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Anaplastic Oligodendroglioma with Cervical Metastases after Prolonged Remission Period

Hanzali Jumastapha[1,2*] and Sakina Ghauth[1]

[1]Department of Otolaryngology, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Malaysia.
[2]Faculty of Medicine and Health Science, Universiti Malaysia Sarawak (UNIMAS), Kota Samarahan, Sarawak, Malaysia.

Authors' contributions

This work was carried out in collaboration between both authors. Author HJ wrote the first draft of the manuscript and managed the literature search. Author SG was actively involved in the management of the patient and critically reviewed the draft of the manuscript prior to submission. Both authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Aims: Oligodendroglioma is thought to never metastasize outside the brain. We report a case of oligodendroglioma with cervical metastasis and to share our experience in managing this case.
Presentation of Case: A 72-year-old gentleman was referred to our clinic with a history of painless left-sided neck swelling. He had a previous history of anaplastic oligodendroglioma which was treated with surgery, radiotherapy, and chemotherapy. Fine needle cytology showed metastatic carcinoma suggestive of glial origin. We proceeded with excision of the tumour and histopathological examination confirmed it to be metastatic oligodendroglioma.
Discussion: Oligodendrogliomas account for 2.9% of all gliomas. It was previously thought to never metastasize extra-cranially. However, there have been many case reports that have proven otherwise. Literature reviews have shown that it can metastasize to any site, albeit rarely.
Conclusion: In a patient with a history of anaplastic oligodendroglioma with a progressively enlarging mass elsewhere, a diagnosis of metastatic oligodendroglioma must be included as the main differential diagnosis.

**Corresponding author: E-mail: jhanzali@unimas.my;*

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1. INTRODUCTION

Malignant gliomas are thought to never metastasize. This idea has been proven incorrect. Malignant gliomas account for about 60% of all primary brain tumours in adults. They are generally categorized into 3 types – astrocytomas, oligodendrogliomas and glioblastomas. Oligodendrogliomas account for 2.9% of all gliomas [1]. Surgical resection followed by radiotherapy and chemotherapy is the mainstay of treatment for many decades and median survival is 60 months [2,3]. We report on a case of anaplastic oligodendroglioma (AO) which has metastasized to the parotid gland and cervical lymph nodes.

2. PRESENTATION OF CASE

A 72-year-old gentleman was referred to our department from the neurosurgery unit. He had a history of hypertension and more significantly, left frontal AO diagnosed in 2004. For this, he received 3 cycles of procarbazine, lomustine, and vincristine (PCV) chemotherapy. He had local disease recurrences twice, in 2011 and 2012, where resection was done. In the former, the patient defaulted on adjuvant radiotherapy. In the latter, he completed adjuvant radiotherapy in 2013. Annual surveillance magnetic resonance imaging (MRI) showed stable disease until 2018.

He was referred to our clinic with a one-month history of left sided neck swelling and no other associated symptoms. Physical examination revealed multiple left sided neck nodes at level I, II, III, and IV. Most lymph nodes were more than 3 cm with the largest measuring 5 x 3 cm. Flexible naso-pharyngo-laryngoscopy was normal. Fine needle aspiration cytology (FNAC) showed metastatic neoplasm suggestive of glial origin.

Computed tomography (CT) scan and MRI showed multiple enlarged left intra-parotid, bilateral cervical and left supraclavicular lymph nodes of varying sizes, worse on the left, with some appearing matted. The largest one being 3.5 x 5.0 cm at left level II. The carotid arteries, internal jugular vein, and parapharyngeal space were preserved. There was no evidence of distant metastases.

We proceeded with left partial parotidectomy and left neck dissection. Histopathological examination (HPE) confirmed the diagnosis of metastatic glial tumour consistent with metastatic anaplastic oligodendroglioma. The patient did not attend his radiotherapy sessions post-operatively. He presented to our clinic again a few months later with enlarging left-sided neck nodes. A completion left parotidectomy with left neck dissection was subsequently undertaken to debulk the tumour load. He completed post-operative radiotherapy to the neck. However, the patient decided not to continue with chemotherapy.

