Review and Research on Cancer Treatment
Volume 8, Issue 1 (2022)

If subarachnoid haemorrhage occurs, is it worth to look further to rule out cancer? A Case Report of a young man for whom neurosurgery saved vitality, behaviour and abilities

Marta Donderska[1], Zuzanna Czudy[1], Milena Matuszczak[1], Zuzanna Wardęga[1], Piotr Defort[1], Marcin Kot[1]

[1]Neurosurgery Center University Hospital, Collegium Medicum University of Zielona Gora, 28 Zyty Str., 65- 417 Zielona Gora, Poland

Corresponding author: Marcin Kot, Neurosurgery Center University Hospital, Collegium Medicum University of Zielona Gora, 28 Zyty Str., 65- 417 Zielona Gora, Poland, m.kot@cm.uz.zgora.pl

ABSTRACT

A 26-year-old patient with suspected SAH was admitted to hospital. A CT scan was performed to exclude haemorrhage. This allowed subarachnoid haemorrhage to be ruled out, and nodular changes from the oedematous zone and the effect of compression of the mass were visualised. An additional imaging study – MRI with contrast – was performed to establish the diagnosis. The examination visualised a tumour measuring 45 x 45 x 32 mm, part of which was located in the nasal cavity and rhinorrhea on the right side with stenosis at the level of the rhinorrheal lamina. The tumour had a heterogeneous structure with cystic spaces, posthemorrhagic foci and an abundant network of pathological vessels. There was oedema, wedging under the brain sickle of approximately 14 mm and compression of the right lateral ventricle. 2 weeks later the patient was admitted to hospital for a seizure, COVID-19 positive. On admission GSC:14. During his stay in the Hospital Emergency Department multiple episodes of convulsions were observed. A CT scan of the head was performed and showed a focal lesion in the anterior cranial fossa located mainly on the right side measuring 63 mm x 50 mm x 53 mm with secondary destruction of bony structures. The tumour caused a mass effect with displacement of brain structures to the left side for a distance of approximately 10 mm with extensive white matter swelling. The patient was qualified for urgent surgical treatment. A bipartite craniotomy was performed, achieving removal of the tumour and plasty of the anterior cranial fossa. Histopathological examination led to the diagnosis of a low-differentiated tumour probably olfactory neuroblastoma with Ki67 expression in more than 90% of the cell nuclei. Olfactory neuroblastoma is a difficult tumour to diagnose, occurring more frequently in young adults and less frequently in people in their 40s and 50s. Olfactory neuroblastoma is an extremely rare malignant neuroectodermal tumour arising in the nasal cavity. It accounts for approximately 2% to 3% of all intranasal tumours, with an incidence of approximately 0.4 cases per million. These tumours arise almost exclusively from the highly specialised sensory olfactory neuroepithelium, which is normally found within the upper nasal vault, including the upper nasal concha, upper septum, nasal roof and sacral plate of the ethmoid. The patient we described, after neurosurgery, was actively and systematically rehabilitated and attended psychotherapy. He has now returned to his previous physical and psychological function and has not been found to have any deficits in lower limb motor function. He has not reported any other complaints and denies any impairment. He reports that his state of health is satisfactory and that his quality of life has improved significantly compared to the period before the surgery. He remains under an ambulatory outpatient follow-up, with no local recurrence or enhancement of treatment.

INTRODUCTION

Neuroendocrine carcinoma (NEC) of the head and neck can be subdivided into well-differentiated NEC (carcinoid), moderately differentiated NEC (atypical carcinoid) and poorly differentiated NEC, the later being subdivided further into small cell and large cell neuroendocrine carcinoma (Sarradin et al., 2018; Mills, 2002). Neuroendocrine carcinoma (NEC) rarely presents primarily in the head and neck. This neoplasm is malignant in nature and associated with a poor prognosis (azevedo). Diagnosis is only possible through the assessment of patholomorphologists and the best treatment method has not been established yet. Small-cell neuroendocrine carcinoma (SmNEC) is a distinct malignancy, arising most commonly in the lungs. Due to the extremely rare occurrence of this neoplasm in the head and neck region, no standard of care has yet been defined (Bellahammou et al., 2017). Diagnosis of this tumour is not easy due to its morphological characteristics and the size of the biopsy, which does not always distinguish NEC from other tumour types. Immunohistochemical staining plays a significant role in confirming the epithelial and neuroendocrine nature of this type of tumour, which secretes specific cytokeratins such as CAM 5.2 and neuroendocrine markers such as synaptophysin, neuron-specific enolase, chromogranin or CD56 (Montone, 2015). The histopathological examination of the patient identified a low-grade tumour, where the differential diagnosis should include neuroendocrine carcinoma. A diagnosis of grade IV olfactory neuroblastoma is less likely. In addition, expression of calretinin and NSE, and a negative response to p63 were observed. Immunohistochemical results established CK (AE1/AE3)+,

