Non-keratinizing undifferentiated carcinoma of the nasopharynx

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Abstract

Nasopharyngeal carcinoma is the predominant tumor type arising in the nasopharynx with cervical lymph nodes present in 60–90% of all cases at the time of presentation. The most frequent pathological varieties include squamous cell carcinoma well-differentiated keratinizing, moderately differentiated non-keratinizing and an undifferentiated type. We present a case of non-keratinizing undifferentiated carcinoma of the nasopharynx with parapharyngeal and middle cranial fossa space involvement in an 18-year-old male who has been admitted in our hospital for recurrent right ear otitis media. Symptoms consisted in mild conductive hearing loss, trigeminal V2 nerve anesthes ia, right ear tinnitus, mild dysphagia, mild dysphonia, right hypoglossal nerve paralysis and right Claude Bernard–Horner’s syndrome. Clinical examination revealed no lymph node masses, chest X-ray corresponding to a normal thoracic image. Cranial contrast enhanced CT scan showed a non-homogenous mass of 5.4/4.5/5.5 cm from the level of the right rhinopharyngeal wall, extending in the right parapharyngeal space, invading the right middle cranial fossa. Cranial MRI with contrast enhancement revealed a rhino- and parapharyngeal mass of 5.5/4.6/5.3 cm with intracerebral extension in the right cavernous sinus, right internal carotid artery being engulfed by the tumor mass with partial compression. Several lymph node masses of 1.7/1.2 cm were also revealed. We performed rhinopharyngeal biopsy, right tympanotomy and grommet tube insertion. The tissue specimens were processed with routine histological technique. Subsequent immunohistochemical reactions for pan-cytokeratin AE1/AE3 and leukocytes common antigen were performed. The histological examination of routine stained slides showed that malignant tumor cells had a syncytial pattern of growth in a background of small lymphocytes. The positivity of tumor cells for pan-cytokeratin established the final diagnosis of non-keratinizing undifferentiated carcinoma. The age of onset, the clinical signs and symptoms and minimum involvement of lymph nodes represents the particular aspects of the case.

Keywords: nasopharyngeal carcinoma, pan-cytokeratin, AE1/AE3, CD45, LCA.

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant tumor of nasopharyngeal epithelium. It is the main type in nasopharyngeal malignant tumors in both endemic areas and regions with low incidence. NPC epidemiological studies focused on etiology and biological behavior of the disease were strongly encouraged because of the International Union against Cancer (UICC) Symposium on Cancer of Nasopharynx held in Singapore in 1964. Investigations in the past four decades have produced many important findings in those aspects [1].

NPC has unique epidemiological features, including obvious regional, racial, and familial aggregation.

NPC is a type of tumor with extremely unbalanced endemic distribution. NPC appears in many countries and areas of the five continents. However, the incidence of NPC is lower than 1/105 in most areas. High-incidence areas are centralized in the southern part of China (including Hong Kong). The highest incidence was found in Guangdong Province, and the incidence in male can reach 20–50/100 000 [1].

Etiological factors are dietary environmental factors,
such as salted fish, a popular dish in southern China, when consumed from a young age, due to its volatile nitrosamines (N-nitroso-dimethylamine and N-nitroso-diethylamine) [2].

**Patient, Methods and Results**

An 18-year-old male patient was admitted in ENT Department of Emergency City Hospital, Timișoara, Romania, in April 2013. Initial diagnosis was right recurrent otitis media.

Hospital admission symptoms and signs consisted in right mild conductive hearing loss, right trigeminal V2 nerve anesthesia, right ear tinnitus, mild dysphagia, mild dysphonia, right hypoglossal nerve paralysis and right Claude Bernard–Horner’s syndrome. Clinical examination revealed no lymph node masses and chest X-ray – normal thoracic image.

Cranial contrast enhanced CT scan showed a non-homogenous mass of 5.4/4.5/5.5 cm from the level of the right rhinopharyngeal wall, extending in the right parapharyngeal space, invading the right middle cranial fossa.

Cranial MRI with contrast enhancement revealed a rhino and parapharyngeal mass of 5.5/4.6/5.3 cm with intracranial extension in the right cavernous sinus, right internal carotid artery being engulfed by the tumor mass with partial compression. Several lymph node masses of 1.7/1.2 cm were identified (Figures 1 and 2).

We performed a rhinopharyngeal biopsy, right tympanotomy and grommet tube insertion.

The tissue specimens were processed according with the routine histological technique. The specimens were fixed in 4% (v/v) buffered formalin and paraffin embedded. Three micrometers thick serial sections were stained with Hematoxylin–Eosin.

Additional immunohistochemical reactions for multi-cytokeratin AE1/AE3 (Novocastra, NCL-L-AE1/AE3, Liquid Monoclonals, clone AE1/AE3) and CD45 (Novocastra, NCL-L-LCA, Liquid Concentrated Monoclonal Antibody, clone X16/99).

For dilution of the antibodies, we used Novocastra IHC Diluent, in a ratio of 1:150. The incubation time with primary antibody was 30 minutes for both antibodies.

