clinical practice guidelines

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Nasopharyngeal cancer: EHNS–ESMO–ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up

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incidence

Cancer of the nasopharynx (NPC) is rare in Europe, with an annual crude incidence rate of 1.1 per 100 000. On the European scale, NPC accounts for 4760 new cases per year. Incidence is higher in men than women.

In Europe the relative survival for NPC was 76% at 1 year and 50% at 5 years in adults. There were no survival differences between sexes. The effect of age on survival is marked. Survival at 5 years was 72% for the youngest age group (15–45 years) and 36% in the oldest group of patients (65–74 years).

diagnosis

Definitive diagnosis is made by endoscopic guided biopsy of the primary nasopharyngeal tumour. The histological type should be classified according to World Health Organization classification. Since the first disease sign in patients is often the appearance of neck nodes it is not infrequent that patients undergo neck biopsy and or neck nodal dissection. This procedure is not recommended since it may reduce cure probability and have an impact on late treatment sequelae.

staging and risk assessment

NPC is clinically staged according to the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) staging system (Table 1). Routine staging procedures include history, physical examination including cranial nerve examination, complete blood cell count, serum biochemistry (including liver function test), chest X-ray, nasopharyngoscopy, computed tomography (CT) scan or magnetic resonance imaging (MRI) of nasopharynx and base of skull and neck. MRI is preferred if available [III, B]. Imaging for distant metastases including isotope bone scan and CT scan of chest and upper abdomen could be considered for at-risk subsets (node positive, especially N3 stage) and for those patients with clinical or biochemical abnormalities detected [III, B]. The use of positron emission tomography/TC can replace the traditional work-up for detection of distant metastatic disease since it has proved to be the most sensitive, specific and accurate diagnostic method. Both the pre-treatment and post-treatment plasma/serum load of Epstein–Barr viral DNA has been shown to be of prognostic value [III, B].

treatment

Radiation therapy (RT) is the mainstay of treatment and is an essential component of curative-intent treatment of non-disseminated NPC. Stage I disease is treated by RT alone, while stage III, IVA, B disease are treated by RT with concurrent chemotherapy [I, A]. Concurrent chemotherapy could be considered for stage II disease [III, B]. Patients should be treated by intensity-modulated radiation therapy (IMRT) if possible [II, A]. RT is targeted to the primary tumour and adjacent regions considered at risk of microscopic spread from the tumour, and to both sides of the neck (levels Ib–V, and retropharyngeal nodes). For patients with lower neck nodes, the supraclavicular fossa should be included as well. Elective nodal irradiation is recommended for N0 stage disease. The consensus is that a total dose of 70 Gy is needed for eradication of gross tumour and either 50–60 Gy or 46–60 Gy for elective treatment of potential risk sites. To minimize the risk of late toxicity (particularly to adjacent neurological structures), fractional dose >2 Gy per daily fraction and excessive acceleration with multiple fractions >1.9 Gy/fraction should be avoided [III, A]. IIMRT may offer improvement in local tumour control [III, B], and reduction in radiation xerostomia

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Table 1. The UICC/AJCC staging system for NPC, seventh edition (2009)

Nasopharynx (T)			
T1	Tumour confined to nasopharynx, with or without extension to oropharyngx, nasal cavity but without parapharyngeal extension		
T2	Tumour with parapharyngeal extension		
T2a	Tumour extends to oropharyngx and/or nasal cavity without parapharyngeal extension		
T2b	Tumour with parapharyngeal extension		
T3	Tumour invades bony structures of skull and/or paranasal sinuses		
T4	Tumour with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, orbit or masticator space		
Regional lymph node (N)			
N1	Unilateral cervical, unilateral or bilateral retropharyngeal lymph node(s), 6_cm or less in greatest dimension, above supraclavicular fossa		
N2	Bilateral cervica lymph nodes, ≤6 cm in greatest dimension, above supraclavicular fossa		
N3	Metastasis in lymph node(s), >6 cm in dimension (N3a) or in the supraclavicular fossa (N3b)		
Distant metastasis (M)			
M0	No distant metastasis		
M1	Distant metastasis		
Stage grouping			
Stage 0	T *in situ*	N0	M0
Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0, N1	M0
Stage III	T1,T2	N2	M0
	T3	N0, N1, N2	M0
Stage VIA	T4	N0, N1, N2	M0
Stage IVB	Any T	N3	M0
Stage IVC	Any T	Any N	M1

UICC, International Union Against Cancer; AJCC, American Joint Committee on Cancer.

in early stage disease [II, B]. The standard agent used in concurrent chemotherapy–RT is cisplatin [I, A]. This provides a benefit in term of overall survival and both on locoregional and distant control. Even though adjuvant chemotherapy on its own has not been documented to confer survival advantage, adjuvant cisplatin and fluorouracil combined with concurrent cisplatin–RT may be beneficial. Cisplatinum-based induction chemotherapy has been shown to improve disease-free survival and may be considered in locally advanced disease although it is not seen as standard treatment [II, B]. In no case should induction chemotherapy negatively affect the optimal administration of concomitant chemoradiation.

follow-up

MRI should be used to evaluate the response to RT or chemoradiotherapy. Follow-up for patients includes periodic examination of the nasopharynx and neck, cranial nerve function and evaluation of systemic complaints to identify distant metastasis. For T3 and T4 tumours, MRI might be used on a 6- to 12-month basis to evaluate the nasopharynx and the base of the skull at least for the first few years after treatment. Evaluation of thyroid function in patients with irradiation to the neck is recommended at 1, 2 and 5 years.

treatment of recurrent or metastatic disease

Small local recurrences are potentially curable and the main issue is choice of the most appropriate therapeutic options, which include nasopharyngectomy, brachytherapy, radiosurgery, stereotactic RT, IMRT, or a combination of surgery and RT, with or without concurrent chemotherapy. Treatment decisions are tailored to the specific situation of individual cases, taking into consideration the volume, location and extent of the recurrent tumour [III, B]. Regional recurrence is managed by radical neck dissection if resectable [III, B].

In metastatic NPC, palliative chemotherapy should be considered for patients with adequate performance status. Platinum combination regimens are commonly used as first-line therapy since cisplatin represents the most effective drug. Other active agents include paclitaxel, docetaxel, gemcitabine, capecitabine, irinotecan, vinorelbine, ifosfamide, doxorubicin and oxaliplatin, which can be used as single agents or in combination [III, C]. Polychemotherapy is more active than monotherapy. In this context treatment choice should be based on previous treatments and the expected toxicity.

notes

Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts.

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