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PRIKAZ SLUČAJA
*CASE REPORT*

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# Nediferencirani nazofaringealni karcinom s oralnim simptomima: prikaz slučaja

# *Undifferentiated Nasopharyngeal Carcinoma with Oral Manifestation: A Case Report*

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**Sažetak**
Nazofaringealni karcinom (NPC) rijetka je maligna bolest u većem dijelu svijeta, pa se zato često pogrešno dijagnosticira. Ta se vrsta raka teško pronađe među karcinomima glave i vrata zbog predilekcijskog mjesta, malignih karakteristika rasta, posebnih teškoća u otkrivanju i određivanju stupnja proširenosti te visoke stope neuspjeha u liječenju, iako je osjetljiv na radioterapiju. O toj bolesti malo se zna i obično na godinu oboli jedna osoba u populaciji od 100 tisuća. Uobičajen je u južnoj Kini i sjevernoj Africi, gdje se njegova etiologija povezuje s prehrambenim navikama. Kako bismo bolje razumjeli etiološku patogenezu i mogli prepoznati klinička obilježja te postaviti ranu dijagnozu i prognozu NPC-a, izvještavamo o rijetkom slučaju nazofaringealnog karcinoma u srednjoj Indiji. Pacijentica je bila u dobi od 19 godina i došla je na liječenje zbog tkivne mase u sklopu vrata intraoralno uključene u meko nepce.

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**Ključne riječi**
karcinom; nazofarinks; Epstein-Barrov virus; Herpesvirus 4, humani; orofarinks; meko nepce; Indija

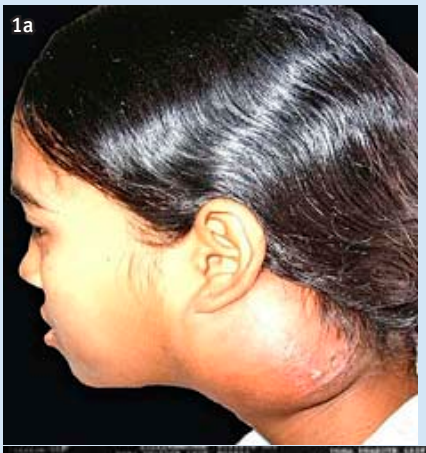
## Uvod

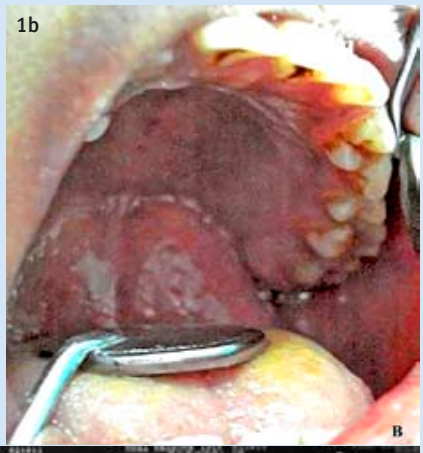
U području nazofaringsa može se pronaći mnogo različitih novotvorina, ali nazofaringealni karcinom (NPC) intrigira naraštaje onkologa, patologa, znanstvenika i epidemiologa zbog varljive etiologije te kliničkih i histoloških svojstava. Za tu vrsta raka u nazofaringealnoj sluznici malo je mikroskopskih i ultrastrukturalnih dokaza skvamozne diferencijacije, s prosjekom od 80 tisuća novih slučajeva na godinu, što iznosi 0,6 posto svih karcinoma (1). Ima određenu rasnu i zemljopisnu rasprostranjenost. U skupinama visokoga rizika incidencija NPC-a raste nakon dobi od 30 godina i vrhunac postiže između 40 i 50 godine, a nakon toga opada. Češće obolijevaju muškarci i to dva do tri puta. Rasna i zemljopisna rasprostranjenost NPC-a i vremenski trendovi te karakteristike opažene kod migranata pokazuju međuovisnost genetske osjetljivosti, infekcije Epstein – Barrovim virusom (EBV-om) i utjecaj okoliša (prehrambeni i neprehrambeni) u etiologiji bolesti (2).

