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Nasopharyngeal Carcinomas: Etiology, Diagnosis, and Current Management

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ABSTRACT

Malignant nasopharyngeal tumors, primarily represented by epithelial nasopharyngeal carcinoma (NPC)—especially the non-keratinizing squamous cell carcinoma (NKSCC) or undifferentiated carcinoma of nasopharynx (UCNT)—differ from other head and neck squamous cell carcinomas (HNSCCs) by their characteristic undifferentiated histology, a lack of association with alcohol and tobacco consumption, and a constant association with the Epstein-Barr virus (EBV). UCNT exhibits an endemic distribution in certain regions such as Southeast Asia and the Mediterranean Basin. Its etiology is multifactorial, involving genetic factors, the EBV virus, as well as environmental factors like salted/smoked foods and nitrosamines. Diagnosis is often delayed due to the deep anatomy of the cavum (nasopharynx). This cancer is characterized by a high rate of nodal and even distant (visceral) metastases, which accounts for some therapeutic failures despite its notable radiosensitivity and good locoregional control. In Algeria, it is the most common ENT cancer and the 12th most common cancer overall (2.4%, intermediate incidence area), primarily affecting males, with a bimodal age distribution (peaks at 10-24 years and 45-60 years). The year 2025 marks a period of dynamic progress in both diagnosis and therapeutic approaches, thereby improving the prognosis of this condition.

Keywords

Nasopharyngeal Carcinoma, Diagnosis, TNM, Radiotherapy, Concurrent Chemoradiotherapy, Immunotherapy.

Introduction

Nasopharyngeal Carcinoma (NPC) is a unique malignancy arising from the epithelial lining of the nasopharynx. It is globally a relatively rare cancer, ranking 23rd in frequency worldwide with over 120,000 new cases annually [1]. However, NPC exhibits a striking geographical disparity, showing endemic distribution patterns with high incidence rates in specific regions, notably Southeast Asia (30–80/100,000/year) and intermediate rates in the Mediterranean Basin, including the Maghreb region (8–12/100,000/year) [2]. For instance, in Algeria, NPC is the most common head and neck cancer [1].

NPC is pathologically distinct from other head and neck squamous cell carcinomas (HNSCCs) due to its strong and constant association with the Epstein-Barr virus (EBV), with viral DNA detectable in 75% to 100% of the most prevalent subtype: the non-keratinizing squamous cell carcinoma (NKSCC) or undifferentiated carcinoma of the nasopharynx (UCNT) [2-4]. The multifactorial etiology of NPC also involves genetic predisposition and environmental factors such as dietary nitrosamines and the consumption of salted/smoked foods [5,6].

Clinically, the deep anatomical location of the nasopharynx often leads to a diagnostic delay [7]. The disease typically presents with cervical adenopathy and otologic symptoms like serous otitis media, and is characterized by a high propensity for nodal and distant metastases [7,8]. Accurate staging is crucial, and recent

advancements, such as the implementation of the AJCC 9th edition TNM classification in 2025, aim to enhance prognostic precision by refining criteria for T and N stages and introducing subdivisions for metastatic disease [9,10,11].

Due to its anatomical site and radiosensitivity, radiotherapy combined with concurrent chemotherapy remains the cornerstone of treatment [12]. Recent advances focus on optimizing systemic treatment through the strategic use of induction chemotherapy and the integration of immunotherapy, particularly anti-PD1 agents, which have shown promising results in improving patient outcomes and potentially reducing chemotherapy-related toxicity in locally advanced and recurrent/metastatic settings [13-15].

This mini-review provides an overview of the etiology, clinical presentation, diagnostic workup, and current evidence-based management strategies for nasopharyngeal carcinoma, highlighting the recent shifts in staging and therapeutic approaches that are improving the prognosis of this unique disease.

Epidemiology

NPC ranks 23rd among the most frequent cancers globally, with 120,434 new cases reported worldwide each year [1]. In Algeria, it is the most common ENT cancer and ranks 12th among all cancers, accounting for over 1,600 new cases and 910 deaths annually [1,2].