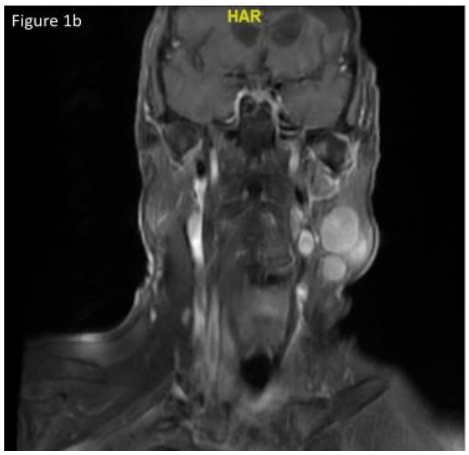

Fig. 1a. Preoperative MRI (T1 flair sequence) showing intraparotid lymph nodes
1b. Preoperative MRI (T1 with contrast) showing multiple left cervical lymph nodes

3. DISCUSSION

Oligodendrogliomas are tumours derived from oligodendrocytes which function as the supporting glial cell of the central nervous system (CNS). They commonly occur in the fourth decade of life. Most are seen in the cerebral hemispheres, especially at the frontotemporal region. They tend to invade white matter and subarachnoid space. A peculiar characteristic is that it can spread along the ventricular cerebrospinal fluid (CSF) pathway [4]. However, extraneural metastasis of primary brain tumours are rare. Liwnicz and Rubenstein reviewed 116 cases and found that extraneural metastasis occurred in 3% of cases [5]. Due to the rarity of cases, the pathway of extraneural metastasis has yet to be proven. Many theories have been postulated to explain extraneural spread of these tumours. These include repeated intracranial surgeries, presence of ventriculoperitoneal shunt, prolonged survival, and the direct impact of tumour on the meninges [6].

Even though it was generally accepted that CNS tumours do not metastasize, Zimmerman have demonstrated that malignant glioma cells are able to grow extracranially by transplanting murine glioma cells into its pleural and peritoneal cavities [7]. Numerous cases of distant metastases of primary gliomas have been published. The most common factor present in all these patients is a history of previous surgical resection [8-10]. This may be due to the incomplete closure of dura or any bony defects after surgery. It was hypothesized that there is a link between the cranial perineural spaces and lymphatic plexus of the neck. In 1983, McComb demonstrated that the lymphatic drainage of CSF into extracranial tissues do exist [11]. This can possibly explain the high incidence rate of metastases in cervical and retro-auricular lymph nodes. Another interesting observation is that post-operative extracranial gliomatous metastases usually occur on the same side. Possibly as a result of tumour cells being washed into the lymphatic drainage system.

Recent research have shown that a type of lymphatic system, termed as the glymphatic (glial-lymphatic) system, functions similar to lymphatic drainage [12]. Animal studies have shown that lymphatic vessels are present in the dura itself [13]. The vessels are located on each side of the main dural sinuses, such as superior sagittal sinus and transverse sinus. They confluence at the base of skull and then drain to the deep cervical lymph nodes. MRI studies in humans using gadobutrol tracer shows *in-vivo* drainage of CSF to cervical lymph nodes [14]. Compared with animal models, CSF drainage to cervical lymph nodes appears to be slower in human models. Also, in humans, it is thought that meningeal lymphatic vessels maybe capable of carrying leukocytes. Immunohistochemical analysis of meningeal lymphatic vessels in mice found T-cells, $MHCII^+$ cells, $CD11^+$ cells and $B220^+$ cells [15].

Other pathways for extracranial spread include the haematogenous pathway and the cerebrospinal pathway. In the former, it is thought that injury to blood vessels during surgery may open a pathway for tumour cells to travel. However, it does not explain why there is a long remission period after surgery [16]. It was reported that a patient had a disease course of 149 months, from initial diagnosis until she succumbed to multi-organ failure due to metastasis [17].

Literature review by Mazza et al found that AO may metastasize to any site. Extracranial sites include bone, bone marrow, lymph nodes, spinal cord, lung, liver, spleen, pancreas, thymus, chest wall, meninges, and breast [18,19]. The median time of initial diagnosis until metastasis is 34 months. In patients who develop extracranial metastases, the median survival after detection of extracranial metastasis is increased to 18 months if treated compared to the untreated patients of 2.5 months [18].

The mainstay of treatment for oligodendroglioma is surgical resection and post-operative radiotherapy. However, in patients with 1p19q deletion, survival time may be doubled with the addition of PCV chemotherapy with radiotherapy [20,21]. Salvage surgery for local recurrences may play a role in preventing disease relapse [22]. Unfortunately, there is no consensus on effective treatment for patients who develop extracranial recurrences. Salvage surgery, chemotherapy, and irradiation to metastatic sites may help prolong survival but there is no concrete data to support this.

4. CONCLUSION

In our case, even though rare, it is possible that cervical lymph node metastasis can occur in patients even without local intracranial recurrence. It is important to keep in mind of possible metastases in patients with history of

long remission of disease. Recent new data on the glymphatic system have shown a connection between the CSF and deep cervical lymph nodes. Debulking of tumour with post-operative chemotherapy may increase survival, however data to support this are scarce.

CONSENT

All authors declare that written consent was obtained from the patient prior to publication of this case report.

ETHICAL APPROVAL

As per international standard, written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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