## Introduction

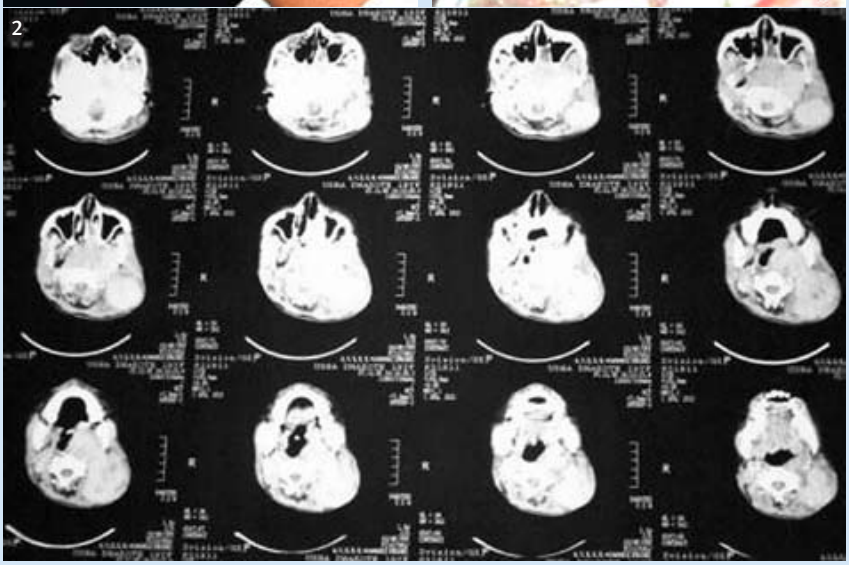
A wide range of tumors arise in the nasopharynx, but it is the nasopharyngeal carcinoma (NPC) that has fascinated generations of oncologists, pathologists, scientists and epidemiologists because of its deceptive etiological, clinical and histological features.

Nasopharyngeal carcinoma is a carcinoma arising in the nasopharyngeal mucosa which shows light microscopic or ultra structural evidence of squamous differentiation, with an average of 80,000 new cases of NPC recorded per year, that is 0.6 % of all cancers (1). It shows a distinct racial and geographical distribution. In high-risk groups, NPC incidence rises after the age of 30 and peaks at 40-60 years, and declines thereafter. It is 2-3 times more common in males than in females. The specific geographical and demographic distribution of nasopharyngeal carcinoma, as well as time trends and patterns observed in migrants reflect the interplay of genetic susceptibility, infection by Epstein-Barr virus

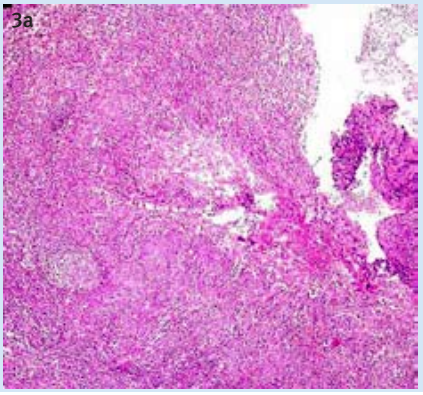


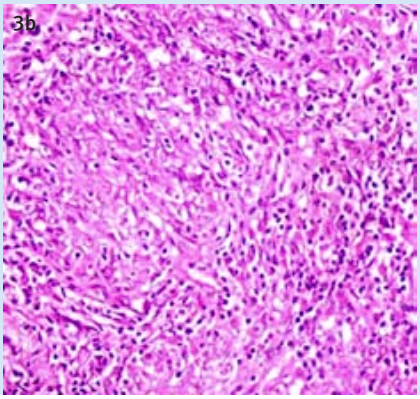




**Slika 1.** a. Ekstraoralni prikaz opsega otekline u lijevom području vrata. b. intraoralni prikaz otekline u anteriorno facio pilarnom području – opstruira orofarings i zahvaća meko nepce.
**Figure 1** Clinical photographs: - A. Extraoral photograph showing extent of swelling in left lateral region of neck. B. Intraoral photograph showing swelling in anterior faucial pillar region, obstructing the oropharynx and involving soft palate.




**Slika 2.** Kompjutorska tomografija – aksijalni pogled
**Figure 2** Photograph of computed tomography showing axial view.




**Slika 3.** Fotomikrografija H i E obojeni rez koji prikazuje: a. Poremećaj u građi limfnog tkiva s područjima bogatima nediferenciranim stanicama (izvorno povećanje x100). b. Stanice sa slabo definiranom citoplazmom i velikom vezikularnom jezgricom, te zrele limfoidne stanice s jednostrukom jezgricom – slabo definirana citoplazma upućuje na ubrzan rast (izvorno povećanje x400).
**Figure 3** Photomicrographs H & E stained section showing: - A. Disturbance in architecture of lymphoid tissue with areas of nests of undifferentiated cells (original magnification x100). B. Cells were seen with poorly defined cytoplasm and large vesicular nucleolus with prominent single nucleolus in stroma of mature lymphoid cells. Poorly defined cytoplasm imparted syncitial growth pattern (original magnification x400).

