CASE REPORT

Olfactory neuroblastoma treated with minimally invasive surgery and adjuvant radiotherapy: a case report and review of the literature

INTRODUCTION

Olfactory neuroblastoma (ON) originates from the olfactory epithelium. Unilateral nasal obstruction and epistaxis are the most common symptoms. Furthermore, headache, sinus pain, excessive lacrimation, rhinorrhea, anosmia and changes in vision may occur. Treatment modalities for ON are surgery combined with radiotherapy (RT) and/or chemotherapy. In this short communication, we report the case of a patient with a mass in the right nasal cavity who was treated by endoscopic resection and adjuvant RT.

CASE REPORT

A 34-year-old male was referred to our hospital where he presented a 6-month history of unilateral nasal obstruction and frontal headache. Endoscopic examination showed a polypoid mass in the right nasal cavity and permitted biopsy of the lesion. Histological findings documented an olfactory neuroblastoma of Grade II according to Hyam's grading system. MRI was performed, revealing a well-circumscribed lesion in the right nasal sinus, hypointense on T1 weighted and hyperintense on T2 weighted sequences (Figure 1). This disease presentation corresponded to Kadish stage B. After discussion in the multi-disciplinary tumour board, a bimodality therapeutic approach consisting of endoscopic resection followed by adjuvant radiotherapy (RT) was chosen. The patient was treated with endoscopic resection and external beam radiotherapy to the right nasal sinus with intensity-modulated radiotherapy (IMRT) technique. After 2 years follow-up, the patient is free of tumour without any late effect related to therapies. We believe that, in such patients, a treatment strategy including endoscopic resection followed by adjuvant radiotherapy may be effective and feasible and should be considered the gold standard of care.
Beam geometry in IMRT plan consisted of five coplanar 6 MV fields. The prescribed dose was 60 Gy in 30 fractions (2 Gy daily) defined as the mean dose planned to the PTV with 95% of the PTV receiving ≥95% of the prescribed dose. Dose–volume histogram was calculated for the IMRT plan for the following volumes: PTVs, spinal cord, brainstem, optic chiasm, eyes, optic nerves and lens. The dose–volume constraints were satisfied: 0.03 cc of the optic chiasm, optic nerves, eyes and brainstem should receive <54 Gy, spinal cord 45 Gy and lens 6 Gy. The dose distribution is shown in Figure 3. Radiation treatment was well tolerated with Grade 1 skin acute toxicity according to Radiation Therapy Oncology Group scale and nasal obstruction. No treatment interruption occurred. The patient is still under regular follow-up based on MRI and nasal endoscopy; after 2 years of observation, he continues to be free from disease without any late complications of therapy.

**DISCUSSION**

ON is a rare malignant tumour of the nasal cavity and it arises from the olfactory neuroepithelium located in the nasal septum. Commonly, this tumour causes unilateral nasal obstruction and epistaxis. Minor manifestations are anosmia, headache, sinus pain, rhinorrhea and epiphora. In the present case, the patient showed unilateral nasal obstruction and frontal headache. Clinically, ON is staged using the Kadish system that is based on the spread of the tumour. According to this system, stage A corresponds to tumours confined to the nasal cavity, stage B includes
lesions involving also the paranasal sinuses, whereas stage C presents masses that extend beyond the nasal cavity and paranasal sinuses. MRI scan is essential to study disease extension and usually reveals a tumour mass presenting a low-intensity signal in T1-weighted images and an iso- or high-intensity signal in T2-weighted images. A key issue consists in early histological diagnosis of ON through endoscopic biopsy. Many studies tend to divide ON into low-grade and high-grade lesions according to Hyams classification identifying two distinct entities. Malouf et al. showed that patients with high-grade ON had larger tumours, frequent lymph node involvement and more often leptomeningeal metastasis compared to low-grade ON. In our case, MRI showed a Kadish stage B ON and endoscopic biopsy revealed a low-grade ON.