The antigen–antibody complex was visualized with 3,3’-diaminobenzidine (from Novolink Max Polymer Detection System, Novocastra). The slides were washed in tap water and counterstained with Mayer’s Hematoxylin and then dehydrated, cleared, and mounted. The signal was brown with cytoplasmic distribution for AE1/AE3 and membranar for CD45.

In each determination, external control slides were included.

Histopathological evaluation was performed with Nikon Eclipse E600 microscope and images were acquired using Lucia G system.

The histological examination at scan magnification of routine stained slides showed that malignant tumor cells had a syncytial pattern of growth in a background of small lymphocytes and plasma cells. The tumor was composed of irregular islands or solid sheets intermingled with non-tumoral lymphoid tissue (Figure 3).

At higher magnification, the tumor cells were small or medium in size, round or oval and had a crowded appearance. In some areas of the tumor, the cells were overlapping or had spindled features (Figure 4).

The scant cytoplasm was either eosinophilic or amphophilic. The nuclei were big, vesicular with prominent nucleoli, situated centrally in the nucleolus. A small number of nuclei were better chromatin-rich rather than vesicular (Figures 5 and 6).

The positivity of tumor cells for pan-cytokeratin and the absence of immune reaction for lymphoid marker established the final diagnosis of non-keratinizing undifferentiated carcinoma (Figures 7 and 8).

Radiochemotherapy represented the therapeutic option for this case.
Discussion

Nasopharyngeal cancer in the western world is relatively rare and typically presents as advanced stage disease. In the United States, only 3% of NPC occurs in patients younger than 19 years of age according to Surveillance, Epidemiology and End Results (SEER) data [3], and pediatric NPC is more prevalent among African-Americans and its geographic distribution favors southern states [4]. Furthermore, approximately 38% of the cases in NPC patients younger than 20 years or between 20 and 40 years were undifferentiated subtype, respectively, whereas patients older than 40 years were often diagnosed with keratinizing squamous cell carcinoma. The randomized study conducted by the Pediatric Oncology Group (POG) enrolled 18 patients from 59 institutions to the POG...
human nasopharyngeal carcinogens [2].

other traditional Chinese foods are important potential NPC is diet related and that Chinese salted fish and the method of cooking the salted fish. These findings first exposure, frequency and duration of consumption and of NPC was found to be increased with earlier age at

50% of NPC cases had exposure to salted fish. The risk NPC when compared with its adult counterpart. Young patients have a higher rate of lymph node metastasis, fewer WHO Type 1 (keratinizing) tumors, and a better prognosis when compared with adults [3].

Khabir A et al. (2000) previously demonstrated that p53 accumulation is much less frequent in younger patients. The same group of researchers investigated Bcl-2 and Bcl-X expression by immunohistochemistry in patients below 30-year-old or those aged over 30 years. The average Bcl-2 score was found to be much lower for patients below 30-year-old, and concluded that this finding strengthened their hypothesis that oncologic mechanisms may be different for pediatric and adult patients. Their comparison of clinical data revealed a major difference between patients below 30-year-old or older in terms of frequency of lymph node involvement also. While all patients below 30-year-old had clinical lymph node invasion, the figure was 66% for patients older than 30-year-old [13]. The same observation was made previously by Maalej M et al. (1995) and they found that almost all the patients in their series with T4N0 disease were over 30-year-old [16].

Historically, radiotherapy alone was used for both early stage and advanced nasopharyngeal carcinoma. Interpreting the results of studies from various parts of the world is difficult, as the prognostic roles of EBV and histological classifications are incompletely understood.

The patient was addressed for radiochemotherapy. The University of Michigan and Washington University have reported reductions in late xerostomia with Intensity-Modulated Radiation Therapy (IMRT) [17]. IMRT has essentially become standard of care for the majority of head and neck cancer sites. IMRT is a useful technique for the nasopharynx, due to the proximity of critical structures to the target. With conventional therapy, there is considerable risk of late morbidity.

While the concomitant chemotherapy and radiation, with or without adjuvant chemotherapy, is the current standard for adult patients with NPC, neoadjuvant chemotherapy with radiotherapy has gained popularity parallel to other pediatric treatment protocols in various solid tumors. The ideal radiotherapy in the nasopharyngeal carcinoma implicates a 40 Gy (2 Gy/fraction) from 70 Gy total dose prescribed [9].

Although multimodality treatment has increased the five-year overall survival to 70–90%, late morbidity is a major concern. Any potential reduction in radiation field and doses is desirable due to the significant chronic morbidity among the long-term survivors.

**Conclusions**

The age of onset, the clinical signs and symptoms and minimum involvement of lymph nodes represent the
particular aspects of the case. The patient was addressed for radiochemotherapy. NPC is a rare disease in children with distinct epidemiological and etiological features, histopathological characteristics, and clinical presentation. Children with NPC usually have the undifferentiated variant of the disease, which is associated with advanced regional spread and distant metastases.

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References

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