Premda je čest u azijskim zemljama, maligni nazofaringsni karcinom relativno je rijetka bolest u Indiji. Danona i njegovi kolege istaknuli su 2009. godine da je 177 pacijenata s NPC-om i udaljenim metastazama imalo median preživljavanja devet mjeseci i 20-postotno ukupno preživljavanje od pet godina (3). To pokazuje da je potrebna rana dijagnoza i kombinirano agresivno liječenje kako bi se povećalo preživljavanje u takvim slučajevima. Za bolje razumijevanje etiološke patogeneze, kliničkih i patoloških svojstava, ranu dijagnozu i prognozu NPC-a opisujemo kao rijedak slučaj nediferenciranog nazofaringealnog karcinoma s oralnim manifestacijama.

(EBV) and environmental factors (dietary and non dietary) in disease causation (2).

Although it is more common in many Asian countries, the malignancy of the nasopharynx is a relatively rare disease in India. Median survival of 9 months and 5-year overall survival of 20% was reported in 177 distant metastatic cases of NPCs in a survey carried out by Dandona et al. in 2009 (3). This indicates the need for an early diagnosis and combined aggressive treatment for improving the survival of such cases. For better understanding of etiopathogenesis, clinical and pathological features, early diagnosis and prognosis of NPC, we report a rare case of undifferentiated nasopharyngeal carcinoma with oral manifestation.

## Prikaz slučaja

Djevojka od 19 godina žalila se liječniku na oteklinu ispod lijevog uha koja se pojavila prije tri mjeseca i već mjesec i pol na bolove u tome području. Ostali simptomi bili su opstruktivna apnea tijekom spavanja te sukrvav, žućkast, gust povremeni iscjedak iz nosa u posljednjih mjesec dana. Istaknula je i promjenu boje glasa u zadnjih 15 do 20 dana te poteškoće u gutanju. Pacijentica se požalila i na gubitak apetita i težine. Fizikalnim pregledom ustanovljena je velika, samostalna, ovalna oteklina 8 x 10 centimetara u području stražnjeg aurikularnog područja na lateralnoj strani vrata uz podignutu ušku (slika 1. a). Na palpaciju je bila mekana s dobro ograničenim rubovima i čvrste konzistencije. Bila je pričvršćena za okolne strukture. Submandibularni limfni čvorovi bili su palpabilni bilateralno kao i desni jugulodigastrični limfni čvorovi, čvrsti u konzistenciji i fiksirani. Intraoralnim pregledom (slika 1. b) ustanovljena je difuzna oteklina u anteriornom faciopilarnom području s opstrukcijom orofaringsa i zahvaćenim mekim nepcem. Bila je blijedo ružičasta s glatkom i čvrstom površinom. Ekstraoralna i intraoralna oteklina je, prema podacima u posljednjih petnaest dana, vrlo brzo rasla. Intraoralna oteklina upućivala je na znatno povećanje i djelomičnu opstrukciju orofaringsa te promjenu glasa.

Analizirajući sve kliničke nalaze, diferencijalnodijagnostički su uzeti u obzir: metastaze limfnih čvorova, limfom, tumor parotidne žlijezde, cistični higrom, cista branhijalnog rascjepa i angiofibrom.

Pacijentica je obavila preglede poput ultrazvuka, citološke analize aspirata (FNAC-a), kompjutorizirane tomografije te incizijske biopsije kako bi se postavila dijagnoza. Na radiogramu prsnog koša oba pluća bila su normalna, bez metastaza. Na ultrazvuku vrata kao da su se nazirale metastatske mase. CT-snimka (slika 2.) otkrila je veliku, dobro definiranu masu u području sfenopalatinalnog foramena koja se uzdizala do vertebralnog prostora pritištući nazofaringealno zračni put s lijeve strane i protežući se do orofaringsa. Na temelju tih nalaza pretpostavili smo da se radi o malignom juvenilnom angiofibromu (drugi stupanj).

FNAC je upućivao na mogući limfanendoteliom jer je dobio vretenast oblik endotelialnih stanica u blizini limfoidnih stanica i histiocite. Incizijska biopsija obavljena je na masi na vratu i pokazala je poremećaj u građi limfoidnog tkiva (slike 3.a i 3.b). Neke su stanice imale loše definiranu citoplazmu te velike vezikularne jezgre i izražene solitarne jezgrice. Slabo definirana citoplazma upućuje na ubrzan rast. Takve stanice nađene su u stromi zrelih limfoidnih stanica. Ti su nalazi upućivali na nazofaringealni karcinom, tip III. prema SZO-u. Postavljena je konačna dijagnoza nazofaringealnog karcinoma – tip III. prema SZO-u (AJCC–stupanj T4N3 aM0 – stupanj 4.). Pacijentica je podvrgnuta radioterapiji tijekom mjesec dana od postavljanja dijagnoze. Na kontrolnom pregledu nakon osam mjeseci njezino se stanje nije poboljšalo i ubrzo je umrla.