The available literature indicates that a combination of surgery and RT is the best treatment approach. Although craniofacial resection is considered the gold standard surgical treatment, some recent reports suggest treating ON with minimally invasive surgery. In fact, endoscopic approaches present some advantages such as shorter surgical time and hospitalization and a better quality of life. Table 1 reports studies including treatment characteristics and outcome for olfactory neuroblastoma. Some reports showed that the addition of postoperative radiation to surgery significantly improves local control rate, and RT is the best treatment approach. Although craniofacial approaches present some advantages such as shorter surgical time and hospitalization and a better quality of life. Table 1 reports studies including treatment characteristics and outcome for olfactory neuroblastoma. Some reports showed that the addition of postoperative radiation to surgery significantly improves local control rate, and RT is the best treatment approach. Although craniofacial approaches present some advantages such as shorter surgical time and hospitalization and a better quality of life. Table 1 reports studies including treatment characteristics and outcome for olfactory neuroblastoma. Some reports showed that the addition of postoperative radiation to surgery significantly improves local control rate, and RT is the best treatment approach.

In our opinion, this case report shows that a combined modality approach with minimally invasive surgery and postoperative RT is the best treatment approach. Although craniofacial resection is considered the gold standard surgical treatment, some recent reports suggest treating ON with minimally invasive surgery. In fact, endoscopic approaches present some advantages such as shorter surgical time and hospitalization and a better quality of life. Table 1 reports studies including treatment characteristics and outcome for olfactory neuroblastoma. Some reports showed that the addition of postoperative radiation to surgery significantly improves local control rate, and RT is the best treatment approach.

In our clinical case, after discussing with the patient about the literature data regarding the prophylactic cervical irradiation, the pros and cons and the side effects, we opted for an RT volume that included the tumour bed and decided not to perform ENI owing to the limited Kadish B stage, radical surgery, absence of clinically and radiologically positive nodes and the possibility of treatment at the time of recurrence.

Furthermore, in addition to surgery and RT, chemotherapy may offer improvement in local control and reduction in the frequency of distant metastasis, especially in patients with unresectable tumours or in case of advanced disease and recurrent and metastatic lesions.

CONCLUSION

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| Study, year | Period | Patients (n) | Treatment | RT technique | Mean Dose (Gy) | Follow-up (months) | Median Survival (months) | 5-year OS | Other Survival |
|-------------|--------|--------------|-----------|--------------|---------------|-------------------|--------------------------|-----------|---------------|
| Dulguerov and Cakaterra, 1992 | 1970–1990 | 24 | S only RT only S + RT ± CT RT + CT | 2D-RT 3D-CRT | 60 | – | – | – | 5-year DSS 74% 5-year RFS 58% |
| Polin et al, 1998 | 1976–1994 | 34 | RT ± CT + S | – | 50.6 | – | 71 | 81 | – |
| Resto et al, 2000 | 1981–1998 | 27 | S only RT only S + RT ± CT | – | 61.8 | – | 71 | – | – |
| Eich et al, 2001 | 1981–1998 | 17 | RT only S + RT | 2D-RT 3D-CRT | 57.3 | 86 | 94 | – | – |
| Simon et al, 2001 | 1978–1998 | 13 | S only RT only S + RT ± CT | – | 59.4 | 75 | 60 | 61 | 5-year DFS 56% |
| Chao et al, 2001 | 1976–1996 | 25 | S only RT ± CT S + RT ± CT | 2D-RT 3D-CRT | 56.4 | 96 | – | 66.3 | 5-year DFS 56.3% |
| Gruber et al, 2002 | 1980–2001 | 28 | RT ± CT S + RT ± CT | 2D-RT 3D-CRT | 60 | 68 | – | – | 5-year LPFS 81% 5-year DFS 70% 5-year CSS 77% |
| Argiris et al, 2003 | 1981–2000 | 16 | S ± CT S + RT ± CT | – | 55 | 51 | 60 | 60 | 5-year DFS 33% |
| Diaz et al, 2005 | 1979–2002 | 30 | S only S + RT RT ± CT | – | 59.4 | 72 | – | 89 | 5-year RFS 69% |
| Castelnuovo et al, 2007 | 1999–2004 | 10 | S only S + RT RT ± CT | 3D-CRT | 56.1 | 37 | 37 | – | – |
| Bachar et al, 2008 | 1972–2006 | 39 | S only RT only S + RT ± CT | 3D-CRT IMRT | 53.13 | – | 140 | 87.9 | 5-year RFS 76% 5-year LRFS 82% 5-year LRRFS 82.5% |
| Otshin et al, 2010 | 1971–2004 | 77 | S only S + RT ± CT RT ± CT | 2D-RT 3D-CRT IMRT | 60 | 72 | – | 64 | 5-year DFS 57% |
| Platek et al, 2011 | 1973–2006 | 511 | S only RT only S + RT Neither S nor RT | – | – | – | – | 73 S + RT 68 S only 35 RT only 26 neither S nor RT | – |

