Reporting of a primary sinonasal neuroendocrine small cell carcinoma in the paediatric age group

M Nandi1, I Arun2, A Bhattacharya2, S Sen2, S Ray2, I Mallick2

Abstract

Introduction

Primary Sinonasal Small Cell Carcinomas, Neuroendocrine type (SCCNET) are rare tumours. Few cases have been reported in the head and neck region of adult patients. They have a fair response to multimodality therapy; but the prognosis remains poor.

Case report

We report here a case of SCCNET in a 5 year old child. He presented with swelling in his right eye with diminution of vision and right sided neck swelling. Cervical lymph node biopsy revealed poorly differentiated metastatic neuroendocrine carcinoma; confirmed by immunohistochemistry. 18 FDG-PET CT scan revealed a nasopharyngeal mass extending to other paranasal sinuses and base of frontal lobe with bilateral extensive cervical lymphadenopathies. He was treated with neoadjuvant platinum based combination chemotherapy followed by radical radiotherapy. At 17 post diagnosis he is alive but on palliative care.

Conclusion

SCCNETs have an unfavourable outcome. Further improvements in our understanding of the pathology and treatment strategies are needed to combat the disease.

Introduction

Primary Sinonasal Small Cell Carcinomas, Neuroendocrine type (SCCNET) are rare tumours which occur more commonly in the lungs and gastrointestinal tract1.

Few cases have been reported in the head and neck region of adult patients, mainly in the paranasal sinuses, salivary glands, nasal cavity, tonsil, larynx, and tongue2,3,4,5. The cell origin of the head and neck small cell carcinomas was initially thought to be from amine-precursor uptake and decarboxylase (APUD or Kulchitsky) cells; however, the current opinion favours their origin from multipotential stem cells6,7. SCCNETs have a fair response to chemotherapy; chemo-radiotherapy but these are aggressive tumours and ultimately the prognosis remains poor8,9,10. There are few reported cases of SCCNETs in the sinonasal region, all in the adult population,11,12,13. To the best of our knowledge this is the first reported case of SCCNET in the paediatric age group.

He was treated with neoadjuvant chemotherapy to which he had a partial response; was followed up with radical radiotherapy. At 17 post diagnosis he is alive and on palliative care.

Case report

We report a case of a 5 year old child who presented to the paediatric oncology outpatient department of our centre in April 2012, with complaints of gradual increase in swelling of the right neck region for the past 1 month and swelling with diminution in vision of the right eye for 2 weeks.

On examination he was found to have bilateral cervical lymphadenopathies, right eye proptosis with no perception of light in the right eye, and no pupillary reaction. The patient was advised for neck node biopsy. Right cervical lymph node biopsy revealed metastatic neuroendocrine carcinoma, poorly differentiated. Cells had increased nuclear cytoplasmic ratio, scanty cytoplasm, monotonous round or oval mitotically active nuclei with powdery chromatin. Immunohistochemical stains done in the pathology department of our centre revealed the neoplastic cells to be strongly positive for Neuron specific enolase (NSE), CD56, and Thyroid transcription factor-1 (TTF-1) (Figure 1). Cells were also positive for CD57 (Figure 1), and showed patchy positivity for synaptophysin and chromogranin (Figure 2); many of the cells showed peri-nuclear dot like positivity for AE1-AE3 (Cytokeratin) (Figure 2). Neoplastic cells were negative for CD45, CD20, CD3, CD2, Desmin, GFAP, Tdt, S100, CD99, and HMB-45. Ki proliferation index was about 75%. Further work up was done to complete staging. CT scan of the orbit revealed a large heterogeneous sinonasal mass of about 5 cm in largest diameter with extension into the ethmoid, sphenoid and maxillary sinus, intracranial extension into the anterior cranial fossa. CT scan of the neck revealed bilateral level IB, II, III, and V cervical lymphadenopathies.