## Case report

A 19-year-old female patient presented with a chief complaint of swelling below the left ear region for three months and pain in the same region for one and half months. Other associated complaints were obstructive sleep apnea and blood tinged, yellowish, viscous, intermittent nasal discharge for one month, change in voice for 15-20 days and difficulty in swallowing. The patient also complained of loss of appetite and weight loss. Local examination showed a single, large, oval shaped swelling of size 8x10 cm in the left posterior auricular region on the lateral side of the neck with raised ear lobule (Figure 1 A). On palpation, the swelling was found to be tender with well-defined margins and it was hard in consistency. It adhered to underlying structures. Bilateral submandibular lymph nodes and right jugulodigastric lymph nodes were palpable, firm in consistency, and fixed. Intraoral examination (Figure 1B) showed a single, diffuse swelling in the anterior faucial pillar region, obstructing the oropharynx and involving the soft palate. The color was pale pink with smooth surface and consistency was firm. The extraoral and intraoral swellings showed rapid increase in size within fifteen days of reporting. The intraoral swelling showed considerable increase in size with partial obstruction of the oropharynx with change of voice.

Considering the history and clinical findings, the patient was differentially diagnosed with Lymph Node Metastasis, Lymphoma, Parotid Tumor, Cystic Hygroma, Branchial Cleft Cyst and Angiofibroma. The patient underwent examinations, procedures and methods such as Ultrasonography (USG), Fine Needle Aspiration Cytology (FNAC), Computed Tomography (CT) scan and an incisional biopsy in order to confirm the diagnosis. On chest X-ray, both lung fields were found to be normal without any metastases. USG neck gave impression of Metastatic Mass. CT scan (Figure 2) showed large, well defined mass in the region of sphenopalatine foramen, which was seen to be extending up to vertebral space, compressing the nasopharyngeal airway from the left side and reaching up to the oropharynx. Based on these findings, we suggested the possibility of Malignant Juvenile Angiofibroma (Grade 2).

FNAC pointed to the possibility of Lymphangioendothelioma as it revealed spindle shaped endothelial cells in proximity to lymphoid cells and histiocytes. The incisional biopsy was performed on the neck mass, which showed disturbance in architecture of lymphoid tissue (Figure 3A & 3B). Some cells were seen with poorly defined cytoplasm and large vesicular nucleoli with prominent single nucleoli. Poorly defined cytoplasm imparted syncytial growth pattern. These cells were seen in stroma of mature lymphoid cells. These features were suggestive of Nasopharyngeal Carcinoma, WHO type 3. Final diagnosis was made as Nasopharyngeal carcinoma-WHO type III (AJCC staging - T4N3aM0- Stage 4). The patient started with radiotherapy within one month of diagnosis. On follow up of eight months, the patient's condition did not improve and she passed away afterwards.

## Rasprava

Posljednjih godina je nazofaringealni karcinom privukao pozornost znanstvenika diljem svijeta zbog složene povezanosti s genetskim, virusnim, okolišnim i prehrambenim čimbenicima koji bi mogli biti povezani s etiologijom te bolesti. NPC je zemljopisno dobro definiran i smatra se da najčešće obolijevaju Kinezi u jugoistočnoj Aziji, Arapi u sjevernoj Africi i Eskimi u arktičkim područjima (4).

