Esthesioneuroblastoma: a case report and review of the literature

Authors
C. Focan, L. Kalala, F. Schils, F. Abraham, P. Reginster, D. Van Den Berge

Key words
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Summary
Olfactory neuroblastoma or esthesioneuroblastoma (ENB) is a rare cancer (one case per one million inhabitants) arising from the neuroepithelium of the olfactory rim located in the nasal cavity (lamina cribosa). Sinusal, orbital and intracranial expansions are common. The anatomopathological diagnosis may be delicate, as it frequently requires immuno-histochemical tests as well as electron-microscopy and genetic testing. Medical imaging with CT scan and MRI is essential for the staging. The case of a young lady with good clinical evolution after combined treatments is reported in this article. (BJMO 2008;vol 2:3:168-71)

Patient history
On July 3rd 2006 a 31-year-old women presented in our hospital with periorbital headache, nausea, photophobia, intermittent diplopia and partial anosmia. Medical imaging (CT-scan; NMR) revealed a tumoural process, poorly delineated which developed from the skull basis around the ethmoïd lamina cribosa towards the orbites, ethmoidal cells and sphenoid bone. An intracranial expansion was also observed (Figures 1 & 2). The tumour images were poorly enhanced through CT-contrast while gadolinium administration defined a cystic component at the superior and inferior borders. A partial resection by an intradural neurosurgical access was performed on august 21st 2006. The histological examination revealed a tumour composed of small cells disposed in sheets with outlined rosette images; diffuse fibrillar material, capillary

Figure 1. Tumoural lesion and local extension at CT scan (A) where the lack of enhancement after contrast and intratumoural calcifications are well defined and at NMR axial-flair sequence (B). (July 07, 2006)

Figure 2. NMR images in T2 sequence, coronal (A) and sagittal with gadolinium contrast (B); note the cystic component after contrast at the lower region and at the intracranial expansion. (July 07, 2006)
dilation and dystrophic calcifications (Figure 3). In line with these pathognomonic images, immunohistochemical tests (S-100 protein; CD56-NCAM protein) further confirmed the diagnosis of ENB. The clinical stage of the ENB was Kadish stage C or T3N0M0 (Table I).\(^1,2\) After cryo-preservation of ovarian fringes (Prof. Donnez; UCL), the patient received 3 courses of chemotherapy with etoposide, ifosfamide and cisplatine (between October 14 and November 27, 2006).\(^3\) A stereotactic radical conformal radiotherapy delivering 55 to 66 gray to the initial tumor volume was delivered from January 03 to February 16, 2007. The whole treatment was very well tolerated. Regular controls of IRM from the sixth week post-radiotherapy confirmed an apparent complete remission with cicatricial gliosis expressed in the zones previously undertaken by the tumour (Figure 4).

Discussion and conclusions
This article reports on a stage T3N0M0 ENB with a favourable evolution after combined multidisciplinary treatment (partial surgery; chemotherapy and stereotactic radiotherapy).

No definite etio-pathogenic agent was recognized for this rare (3-5% of nasal cancers) tumour.\(^4-6\) In 1963 Herrold et al suggested a potential role for industrial solvants such as nitrosoamines in the development of ENB. Herrold et al confirmed this hypothesis in a study where tumours mimicking ENB were induced in Syrian hamsters after treatment with diethylnitrosamine.\(^7\)

The cell of origin of the tumoral ENB cells is now confirmed to lie in the basal layers of the olfactory neuro-epithelium in the cribiform lamina area.\(^4,6,8-12\) Immunohistochemical (protein GAP43, NCAM, type-protein kinase C) and genetical (expression of the mammal analogue of the achaete-scute gene; h-ASH1) studies revealed common characteristics between these basal cells and the tumoral, small, round ENB cells.\(^4,6,8,12\)

The clinical diagnosis of ENB is based upon direct nasal endoscopy and medical imaging. Microcalcifications inside the tumour and hollows at the brain-tumour interface are pathognomonic (Figure 1 & 2 on page 168).\(^14,15\) In case of well-differentiated ENB, the observation of true rosettes (Flexner-Weiterscheiner) or pseudo-rosettes with an interstitial fibrillar material in histological examinations also allows a reliable