NPC exhibits significant geographical disparity (Figure 1). Incidence is low in Europe (0.5–2/100,000/year), intermediate in the Maghreb region (8–12/100,000/year), and very high in Southeast Asia (30–80/100,000/year).
Its incidence is subject to geographical and ethnic variations. Certain ethnic groups have a higher risk, with incidence rates exceeding 16 per 100,000 inhabitants among men. Examples include the Bidayuh in Borneo, the Nagas in Northern India, and the Inuits in the Arctic [2]. Eighty-one percent (81%) of new cases are diagnosed in Asia, 9% in Africa, and the remaining 10% across the rest of the world [2,16].

The peak age of frequency varies according to the region and histological type, showing a bimodal distribution in Mediterranean basin countries (children and middle-aged adults). The male-to-female sex ratio is 2:1 to 3:1, with a male predominance [1,16].

Etiological Factors

Viral factors are dominated by the Epstein-Barr virus (EBV), whose oncogenic role is well-established; viral DNA is detected in the majority of undifferentiated nasopharyngeal carcinoma (UCNT) tumors [2,5,6,16]. The etiology of NPC is also influenced by environmental factors, which include exposure to dietary nitrosamines, the consumption of salted fish and smoked foods during childhood, as well as tobacco and alcohol use, particularly associated with the keratinizing forms [5]. Furthermore, an existing genetic predisposition is evidenced by familial clusters of UCNT observed in endemic areas [6,16]. Other external risks include occupational exposure to chemical fumes, notably formaldehyde and wood dust [17]. It is also important to note that the keratinizing subtype can manifest as a secondary malignancy, often years after initial radiotherapy treatment for a non-keratinizing nasopharyngeal carcinoma [3,17].

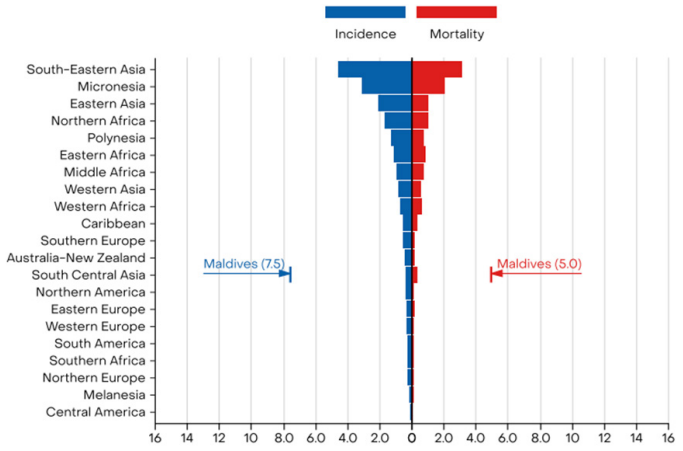

Figure 1: Incidence and Mortality Rates of Nasopharyngeal Carcinoma Worldwide by Region [1].

Pathology

Nasopharyngeal Carcinoma (NPC) originates in the nasopharyngeal mucosa and exhibits a squamous differentiation pattern [3]. The World Health Organization (WHO) classification distinguishes several types of NPC. The most frequent histological type is the non-keratinizing squamous cell carcinoma (which is further divided into differentiated and undifferentiated subtypes), representing nearly 70–90% of cases in high-incidence areas. Other types include keratinizing squamous cell carcinoma (which is radioresistant and carries a poorer prognosis), basaloid squamous cell carcinoma, as well as lymphomas, sarcomas, and adenocarcinomas [18]. In endemic regions (China, Southeast Asia, and North Africa), NPCs are strongly associated with the Epstein-Barr virus (EBV); detection of the EBV virus by PCR or *in situ* hybridization (EBER) is found in 75% to 100% of cases [4]. On the immunohistochemical level, NPC shows positivity for EBV LMP antibodies, Pan-keratin, p63, and p40, and negativity for CK7 and CK20 [3].