U usporedbi s ostalim područjima, indijski potkontinent ima vrlo nisku incidenciju NPC-a, osim etničke skupine na sjeveroistoku gdje je velika incidencija u Nagalandu (na godinu oko 4,3 slučaja u populaciji od 100 tisuća)(5). Tri etiološka čimbenika koji pridonose zemljopisnoj rasprostranjenosti NPC-a su: (A) ubikvitaran Epstein-Barrov virus, (B) opće određena primljivost i (C) okolišem povezani čimbenici koji sugeriraju da je etiologija te bolesti višestupanjski proces (7). Otkrivanje nuklearnog antigena povezanog s Epstein-Barrovim virusom (EBNA-om) i virusni DNK u NPC-u tipa II. i III. pokazalo je da EBV može inficirati epitelne stanice i da je povezan s njihovom transformacijom. Otkriveno je također da genska sekvencija EBV-a sudjeluje u raznim imunskim izbjegavanjima i regulaciji različitih staničnih signalnih kaskada. Činjenica da se genom EBV-a nalazi u gotovo svakom tkivu NPC-a, čini ga gotovo idealnim biljegom za tu bolest. Kvantitativne analize protutijela EBV-a i EBV-ov DNK pokazali su se klinički korisnima u ranom otkrivanju, praćenju i prognozi te bolesti (8). Premda razvoj te vrste raka uključuje osjetljivost na genetske mutacije, genski polimorfizam i latentnu infekciju EBV-om, patogeneza se razlikuje od endemičnih do povremenih slučajeva. Kod endemičnih naslijeđenih slučajeva, genetske bi promjene mogle biti prvi stupanj, a EBV može pridonijeti drugi, te zato u takvim slučajevima bolest ranije počinje. Suprotno tomu, kod povremenih, sporadičnih slučajeva, infekcija EBV-om djeluje kao prvi stupanj zajedno s okolišnim kancerogenima koji prelaze drugi stupanj. U takvim slučajevima NPC se pojavljuje u starijoj populaciji (1). Uzevši u obzir taj model razvoja povremenih i endemskih oblika bolesti, povremeni slučajevi NPC-a trebali bi se pojavljivati u starijoj populaciji, što u ovom istraživanju nije tako jer je naša pacijentica imala samo 19 godina.

Klinički podaci dobiveni od 722 pacijenta liječenih u Pamela Youde Nothersole Eastern bolnici u Hongkongu od 1994. do 2001. godine otkrivaju da je glavni simptom u 42 posto slučajeva bio oteklina vrata, dva posto bili su problemi s govorom i gutanjem, a zahvaćenost orofaringsa i mekog nepca bila je zabilježena u 21 posto slučajeva (1). Naša pacijentica javila se zbog otekline na vratu i gubitka glasa te poteškoća s gutanjem zbog opsežne zahvaćenosti orofaringsa i mekog nepca. NPC je problem u postavljanju kliničke dijagnoze zbog blagih simptoma i teškoća tijekom pregleda nazofaringsa.

U našem slučaju pacijentica je imala otečen vrat, što se na početku diferencijalno-dijagnostički vodilo kao tumor parotide, cista branhijalnog rascjepa i metastatska masa. Nalaz FNAC-a davao je naznake da bi se moglo raditi o lymphangioendotheliomu, ultrazvuk da je riječ o metastatskoj masi, a CT mogućnost malignoga juvenilnog nazofaringealnog angiofibroma (II. stupnja). Neobična i varljiva histološka slika

## Discussion

In recent years, nasopharyngeal carcinoma has attracted worldwide attention because of complex interactions of genetic, viral, environmental and dietary factors, which might be associated with the etiology of the disease. It has well defined geographical distributions and has been reported to be prevalent in Chinese in South East Asia, Arabs in North Africa and Eskimos in the Arctic region (4).

When compared to some other parts of the world, the Indian subcontinent has a very low incidence, except amongst the ethnic groups of Northeastern parts of India with a high incidence in Nagaland (about- 4.3per100000/year) (5). Three etiological factors which contribute to particular geographic distribution of NPC are (A) the ubiquitous Epstein Barr virus, (B) genetically determined susceptibility and (C) associated environmental factors, which suggest that the etiology of NPC is a multi-step process (7). The detection of nuclear antigen associated with Epstein-Barr virus (EBNA) and viral DNA in NPC type 2 and 3 has revealed that EBV can infect epithelial cells and is associated with their transformation. EBV encoded genes have been shown to be involved in immune evasion and in the regulation of various cellular signaling cascades. The fact that EBV genome is present in almost all NPC tissues renders it an ideal tumor marker for NPC. Quantitative analyses of EBV antibodies and EBV DNA have been shown to be clinically useful for early detection, monitoring and prognostication of NPC (8).

Though the NPC development involves the susceptibility to gene mutations, gene polymorphisms and latent EBV infections, the pathogenesis differs in endemic and sporadic cases. In endemic inherited cases, inherited genetic alterations could be the first hit and EBV may contribute as the second hit, therefore, such cases usually have younger age of onset. On the other hand, in sporadic cases, EBV infection acts as a first hit with environmental carcinogens acting as second hit and therefore in such cases NPC usually occurs in older age groups (1). Considering this putative model for the development of sporadic and endemic forms of NPC, sporadic cases should occur in older age groups but in our patient, the age of occurrence was 19 years.