Table 1. Clinical classifications of esthesioneuroblastoma

<table>
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<tr>
<th>KADISH (1976)</th>
<th>TNM according to DULGUEROV et CALCETTARA (1992)</th>
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<tr>
<td>Stage A: tumour localised to the nasal cavity</td>
<td>T1: tumour localised to the nasal cavity and paranasal sinuses with a space between tumour and lamina cribosa</td>
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<td>Stage B: spread to sinuses</td>
<td>T2: tumour developed in nasal cavity or sinuses but in contact with cribiform lamina and/or sphenoid extension</td>
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<tr>
<td>Stage C: extension over paranasal sinuses</td>
<td>T3: tumour with intracranial extradural and/or orbital expansion</td>
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<td>T4: tumour with intracranial intradural extension</td>
<td>N0: no metastatic cervical nodes</td>
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<tr>
<td>N1: metastatic cervical nodes</td>
<td>M0: no distant metastases</td>
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<td>M1: distant metastases</td>
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Figure 3. Histological picture of the described ENB showing the monomorphism of tumour cells, some rosettes, fibrillar material, capillary dilation and dystrophic calcification.

Figure 4. NMR with contrast after treatment: T1 coronal (A) and sagital (B). Note the clearance of contrast enhancement and the presence of a liquid cavity in place of previous tumour. The absence of apparent tumoral regrowth (radiological complete response) is also visible.

A

B
diagnosis.8,9 In less-differentiated or undifferentiated ENB, further immunohistochemical, electron microscopical (which will show neuro-secretory grains, neuron-filaments or fibrillar material) or even genetic tests (i.e. determination of h-ASH1-m-RNA levels from PCR) may be required to distinguish ENB from some types of non-hodgkin lymphoma, undifferentiated sino-nasal carcinoma, neuro-endocrine tumours or even Ewing sarcoma.10-13

The treatment of these tumours will generally be based on a combination of surgery and radiotherapy. The surgery requires a combined transfacial and neurosurgical access allowing en-bloc resection of the tumour in optimal cases16, this was however not possible in the patient presented here. As surgery is rarely complete, in most cases complementary radiotherapy will be proposed.17 Due to the excellent radio-sensitivity of ENB, this approach improves the patients’ prognosis.17 Additional, sophisticated techniques, such as targeted treatment from stereotactic conformal delivery (as performed in our patient) will allow the preservation of normal brain and eye structures despite administering an optimal dose-intensity to the tumoural bed.17 Chemotherapy, which is initially reserved for palliation, may now be progressively implemented in the multidisciplinary program, i.e. in neo-adjuvant treatment before surgery and radiotherapy.5,18,19

Key messages for clinical practice

1. Esthesioneuroblastoma (ENB) or olfactory neuroblastoma is a rare tumour developing from the nasal cavity (1 case per 1,000,000 per year; 3-5% of nasal tumours).
2. The tumour arises from the basal layer of the olfactory neuroepithelium and spreads in all directions from the olfactory rim area.
3. In medical imaging, dystrophic calcifications, poor enhancement at CT-contrast and small hollows at tumour border at NMR are pathognomonic features.
4. The presence of (pseudo-)rosettes surrounded by fibrillar material, dilatation of capillars and calcifications allows accurate histological diagnosis.
5. Further specific immuno-histochemical, electron microscopical or genetic tests may support diagnosis in case of poorly- or undifferentiated ENB.
6. Despite adequate surgery ideally by a cranio-facial access and adjuvant targeted radiotherapy, the prognosis remains poor with more than 50% relapses.

References

18. Mishima Y, Nagasaki E. Terui Y et al. Combination chemotherapy (cyclophosphamide, doxorubicin, and vincristine with continuous-infusion cisplatin and etoposide) and radiotherapy with stem cell support can be beneficial for adolescents and adults with esthesioneuroblastoma. Cancer 2004; 101:1437-77.