Clinical Presentation

The anatomical depth of the nasopharynx contributes to the deceptive nature of the symptoms and the resultant diagnostic delay (Figure 2).

The most common presenting signs are cervical adenopathies (lymph node enlargement) in 50% to 75% of cases. These are typically unilateral or bilateral, most often located high and posterior, sub-digastric, jugulo-carotid, posterior spinal, or, more rarely, supraclavicular [7]. Otologic signs are the presenting circumstances in 40% to 60% of cases, typically manifesting as serous otitis media (otitis sero-muqueuse) [8]. In 20% of cases, the reason for the first consultation is rhinological signs such as unilateral nasal obstruction or epistaxis [7]. Neurological signs are indicative of NPC in 10% to 15% of cases. The presence of distant metastases is more frequent in NPC than in other cancers

of the upper aerodigestive tract (UADT). These metastases are symptomatic and revealing of NPC in 5% to 10% of cases [8]. Finally, in less than 5% of cases, a paraneoplastic syndrome may be present and lead to the diagnosis of NPC [8,19,20].

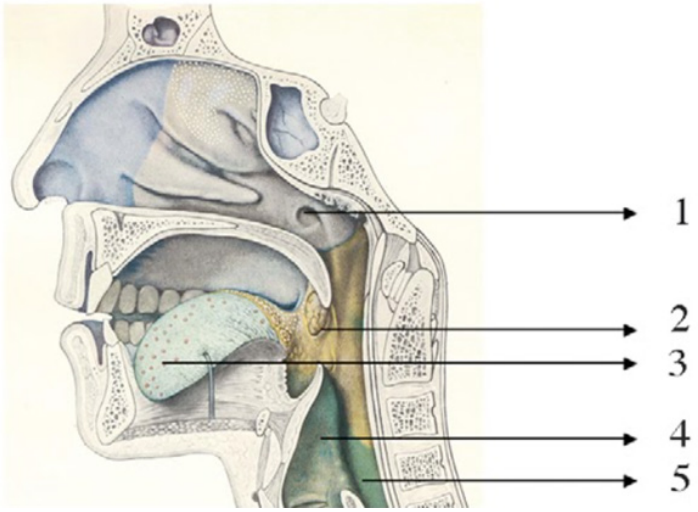

Figure 2: Anatomy of the Nasopharynx (Cavum) Showing its Deep Location and Consequent Diagnostic Delay [16].

Diagnosis and Staging Workup

In areas of high or intermediate incidence, any high-level cervical adenopathy, whether or not associated with otologic or rhinological symptoms, necessitates a focused clinical examination of the nasopharynx [7,20,21]. A rigid tube nasofibroscopy is the most suitable method for performing biopsies of the cavum (nasopharynx). This procedure is typically done under local anesthesia, or under general anesthesia for patients who are difficult to examine.

Magnetic Resonance Imaging (MRI) is the preferred modality for characterizing locoregional extension and localized forms of the disease [21]; Computed Tomography (CT) scan is indicated for the analysis of bone involvement and lymph nodes [21,22]. Positron Emission Tomography-Computed Tomography (PET-CT) is recommended for locally advanced or recurrent forms [9]. EBV serology (IgA, IgG, circulating viral DNA) plays a crucial role in diagnosis, risk stratification, and surveillance [10].

TNM Classification

Since January 2025, a new TNM classification has been in effect [10]. The 9th edition of the AJCC (American Joint Committee on Cancer) TNM staging system for Nasopharyngeal Carcinoma

Table 1: AJCC/UICC TNM Staging Classification and Grouping: Changes from the 8th to the 9th Edition.