Clinical data from 722 patients treated at Pamela Youde Nothersole Eastern Hospital, Hongkong during 1994 to 2001 showed neck mass as presenting symptom in 42 % and speech and swallowing problems in 2% of cases, whereas oropharyngeal and the soft palate involvement in 21% of cases (1).[1] In our case, the patient presented with neck mass and congestion of voice and difficulty in swallowing due to extensive involvement of the oropharynx and the soft palate. NPCs always pose a problem in clinical diagnosis due to vague presenting symptoms and the difficulty of the examination of the nasopharynx. In our case, the patient also presented with the neck mass, which was initially differentially diagnosed as parotid tumor, branchial cleft cyst and metastatic mass. FNAC was suggestive of lymphangioendothelioma, USG was suggestive of metastatic mass, and CT suggested the possibility of Malignant Juvenile Nasopharyngeal Angiofibroma (grade2).

NPC-a stvorila je suprotna mišljenja o prirodi toga tumora te još i danas predstavlja izazov kirurzima-patolozima. Na temelju klasifikacije prema SZO-u, novotvorine nazofaringsa dijele se na nekeratinizirajući karcinom, keratinizirajući karcinom skvamoznih stanica te karcinom bazalnih skvamoznih stanica. Histopatološka dijagnoza može se potkrijepiti imunohistokemijskim istraživanjima – na temelju tih podataka potvrđeno je da je NPC maligna neoplazma epitela (9). Premda nediferencirani NPC ne daje posebne biljege citokeratina (10), čini se da je karcinom bazaloidnih stanica pozitivan posebice na CK14 (11). U našem slučaju je pacijentici histopatološki bio dijagnosticiran nediferencirani nekeratinizirajući nazofaringealni karcinom.

Ti tumori su vrlo maligni jer se vrlo rano i brzo šire limfom (zbog bogatoga limfatičkog pleksusa) te visoke incidencije hematološkog širenja. Uobičajeno je širenje prema bazi lubanje, paranazalnim sinusima, orbiti i bazalnim foramenima. Kod oko 50 posto pacijenata metastaze u limfnim čvorovima nalaze se odmah nakon što se bolest otkrije. Jugulogastrični čvorovi i posteriorni cervikalni lanac limfnih čvorova češće su zahvaćeni negoli u slučaju bilo kojeg raka glave i vrata. Usporedna kemoterapija jedna je od najučinkovitijih strategija da bi se tumor stavio pod nadzor u uznapredovalim slučajevima NPC-a jer može pojačati lokalno djelovanje i uništavati maligne stanice (12). U našem slučaju pacijentici je preporučena radioterapija paralelno s kemoterapijom, ali je odbila kemoterapiju. Ordinirana doza radioterapije bila je 68 Gya za centralnu masu u nazofaringsu (GTVnx) i 60 do 64 Gya za pozitivne limfne čvorove na vratu (GTVnd). Pacijentica je na žalost podlegnula bolesti osam mjeseci nakon terapije.

Od nedavno prihvaćenih protokola, najbolji se rezultati postižu Mertensovim protokolom NPC-91-GPOH (Society of Pediatric Oncology and Hematology). Njegova posebnost je u tome da uključuje imunoterapiju s interferonom beta nakon kemoterapije i radioterapije, što bi moglo objasniti veću uspješnost u odnosu prema protokolima bez primjene interferona. Visokorizični pacijenti dobivaju cisplatinum (100 mg/m$^2$ šest sati prvi dan sa standardnom hidratacijom), manitol i elektrolitne zamjene, folnu kiselinu (25 mg/m$^2$ svakih šest sati – ukupno šest doza) te 5-fluorouracil (1000 mg/m$^2$ na dan pet dana, počevši od drugog dana) kao neprekidnu infuziju. Bolesnici dobivaju tri slijeda kemoterapije svaka tri tjedna ili dok se ne obnovi krvna slika, a zatim slijedi iradijacija i interferon beta (13).

Ukupno preživljavanje od pet godina u SAD-u je oko 40 do 80 posto (ovisno o endemičnom ili sporadičnom tumoru) kod nediferenciranog NPC-a (65 posto). Jedan od loših prognostičkih pokazatelja uključuje uznapredovalu kliničku sliku (14, 15), a u našem slučaju pacijentica je imala IV. stupanj NPC-a. Lee i suradnici su 2009. ispitali utjecaj zahvaćanja prevertebralnih ili faringealnih područja te veliki volumen tumora na terapijski rezultat kod 105 pacijenata s NPC-om (16). Ustanovili su da oni s dijagnozom NPC-a te dva ili nekoliko tih čimbenika imaju više recidiva tumora i manju stopu preživljavanja (16). Naša pacijentica imala je ne samo velik tumor, nego se proširio sve do vertebralnog područja.

