Figure 4).

A total dose of 60 Gy is divided into 25 fractions. All organs-at-risk (OARs) doses were within the tolerance limits of conventional dose constraints, with maximum doses of adjacent organs as follows: right eye, 2116.4 cGy; left eye, 2729.3 cGy; and pituitary gland, 4921.4 cGy. The mean haemoglobin level during this treatment is 13.5 mg/dL. Serial

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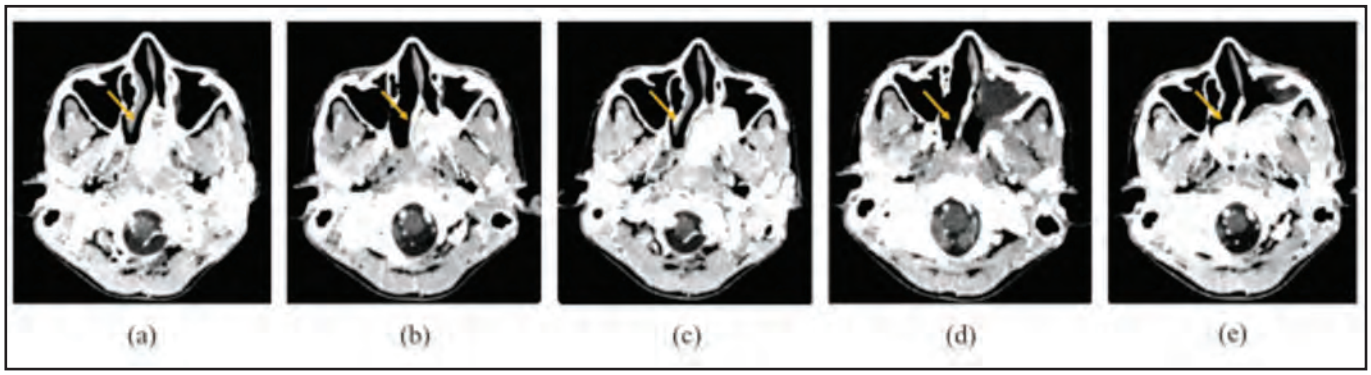

Fig. 1: Serial multislice computed tomography (MSCT) before radiotherapy: (a) pre-operative 1 in 2018, (b) pre-embolisation pre-operative 2 in 2019, (c) post-operative 2 in 2019, (d) post-operative 3 in 2020, (e) post-operative 4 in 2021. Orange arrows indicate the tumour

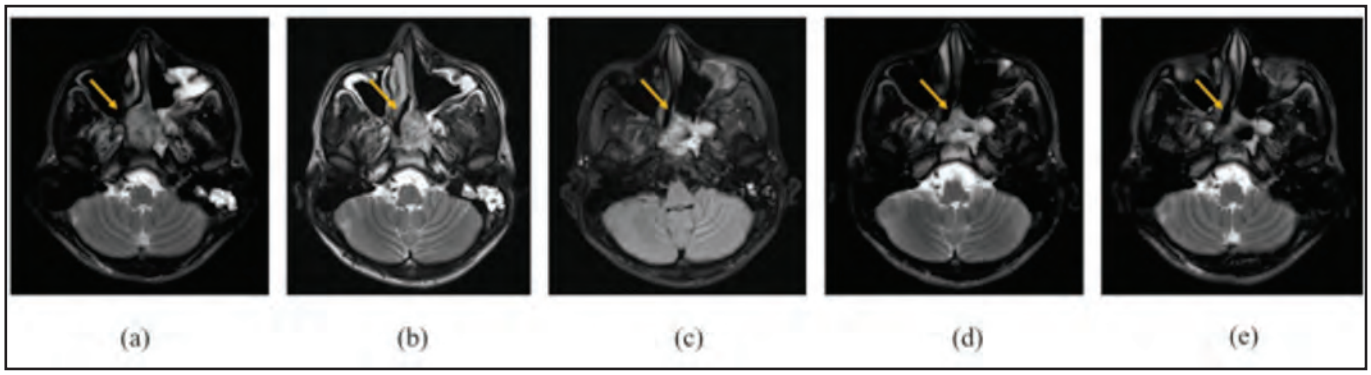

Fig. 2: Serial magnetic resonance imaging (MRI) T2 images showing tumour size: (a) Pre-radiotherapy (RT) (AP 3.7 × LL 2.6 × CC 2.73 cm), (b) 6 weeks after RT, (c) 6 months after RT, (d) 12 months after RT, and (e) 18 months after RT (AP 2.5 × LL 2.13 × CC 1.3 cm)