(Continued)
Table 1. (Continued)

| Study, year | Period     | Patients (n) | Treatment | RT technique | Mean Dose (Gy) | Follow-up (months) | Median Survival (months) | 5-year OS | Other Survival |
|-------------|------------|--------------|-----------|--------------|----------------|---------------------|--------------------------|-----------|----------------|
| Back et al, 2012 | 1990–2009 | 17           | S only S + RT ± CT RT ± CT | 2D-RT 3D-CRT IMRT | 60 | 57.5 | 60 | 68 | 5-year DFS 62% |
| Michel et al, 2012 | 1978–2006 | 11           | S only S + RT RT + CT | – | – | – | – | 90 | 5-year DFS 54.5% |
| Modesto et al, 2013 | 1998–2010 | 43           | Multimodal therapy | 3D-CRT IMRT | 64 | 77 | – | 65 | 5-year PFS 57% |
| Kumar et al, 2013 | 2006–2010 | 15           | S + RT ± CT RT ± CT | 2D-RT 3D-CRT IMRT | 54 | 23 | 35 | 45 (4 year) | 4-year LRC 25% |
| Ow et al, 2014 | 1992–2007 | 70           | S only S + RT ± CT | – | – | 91.4 | 126.3 | 90 | 5-year DSS 90% |
| Rimmer et al, 2014 | 1978–2013 | 95           | S only S + RT ± CT | 2D-RT 3D-CRT IMRT | – | 88.6 | 224 | 83.4 | 5-year DFS 80% |
| Feng et al, 2015 | 2001–2012 | 24           | S only S + RT ± CT | – | 60 | 44 | – | 82 (3 year) | 3-year DFS 70.8% |
| Mori et al, 2015 | 1992–2013 | 17           | S + RT Multimodal therapy | 3D-CRT IMRT | – | 95 | – | 88 | 5-year RFS 74% |
| Lapierre et al, 2016 | 1993–2015 | 10           | S only S + RT ± CT | 3D-CRT IMRT | 61 | 136 | – | 90 (10 year) | 5-year PFS 70% |

2D-RT, 2-dimensional radiotherapy; 3D-CRT, 3-dimensional conformal radiotherapy; CSS, cancer-specific survival; CT, chemotherapy; DFS, disease-free survival; DSS, disease-specific survival; IMRT, intensity-modulated radiation therapy; LPFS, local progression-free survival; LRC, locoregional control; LRFS, local relapse-free survival; LRRFS, locoregional relapse-free survival; OS, overall survival; PFS, progression-free survival; RFS, relapse-free survival; RT, radiotherapy; S, surgery.
IMRT can be effective in this setting. Two years after treatment, there is no local recurrence in the nasal cavity nor late effects. Nevertheless, the possibility of late relapse requires an extended follow-up time.

**LEARNING POINTS**

1. In this case report of a rare clinicopathological entity, we showed the impact of bimodal therapy with minimally invasive surgery and adjuvant RT. This strategy has proved to be successful, representing a proof of principle for potential future studies.

2. Minimally invasive surgery is potentially feasible in olfactory neuroblastoma.

3. Adjuvant radiotherapy increases local control.

4. High-tech radiation provides a good balance between tumor control and normal tissue sparing.

5. Combination therapy is safe and effective in this setting.

**CONSENT**

Written informed consent for the case to be published (including images, case history and data) was obtained from the patient(s) for publication of this case report, including accompanying images.

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