U literaturi je istaknuto petogodišnje preživljavanje, bez bolesti, bez pojave bolesti i bez lokalnih simptoma (55 po-

The unusual and deceptive histological features of NPC have generated controversies over the nature of the tumor and still pose challenge to surgical pathologists. WHO histological classification of tumors of the nasopharynx has divided nasopharyngeal carcinoma into nonkeratinizing carcinoma, keratinizing squamous cell carcinoma and basaloid squamous cell carcinoma. Histopathological diagnosis can be supported by immunohistochemical studies and it has been found in various studies that NPC is a definite malignant epithelial neoplasm (9). Although undifferentiated NPC reveals no specific pattern of cytokeratin expression (10), basaloid squamous cell carcinoma is seen to be positive for CK14 in particular (11). In our case, the patient was histopathologically diagnosed as having Undifferentiated Nonkeratinizing Nasophryngeal Carcinoma.

These tumors are highly malignant with extensive and early lymphatic spread (due to a rich lymphatic plexus) and a high incidence of hematogenous spread. Direct extension into the base of the skull, paranasal sinuses, orbit and basal foramina is common. About 50% of patients will have lymph node metastasis at presentation. Specifically, the jugulo-digastric node and the posterior cervical chain are more frequently affected than by any other head and neck cancer. Concurrent chemoradiotherapy is one of the most promising strategies for improving tumor control in advanced NPC, as this has potential for both enhancing the local effect of radiotherapy and eradicating micrometastases (12). In our case the patient was also advised to start radiotherapy with concurrent chemotherapy but the patient refused to take chemotherapy. The prescription dose for radiotherapy was 68 Gy to the nasopharynx gross tumor volume (GTVnx), 60-64 Gy to positive neck lymph nodes (GTVnd). Unfortunately, the patient succumbed to the illness within eight months of therapy.

With recent update, the most promising results are those obtained using the Mertens protocol NPC-91-GPOH (Society of Pediatric Oncology and Hematology). Uniquely, the NPC-91-GPOH protocol includes immunotherapy with interferon-beta after chemotherapy and radiotherapy, which may explain its superior results compared to regimens without interferon treatment. High-risk patients receive cisplatinum (100 mg/m$^2$ over 6 hours on day 1 with standard hydration), mannitol and electrolyte replacement, and folinic acid (25 mg/m$^2$ every 6 hours for a total of six doses) as well as 5-fluorouracil (1000 mg/m$^2$ per day from day 2 for 5 days) as a continuous infusion. They receive three courses of chemotherapy every 21 days or on full blood count recovery, followed by irradiation and IFN beta (13).

Overall 5-year survival reported in the United States is about 40–80% (depending on endemic versus sporadic tumor) with undifferentiated NPC (65%). One of the poor prognostic indicators include advanced clinical stage (14, 15) and, in our case the patient had stage IV NPC. The impact of invasion of the prevertebral or parapharyngeal spaces and large tumor volume on treatment outcomes in patients with NPC was evaluated on 105 patients by Lee CC et al. in 2009 (16). NPC patients with two or more of these factors were found to have more recurrence and poor survival rates (16). Our patient also had a large tumor volume and the tumor was seen to be extending to vertebral space as well.

sto, 36 posto, 58 posto i 59 posto) kod 58 pacijenata s NPC-om u razdoblju od 10 godina. Svi su bili na terapiji u izmirskom Onkološkom centru (IOC-u) (17). Devetomjesečni medijan preživljavanja (95-postotni interval pouzdanosti: 7 do 13 mjeseci) i 20-postotno ukupno preživljavanje pet godina (OS) (95-postotni interval pouzdanosti: 14 do 26 %) objavili su Dandoda i suradnici za 77 udaljenih metastatskih bolesti NPC-a godine 2009. (3). Niska stopa preživljavanja bez bolesti kod takvih pacijenata upućuje na potrebu ranog dijagnosticiranja i agresivnu terapiju kako bi se povećalo preživljavanje.

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The 5-year overall survival, disease-free survival, local failure-free survival, and distant failure-free survival rates were reported to be 55, 36, 58 and 59%, respectively in 58 patients of NPC over a period of 10 years treated at Izmir Oncology Center (IOC) (17). Median survival of 9 months (95%CI: 7-13 months) and 5-year overall survival (OS) of 20% (95%CI: 14-26%) was reported in 177 distant metastatic cases of NPC in a survey carried out by Dandona MA et al. in 2009 (3). Low disease-free survival rate in such patients indicates a need for an early diagnosis and combined aggressive treatment in order to improve their survival.