An 18-FDG PET scan showed a nasopharyngeal mass lesion of 4.2x5.5x4.1 cm (SUV max 6.4) involving nasal cavity, anterior and posterior ethmoid air cells and sphenoid sinuses bilaterally. Lesion involved extracranial space in both orbits, not separable from the medial rectus muscle. Destruction of lamina papyracea, cribriform plate was present with intracranial extension to the base of the frontal lobe. FDG avid lateral retropharyngeal node (SUV max 4.1), bilateral conglomerated cervical nodal mass involving level II & III, abutting carotid vessels was also noted. Staged as T4N3M0, the patient was started on neo-adjuvant chemotherapy comprising cisplatin and etoposide.
Case report

After completion of 3 cycles of chemotherapy, interim CT scan of orbit was done to assess response. It revealed enhancing lesion in the sphenoid sinus measuring 22x12mm, mucosal thickening in maxillary, ethmoid and frontal sinuses. Small enhancing intracranial lesion was seen at the base of the anterior cranial fossa measuring 7x8mm (Figure 3). As there was partial response with chemotherapy, multi-disciplinary tumour board (MDT) of the institution decided to continue with chemotherapy for a further 3 cycles. At the end of 6 cycles of chemotherapy, CT scan face reported a small increase in size of the lesion at the base of the anterior cranial fossa measuring 24x18mm; bilateral cervical nodes were seen in level II with the largest measuring 15x12mm. There was no radiological residual in the nasal cavity and para-nasal sinuses. He was then planned for external beam radiotherapy with image-guided intensity modulated radiotherapy on Helical Tomotherapy to a 30 fraction schedule over 6 weeks. The gross residual disease was planned for 63Gy. The entire pre-treatment volume covering the sinonasal region and bilateral level I-III+V lymph nodes received 60Gy. The frontal brain and level IV nodes were planned for 54Gy. Concurrent chemotherapy was not planned in view of the fact that the child had received a full course of cisplatin and etoposide (6 cycles). He completed the treatment successfully without treatment breaks, but with manageable Grade 3 mucositis and dysphagia.

He remained on close follow-up. In the first 2 months his acute radiation reactions had subsided and he did not have any symptoms attributable to disease. However, he presented with recurrent headache at 3 months. An MRI of the neck and brain suggested a large progressive lesion in the frontal lobe with haemorrhage. There was no radiological evidence of disease in the rest of the head and neck region. The lesion was not operable. A further multidisciplinary discussion recommended best supportive care only. At 17 months following diagnosis he is moribund but alive receiving palliative treatment.

Discussion

To the best of our knowledge this is the first immunohistochemically confirmed case of primary sinonasal small cell carcinoma, neuroendocrine type being reported in a child. SCCNET of the sinonasal region are rare. In a review of literature by Han et al. in 2012, 55 prior reported cases have been compiled. All were positive for CD56, Synaptophysin and chromogranin A. The largest reported series of 16 cases by Babin et al. is from a consortium of 8 French hospitals. Other large series include those by Perez-Ordonez and Rosenthal. Table 1 summarizes a few of the larger series. In all the reports, the patients...
Case report


Figure 3a: 18FDG-PET SCAN reveals bilateral cervical lymphadenopathies.

Figure 3b-d: Reveal initial lesion in the frontal lobe on CT scan, subsequent response with chemotherapy (on a CT scan) and the progression after completion of treatment on MRI scan (at 3 months of follow up).

were adults. The mean age of all the previously reported cases summarized by Ho et al. was 51.3 years. We believe that this is the first report of this histology in a child. Initial clinical differentials included lymphoma but the pathology was confirmed from a lymph node biopsy. The closest histopathological differential diagnosis considered was Olfactory Neuroblastoma. Presence of diffuse perinuclear dot like positivity for AE1-AE3 (Cytokeratin), strong and diffuse TTF-1 positivity and absence of S100 positive sustentacular cells were in favour of SCCNET. Radiotherapy is also very commonly used either with concurrent chemotherapy or alone in sequence with chemotherapy. Our patient being a young child and considering his advanced disease presentation was taken up for neo–adjuvant combination chemotherapy followed by radical radiotherapy. Despite completing his planned treatment he developed early large-volume local failure in the brain that could not be salvaged.