CD 56+, SYN +/-, EMA+/-, CD 117, S100 and p53 -/+, expression of the proliferative antigen Ki67 in more than 90% of cell nuclei. The expression of cytokeratins and neuroendocrine markers can vary from case to case. As described in the literature, most cases showed expression of chromogranin, synaptophysin and CD56, with only one expressing enolase (Aguiar et al., 2015; Bellahammou et al., 2017; Lee et al., 2011; Lin et al., 2007).

Small cell neuroendocrine carcinomas of the nasopharynx are highly malignant tumours and therefore carry a poor prognosis. Therapeutic options for these tumours are variable: chemo-radiotherapy, radiotherapy, surgery (and their combinations). However, the treatment of choice is still undefined, as few cases of such patients have been described in the literature so far. Of these, only one patient described so far has been treated surgically and survived 11 months after surgery (Deviprasad et al., 2008).

Very similar immunohistochemistry results were obtained in another publication by Bhardwaj et al. They describe at the time of the first biopsy positive pancytokeratin (CK) and negative

leukocyte common antigen (LCA), chromogranin and synaptophysin. Due to the destruction of the slide, it was decided to re-biopsy, which revealed SmNEC. This finding was based on immunopositivity for CD56, CK, and chromogranin (focal); synaptophysin and p40 were negative. The Ki-67 labelling index was high (90%) and almost identical to that described in our patient (Ki-67> 90%) (Bhardwaj et al., 2018). No universal principles have led individual centres to develop their own, often controversial, management recommendations. The most specialised centres adopt surgery and complementary radiotherapy as the 'gold standard' of management (Ow et al., 2014). The significance of neoadjuvant or adjuvant chemotherapy in more advanced cases remains unknown, and the indications for regional lymph node resection or radiation coverage are debatable (Fukushima et al., 2012). Olfactory neuroblastoma (esthesioneuroblastoma) is a neoplasm originating in the sinuses of the nose and nasal cavity, with specific clinical and pathological features and a varied presentation and natural history. The tumour characteristics are remarkably heterogeneous.

The exact location and cell type from which the neoplasm originates have not yet been determined, and in recent decades the same type of neoplasm has been referred to by different names, such as olfactory neuroblastoma, neuroendocrine carcinoma, esthesion-euroepithelioma or esthesioneurocytoma. Nevertheless, the common origin was defined as neural crest/immature olfactory neurons, as suggested by the presence of typical neuronal filaments in the tumour cells and the results of molecular analyses (Su et al., 2014) Commonly accepted name remains (Sampath et al., 2006) is a rare malignant neoplasm of the nasal passages and sinuses, first described by Berger and Richard in 1924 (Hassoun et al., 1981). Tumours of the nasal cavity and nasal sinuses are a relatively rare, diverse and heterogeneous group of malignancies. Olfactory neuroma accounts for only 3% of all nasal cavity and sinus tumours (Broich et al., n.d.). Tumours involving the frontal lobes affect the behavioural, complex and directed activities of humans. Forntal lobes are the site of arbitrary and conscious actions, the highest organised area of the cerebral cortex, controlling our behaviour, cognitive functions and emotional states. Traditionally, this area is referred to as the 'silent area' because no obvious neurological symptoms are found as a result of its damage. Despite the absence of neuropsychological deficits such as perceptual disorders (agnosias), motor disorders (apraxias and paresias) or speech disorders of the aphasia type, behavioural and personality changes characteristic of prefrontal area pathology do occur. These changes significantly interfere with the social functioning of patients (*Cognitive impairments in the examination of a patient after surgical treatment of anterior cranial base meningioma – case study*, 2010). Following the surgical intervention, favourable changes in personality and a significant improvement in the patient's social life were observed. The patient has been under outpatient control since then, he reports no somatic complaints and his standard of living is satisfactory. Without recurrence or metastasis, he did not require intensification of treatment.