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**Abstract**
Nasopharyngeal carcinoma (NPC) is a rare malignancy in most parts of the world and is one of the most confusing, commonly misdiagnosed, and poorly understood diseases. It is unusual among all the head and neck cancers due to its marked geographical predilection, highly malignant tumor growth characteristics, special difficulties in detection and staging and a high rate of treatment failure despite of its radiosensitivity. This carcinoma is rare in most parts of the world with reported incidence of around 1 case per 100,000 population per year. Nasopharyngeal carcinoma is common in Southern China and North Africa, where the etiology is related to dietary habits but it is rare in other parts of the world. Therefore, for better understanding of etiopathogenesis, clinical pathological features, early diagnosis and prognosis of NPC, we report a rare case of a nasopharyngeal carcinoma in Central India, of a 19 year old female patient who presented with a mass in her neck and intraoral involvement of the soft palate.

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**Key words**
Nasopharyngeal carcinoma (NPC), Central India, Epstein Barr Virus (EBV), oropharynx, soft palate.

## References

1. Chan JK, Bray F, McCarron P, Foo W, Lee AW, Yip T et al. Nasopharyngeal carcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. World health organization classification of tumors: Pathology and genetics of head and neck tumors. Lyon: IARC Press; 2005. p. 85-97.
2. Fedder M, Gonzalez MF. Nasopharyngeal carcinoma. Brief review. Am J Med. 1985 Sep;79(3):365-9.
3. Dandona MA, Morgensztern D, Auethavekiat V, Adkins D, Thorstad W, Nussenbaum B, et al. Survival for nasopharyngeal cancer with distant metastatic disease at presentation. J Clin Oncol. 2009;27 Suppl 15:e17004.
4. Chan AT, Teo PM, Johnson PJ. Nasopharyngeal carcinoma. Ann Oncol. 2002 Jul;13(7):1007-15.
5. Epidemiological and etiological factors associated with nasopharyngeal carcinoma. ICMR Bulletin. 2003 Sept;33:1-9.
6. Ho JH. An epidemiologic and clinical study of nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys. 1978 Mar-Apr;4(3-4):182-98.
7. Brennan B. Nasopharyngeal carcinoma. Orphanet J Rare Dis. 2006 Jun 26;1:23.
8. Cho WC. Nasopharyngeal carcinoma: molecular biomarker discovery and progress. Mol Cancer. 2007 Jan 2;6:1.
9. Nomori H, Kameya T, Shimosato Y, Saito H, Ebihara S, Ono I. Nasopharyngeal carcinoma: immunohistochemical study for keratin, secretory component and leukocyte common antigen. Jpn J Clin Oncol. 1985 Mar;15(1):95-105.
10. Friedrich RE, Bartel-Friedrich S, Lobeck H, Niedobitek G, Arps H. Epstein-Barr virus DNA and epithelial markers in nasopharyngeal carcinoma. Med Microbiol Immunol. 2003 Aug;192(3):141-4.
11. Coletta RD, Cotrim P, Almeida OP, Alves VA, Wakamatsu A, Vargas PA. Basaloid squamous carcinoma of oral cavity: a histologic and immunohistochemical study. Oral Oncol. 2002 Oct;38(7):723-9.
12. Lee AW, Lau WH, Tung SY, Chua DT, Chappell R, Xu L et al. Preliminary results of a randomized study on therapeutic gain by concurrent chemotherapy for regionally-advanced nasopharyngeal carcinoma: NPC-9901 Trial by the Hong Kong Nasopharyngeal Cancer Study Group. J Clin Oncol. 2005 Oct 1;23(28):6966-75.
13. Rodriguez-Galindo C, Wofford M, Castleberry RP, Swanson GP, London WB, Fontanesi J et al. Preradiation chemotherapy with methotrexate, cisplatin, 5-fluorouracil, and leucovorin for pediatric nasopharyngeal carcinoma. Cancer. 2005 Feb 15;103(4):850-7.
14. Thompson LD. Update on nasopharyngeal carcinoma. Head Neck Pathol. 2007 Sep;1(1):81-6.
15. Cheng SH, Yen KL, Jian JJ, Tsai SY, Chu NM, Leu SY et al. Examining prognostic factors and patterns of failure in nasopharyngeal carcinoma following concomitant radiotherapy and chemotherapy: impact on future clinical trials. Int J Radiat Oncol Biol Phys. 2001 Jul 1;50(3):717-26.
16. Lee CC, Chu ST, Chou P. Concurrent chemoradiotherapy with adjuvant chemotherapy for high-risk nasopharyngeal carcinoma. Auris Nasus Larynx. 2009 Dec;36(6):688-94.
17. Gokce T, Unlu I, Akcay C. Evaluation of overall survival of nasopharyngeal carcinoma patients treated in ten years at a single institution. J BUON. 2010 Jan-Mar;15(1):36-42.