Category	8th Edition TNM	9th Edition TNM
T Category: No Change in T0		
T1	Tumor confined to the nasopharynx or extension to the oropharynx and/or nasal cavity without parapharyngeal extension.	Tumor confined to the nasopharynx or extension to one of the following sites without parapharyngeal extension: (1) oropharynx; (2) nasal cavity (including nasal septum).
T2	Tumor extension to the parapharyngeal space and/or involvement of adjacent soft tissue (medial, lateral, prevertebral pterygoid muscles).	Tumor extension to one of the following sites: (1) parapharyngeal space; (2) adjacent soft tissue (medial, lateral, prevertebral pterygoid muscles).
T3	Tumor infiltration into bony structures: base of skull, cervical vertebrae, pterygoid structures, and/or paranasal sinuses.	Unequivocal infiltration into one of the following bony structures: (1) base of skull (including pterygoid structures); (2) paranasal sinuses; (3) cervical vertebrae.
T4	Intracranial extension, cranial nerve involvement, hypopharynx, orbit, parotid gland, extensive soft tissue infiltration beyond the lateral face of the lateral pterygoid muscle.	Extension/infiltration to one of the following sites: (1) intracranial extension; (2) unequivocal radiological or clinical involvement of cranial nerves; (3) hypopharynx; (4) orbit (including inferior orbital fissure); (5) parotid gland; (6) extensive soft tissue infiltration beyond the anterolateral face of the lateral pterygoid muscle.
N Category: Addition of Advanced Extranodal Extension as N3 Criterion		
N0	No regional lymph node metastasis.	No regional lymph node metastasis.
N1	Unilateral metastasis in cervical lymph nodes and/or unilateral or bilateral metastasis in retropharyngeal nodes, ≤6cm, above the caudal border of the cricoid cartilage.	Metastatic nodal involvement of: (1) unilateral cervical nodes; (2) unilateral or bilateral retropharyngeal nodes; all: (1) ≤6cm; (2) above the caudal border of the cricoid; (3) without advanced extranodal extension.
N2	Bilateral metastases in cervical lymph nodes, ≥6cm, above the caudal border of the cricoid cartilage.	Metastatic involvement of bilateral cervical nodes and: (1) ≥6cm; (2) above the caudal border of the cricoid; (3) without advanced extranodal extension.
N3	Unilateral or bilateral metastases in cervical lymph nodes >6cm or extension below the caudal border of the cricoid cartilage.	Metastatic involvement of cervical nodes (unilateral or bilateral) and: (1) >6cm; (2) extension below the caudal border of the cricoid; (3) advanced radiological extranodal extension (involvement of adjacent muscles, skin, neurovascular bundle).
M Category: Subdivision of M1 into M1a and M1b		
M0	No distant metastasis.	No distant metastasis.
M1	Presence of distant metastases.	M1: Distant metastases; M1a: ≤3 metastatic lesions in ≥1 organs/sites; M1b: > 3 metastatic lesions in more than 1 organs/sites.
Stage Grouping		
Stage I	T1 N0 M0	**IA** T1-2, N0, M0
Stage II	T1 N1 M0 / T2 N0-1 M0	**IB** T1-2, N1, M0
Stage III	T1-2 N2 M0 / T3 N0-2 M0	**II** T1-2, N2, M0; T3, N0-2, M0
Stage IVA	T4 N0-2 M0 / Any T N3 M0	**III** T4, Any N, M0; Any T, N3, M0
Stage IVB	M1 (Any T, Any N)	**IVA** Any T, Any N, M1a
		IVB Any T, Any N, M1b

(NPC) introduces significant adjustments aimed at improving prognostic accuracy, clarity, and clinical relevance. Building upon the 8th edition, it refines the TNM classifications to address certain limitations in stratifying survival outcomes and incorporates new criteria (Table 1). Specifically, this 9th version clarifies the criteria for T3 stage, which now requires unequivocal evidence of bone infiltration, notably involving the skull base (including pterygoid structures), cervical vertebrae, or paranasal sinuses [9,23]. It also introduces advanced radiological extranodal extension (ENE) as a criterion for the N3 category [9,24]. Furthermore, it subdivides M1 metastatic disease into M1a (three metastatic lesions or fewer) and M1b (more than three lesions) to better assess risk [9,11]. Developed from comprehensive multicenter studies and validated by international expert groups, this version redefines the stage groups for NPC, aligning clinical management with evidence-based practices and enhancing prognostic reliability.