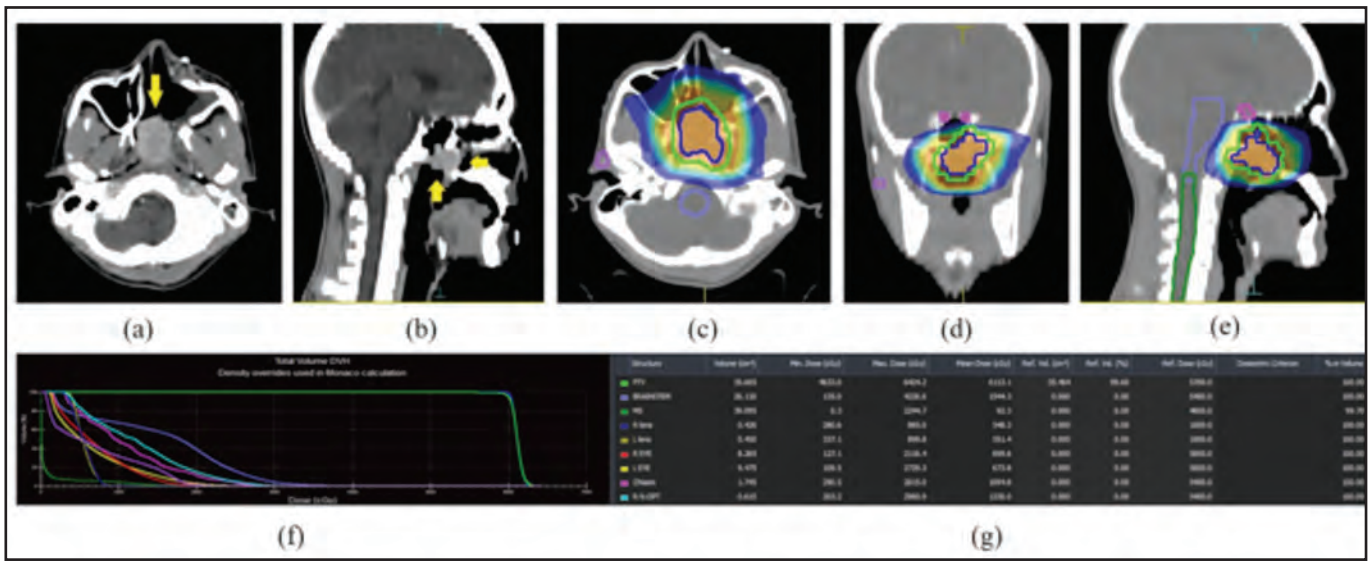

Fig. 4: Illustration of computed tomography (CT) simulation showing the location of the tumour in (a) axial and (b) sagittal views; delineation and dose distribution in (c) axial, (d) coronal and (e) sagittal views. Gross tumour volume (GTV) marked in blue, planning target volume (PTV) marked in green (expanded 5 mm from GTV); (f) dose volume histogram, and (g) dose volume statistic

MRIs were performed and always showed a decreasing size tumour even after 18 months post radiotherapy with no more epistaxis happening and no radiation side effects observed. Additionally, no growth retardation, panhypopituitarism, temporal lobe necrosis, cataracts and radiation keratopathy were observed after follow-up.

DISCUSSION

Treatment options for JNA are surgery and embolisation.[4,5] In this case, the patient already went for four surgeries with prior embolisation, each of them confirmed pathologically as JNA, followed by the recurrent chief complaint which was epistaxis. The surgical approach is still the first-line treatment for JNA, which is benign, proliferative and destructive.[5]

Our following approach for this case was radiotherapy given locally with the IMRT technique preferred over stereotactic radiosurgery (SRS). There are two kinds of approaches for radiotherapy conventional dose or SRS (hypofraction). Stereotactic radiosurgery is still controversial due to the tumour margin being usually unclear.4 In this case, a slightly hypofractionated radiation dose of 60 Gy in 25 fractions was selected due to the patient's highly recurrent JNA and persistent rebleeding despite prior surgeries and embolisation. This aggressive recurrence pattern necessitated a more intensive treatment approach to achieve long-term control and prevent further relapses. A previous study has shown that the radiation dose used was variable, ranging between 3,000 and 5,500 cGy, with a 2-year local control rate of 87.5% and no remarkable adverse effects.[5] Additionally, the tumour's size and anatomical location in our case posed significant challenges for complete surgical resection, requiring a higher radiotherapy dose to ensure adequate tumour control and minimise the likelihood of further recurrence. Radiotherapy is the last treatment option for JNA due to its possibility to induce secondary malignancy.[6] A previous study using proton radiotherapy reported considerable tumour shrinkage and complete remission in five out of ten patients with JNA, with the potential to provide partial or complete symptom relief.[7] However, our facility was not able to administer proton radiotherapy treatment. Additionally, proton therapy is often limited to only few medical facilities in other countries and may not be accessible to all patients. Nevertheless, in our case, the dose was also used to effectively control bleeding. Follow-up examinations and serial MRI over 18 months showed no late complications. The tumour size has decreased significantly with more necrotic regions and no further episodes of epistaxis. The MRI was performed 6 weeks after radiation, every 6 months after radiation for 2 years, and will still be performed annually or if the patient has symptoms in the future.

Based on this patient, there are a few things that can be evaluated from this case. Treatment of JNA should be done directly due to uncontrolled epistaxis could lead to hypovolemic shock. Multidisciplinary team management is important for planning and evaluating how and when to use which modalities are available in our centre. The MRI is the best non-invasive modality to evaluate disease and treatment side effects of JNA. Even though radiation-induced malignancy is still a mystery the incidence varies only from 3 to 26% in >20 years.6 Radiation dose and technique for JNA should be explored more with randomized clinical trials.

CONCLUSION

Radiotherapy can still be a reliable alternative for JNA despite its considerably small potential to induce secondary malignancy. The successful use of a slightly hypofractionated radiation dose in a highly recurrent case of JNA underscores the potential benefits and safety of higher doses in specific clinical scenarios. Radiotherapy doses and techniques for JNA are selected based on clinical judgment considering clinical symptoms, location, size of the tumour, and radiotherapy equipment owned by the centre.

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