CASE REPORT

Patient, 26-year-old male admitted to the Hospital Emergency Department. A computer tomography (CT) was performed to exclude subarachnoid haemorrhage (SAH), as indicated by the referral. It showed the presence of a tumour-like lesion surrounded by a zone of

palpable oedema and showing a mass effect. It was recommended to extend the diagnosis with contrast-enhanced magnetic resonance imaging (MRI). An MRI visualised a 'dumbbell' shaped tumour, part of which was located in the nasal cavity and situs on the right side with a constriction at the level of the situs lamina. The tumour had a heterogeneous structure with cystic spaces, posthemorrhagic foci and an abundant network of pathological vessels. Its dimensions were 45 mm x 45 mm x 32 mm. Oedema, wedging under the brain sickle of approximately 14 mm and compression of the right lateral ventricle were also evident. 2 weeks later the patient was admitted to hospital due to a seizure, COVID-19 positive. On admission GSC:14. During the residence in the Hospital Emergency Department, multiple episodes of convulsions. A CT scan of the head was performed and showed a focal lesion in the anterior cranial fossa located mainly on the right side measuring 63 mm x 50 mm x 53 mm with secondary destruction of bony structures. The tumour caused a mass effect with displacement of the brain structures to the left side for a distance of approximately 10 mm with extensive white matter swelling. A CT scan of the chest was also performed and showed a single focal parenchymal lesion in the left lung area. The patient was qualified for urgent surgical treatment. A bifrontal craniotomy resulting in tumour removal and anterior cranial fossa plasty was performed. Patient was systematically rehabilitated after surgery and no deficits in lower limb motor function were observed. Discharged home with a healed postoperative wound. Oncology and psychiatric consultations were also recommended. Histopathological examination led to the diagnosis of a low-differentiated tumour probably of olfactory neuroblastoma character with Ki67 expression in more than 90% of cell nuclei.

DISCUSSION

Olfactory neuroblastoma (ONB) is an extremely rare malignant neuroectodermal tumour arising within the nasal cavity. It has incidence is about 2% to 3% of all intranasal tumours with an incidence of approximately 0.4 cases per million. These tumors arise almost exclusively from the highly specialized sensory olfactory neuro-epithelium nor-mally encountered within the superior nasal vault, including the superior nasal concha, superior septum, roof of nose, and the cribriform plate of ethmoid (Thompson, 2009). It can manifest at any period of life, although it predominates in young people. A second peak of incidence prevails later in adult life. There are two peaks of increased incidence of ONB – the first in the second decade of life and the second in the sixth decade of life (Al-Osaimi et al., 2021). There is no definitive gender or racial predilection. To date, the etiological basis and risk factors are unknown. There is also no link to occupational exposure (Faragalla & Weinreb, 2009). Typically, these are slow growing tumors with long-standing symptomology, often resulting in delayed biopsy and definitive diagnosis. Implementation of treatment each time should be preceded by confirmation of the histological subtype of the lesion and exclusion of similar neuroendocrine tumours in the differential diagnosis. Other non-ONB neuroendocrine tumours have a high percentage of systemic failure and require the initiation of systemic management. In comparison, ONB is linked to excellent outcomes with locoregional-only therapy. Non-specific initial symptoms characteristic of this neoplasm, such as nasal obstruction and recurrent epistaxis, make a correct diagnosis much more difficult and delay the implementation of treatment. The initial diagnostic studies, besides Computer Tomography, can include MRI or PET CT to more clearly define the local extent of the malignancy. Local recurrence that may occur many years after the surgical excision of the lesion or distant progression remains a major problem in the medical treatment of ONB. Salvage therapy involves operation, surgery and postoperative radiotherapy, radiotherapy itself, palliative chemotherapy or supportive care according to the nature of the recurrence and the initial treatment of the patient. New strategies involving combined CT and/or escalation of dose made possible by sophisticated irradiation techniques such as IMRT or proton therapy ought to be explored potentially (Ozsahin et al., 2010). The relapsing remitting disease is frequently very treatable, with prolonged survival and success, so extended follow-up is indicated for detection and suitable medical treatment (Rimmer et al., 2014).

CONCLUSION

In summary, neuroblastoma has a difficult diagnosis. Histological diagnosis should always be complemented by immunohistochemistry. Surgical resection with adequate margins is the first treatment for resectable lesions. Olfactory neuroblastoma demands advanced aggressive surgical resection and radiation therapy. The patients should be carefully supervised in the awareness that Iocoregional recurrences are frequent and can appear some years after treatment. The long-term survival prognosis is bad.

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