Conclusion

The reported literature also shows an unfavourable outcome with this histology and a short disease-free and overall survival using commonly used treatment protocols. Further improvements in our understanding of the pathology and treatment strategies are needed to combat this disease.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

References


for CD45, CD3 and CD2 which ruled out Lymphomas including NK/T cell lymphomas (Table 2 below gives the differential diagnosis for SNEC). Therefore our case was diagnosed as a case of Primary Sinonasal Small Cell Carcinoma, Neuroendocrine type. The clinical presentation of cervical lymphadenopathies, sinonasal symptoms and unilateral blindness was in keeping with the usual presentation of sinonasal cancers. The treatments of sinonasal small cell carcinomas have been varied, with reports of chemotherapy, radiotherapy and surgery being used. The use of cisplatin based chemotherapy is common. The treatments of sinonasal small cell carcinomas have been varied, with reports of chemotherapy, radiotherapy and surgery being used. The use of cisplatin based chemotherapy is common. Radiotherapy is also very commonly used either with concurrent chemotherapy or alone in sequence with chemotherapy. Our patient being a young child and considering his advanced disease presentation was taken up for neo–adjuvant combination chemotherapy followed by radical radiotherapy. Despite completing his planned treatment he developed early large-volume local failure in the brain that could not be salvaged.

Conclusion

The reported literature also shows an unfavourable outcome with this histology and a short disease-free and overall survival using commonly used treatment protocols. Further improvements in our understanding of the pathology and treatment strategies are needed to combat this disease.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

References


were adults. The mean age of all the previously reported cases summarized by Ho et al. was 51.3 years. We believe that this is the first report of this histology in a child. Initial clinical differentials included lymphoma but the pathology was confirmed from a lymph node biopsy. The closest histopathological differential diagnosis considered was Olfactory Neuroblastoma. Presence of diffuse perinuclear dot like positivity for AE1-AE3 (Cytokeratin), strong and diffuse TTF-1 positivity and absence of S100 positive sustentacular cells were in favour of SCCNET. S100, CD99, and Desmin, were negative excluding Melanoma, Ewing/PNET and Rhabdomyosarcoma respectively. Neoplastic cells were immunonegative for CD45, CD3 and CD2 which ruled out Lymphomas including NK/T cell lymphomas (Table 2 below gives the differential diagnosis for SNEC). Therefore our case was diagnosed as a case of Primary Sinonasal Small Cell Carcinoma, Neuroendocrine type.
Table 1: Summary of cases of neuroendocrine carcinoma of paranasal sinuses and nasal cavity

<table>
<thead>
<tr>
<th>Authors</th>
<th>Patients (N)</th>
<th>Gender</th>
<th>Age (mean)</th>
<th>Location</th>
<th>Treatment</th>
<th>Disease progression</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koss et al.</td>
<td>4</td>
<td>M-2, F-2</td>
<td>41</td>
<td>NA</td>
<td>S-3,5,RT-1</td>
<td>Rec-1</td>
<td>A-8yr, D-8mo,11mo,16mo</td>
</tr>
<tr>
<td>Perez-Ordonez et al.</td>
<td>6</td>
<td>M-3, F-3</td>
<td>50</td>
<td>Ethmoid, maxillary, nasal, Ethmoid, nasal, Maxillary, Ethmoid</td>
<td>S-2, RT,S-1, CT,RT-1, S,RT,CT-2</td>
<td>Rec-2, Met-1, Rec-1, Met-1</td>
<td>A-19mo, A-24mo, D-21mo, A-96mo, D-6mo</td>
</tr>
<tr>
<td>Rosenthal et al.</td>
<td>7</td>
<td>M-5, F-2</td>
<td>48</td>
<td>NA</td>
<td>RT-2, CT/S/RT-5</td>
<td>5yr rec rate 44%, 5yr met rate 75%</td>
<td>5yr OS rate 28.6%</td>
</tr>
<tr>
<td>Babin et al.</td>
<td>25</td>
<td>M-12, F-9</td>
<td>55</td>
<td>B-3, B-1, C-2, C-2, B-1, C-2, B-1, C-2, C-2, B-3, C-1</td>
<td>S-3, CT-3, RT-3, S,RT-3, CT, S,RT, CT-3, CT, CRC-2, S,RT, CT-4</td>
<td>Rec-2, Met-1, Met-1, Rec-1, Rec-1, Rec-1, Met-1</td>
<td>A-3yr, 14yr, D-6mo, A-1mo, 1yr, D-3yr, D-5mo, 1yr, A-6mo, 2yr, 4yr, D-18mo, A-3mo, 8yr, D-20mo, A-1yr (both patients) A-3mo, D-8mo, 1yr, 4yr,</td>
</tr>
<tr>
<td>Menon et al.</td>
<td>4</td>
<td>M-4</td>
<td>40</td>
<td>Maxillary, Ethmoid, Sphenoid, Nasal, Ethmoid, Nasal, Ethmoid, Ethmoid, Nasal</td>
<td>CT, RT, S, RT, S, RT, CT, RT</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nandi et al. (present case)</td>
<td>1</td>
<td>M</td>
<td>6</td>
<td>Maxillary, ethmoid, nasal extending to brain with cervical lymphadenopathy</td>
<td>CT, RT</td>
<td>Rec</td>
<td>A-17mo</td>
</tr>
</tbody>
</table>

PNET- Primitive neuroectodermal tumour, TTF-1- Thyroid transcriptase factor-1, NSE-Neuron specific enolase, AE1-AE3- Cytokeratin


Licensee OAPL (UK) 2014. Creative Commons Attribution License (CC-BY)


### Table 2: Differential diagnoses considered for the case

<table>
<thead>
<tr>
<th>No.</th>
<th>Tumour</th>
<th>Age</th>
<th>Histopathological features</th>
<th>Immunohistochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Small cell carcinoma neuroendocrine type</td>
<td>26-77</td>
<td>Sheets, ribbons or nests of monotonous small or medium sized cells with inconspicuous nucleoli and minimal cytoplasm.</td>
<td>CD56, Cytokeratin (punctate perinuclear), Variable positivity for Chromogranin, Synaptophysin, S100 (Sustentacular cells).</td>
</tr>
<tr>
<td>2.</td>
<td>Olfactory neuroblastoma</td>
<td>10-80</td>
<td>Lobular to solid growth pattern, rosettes may be present. Uniform small round /oval cells, scant cytoplasm, fine to coarse granular chromatin and occasional small nucleoli.</td>
<td>NSE, CD56, Synaptophysin, S100 (Sustentacular cells), Variable CD57, Chromogranin, GFA and Keratin.</td>
</tr>
<tr>
<td>3.</td>
<td>Ewing sarcoma/PNET</td>
<td>&lt;30</td>
<td>Sheets, lobules, trabeculae +/- rosettes, small to intermediate sized cells with scant vacuolated cytoplasm, round nuclei, fine chromatin.</td>
<td>CD99 (membranous pattern), Vimentin, FLI1, variable NSE, Synaptophysin, occasional AE1/AE3 and CAM5.2</td>
</tr>
<tr>
<td>4.</td>
<td>Rhabdomyosarcoma</td>
<td>&lt;20</td>
<td>Embryonal and alveolar type with small round cells with scant cytoplasm scattered cells with eosinophilic cytoplasm and cross striations.</td>
<td>Desmin, Myogenin (nuclear), MyoD1, Myoglobin (cytoplasmic). Usually positive for Vimentin and CD 56, Myosin variable.</td>
</tr>
<tr>
<td>5.</td>
<td>Extraneal NK/T cell lymphoma</td>
<td>50-70</td>
<td>Diffuse infiltrate of small or medium sized to large transformed cells with angiocentric/angiodestructive growth pattern.</td>
<td>CD2, CD3 (epsilon) cytoplasmic, CD56, Granzyme B, Perforin, TIA-1</td>
</tr>
<tr>
<td>6.</td>
<td>Desmoplastic small round blue cell tumour (DSRCT)</td>
<td>15-35</td>
<td>Nests of cells with small round or oval nuclei with inconspicuous nuclei, scant or moderate cytoplasm in a desmoplastic stroma.</td>
<td>Desmin (Perinuclear dot like), AE1-AE3, EMA, Vimentin, WT-1, usually positive for NSE and CD57, Occasionally positive for CD99 and Synaptophysin.</td>
</tr>
<tr>
<td>7.</td>
<td>Sinonasal undifferentiated carcinoma</td>
<td>20-80</td>
<td>Nests, lobules, sheets, trabeculae of cells with medium sized nuclei, prominent nucleoli and scant eosinophilic cytoplasm.</td>
<td>Pankeratin, CK7, CK8, CK19, Occasional NSE and EMA, Rare positivity for CD99, Synaptophysin, S100, Chromogranin.</td>
</tr>
<tr>
<td>8.</td>
<td>Squamous cell carcinoma (non keratinising)</td>
<td>55-65</td>
<td>Ribbons, nests/strands of poorly differentiated cells morphologically similar to other small round blue cell tumours.</td>
<td>Pankeratin, EMA, CK 5/6, CK8, CK 13, CK14, CK19.</td>
</tr>
</tbody>
</table>