Management

Radiotherapy (RT) is the standard treatment for nasopharyngeal carcinoma due to its difficult surgical access (both for the primary tumor and particularly the retropharyngeal lymph node areas) and its notable radiosensitivity [12]. RT is combined with concurrent chemotherapy for all stages except T1N0M0, provided there are no contraindications. It is performed using Intensity-Modulated Radiation Therapy (IMRT), which allows for better local and regional control, improved overall survival, and reduced salivary toxicity compared to 2D radiotherapy [25].

Role of Chemotherapy

Chemotherapy serves a radiosensitizing role. The benefit of concurrent chemotherapy added to RT for locally advanced NPC has been demonstrated by numerous studies [26,27]. There is no benefit from concurrent chemoradiotherapy for T1N0 tumors [12,27]. Concurrent chemotherapy may be considered for T2N0 tumors depending on the patient's general condition [28].

Several meta-analyses have been conducted to define the contribution and precise role of chemotherapy. The Blanchard meta-analysis [29], which reviewed data from 19 trials and 4,806 patients, updated in 2021 to include 7,000 patients, confirms the benefit of adding chemotherapy to RT with a significant improvement in overall survival and a 5-year benefit of 6.3%. In this study, the benefit of chemotherapy on overall and recurrence-free survival was demonstrated for treatments involving concurrent chemoradiotherapy with or without adjuvant chemotherapy [29].

The standard concomitant chemotherapy regimen is cisplatin 100mg/m² every 3 weeks on days 1, 22, and 43 of radiotherapy [28]. In cases of non-sterilization after 10 weeks post-treatment and histological confirmation, the reference treatment is stereotactic radiotherapy or brachytherapy, with local control rates ranging from 72% to 86% [30]. Surgery may be an alternative for localized residual disease [31].

Induction Chemotherapy

Induction chemotherapy (IC) aims to reduce tumor volume to facilitate RT and to treat micro-metastases early in advanced stages, leading to an expansion of its indications [32]. Its efficacy was long debated, but several recent Phase III studies confirm its value, particularly in improving recurrence-free survival and sometimes overall survival (OS) in patients with stage III/IV NPC [13,33-35]. The Cao study [34], which included 476 T4/N2-N3 patients, found a benefit in recurrence-free survival but not in OS. The Sun study [13] demonstrated that after three cycles of TPF before chemoradiotherapy, the 3-year relapse-free survival was 80% versus 72%, and OS was 92% versus 80% ($p = 0.034$ and 0.029). A Tunisian study [35] also found an improvement in progression-free survival (HR = 0.44) and 2-3 year OS in the induction arm. The tolerability profile remains acceptable, with no significant increase in acute toxicities during chemoradiotherapy [13,32-35].

Immunotherapy and De-escalation

The addition of toripalimab, an anti-PD1 agent, to induction chemotherapy followed by cisplatin-free radiotherapy for locally advanced nasopharyngeal cancer was evaluated in a Phase III trial in China [14]. Among 532 patients included, the 3-year failure-free survival was similar in both groups (88.3% without cisplatin vs. 87.6% standard). Toxicity was markedly lower in the cisplatin-free arm (all-grade nausea/vomiting at 25.6% vs. 69%; Grade 3-4 vomiting at 3.8% vs. 10.3%; Grade 3-4 acute adverse events at 52.3% vs. 63.6%), with no treatment-related deaths. Quality of life was significantly better in the absence of cisplatin, particularly regarding digestive and general tolerance. The conclusion is that eliminating cisplatin in favor of immunotherapy combined with induction chemotherapy and RT offers comparable efficacy while substantially reducing toxicity and improving the quality of life for patients with locoregionally advanced NPC [14].

Adjuvant Chemotherapy

Adjuvant chemotherapy aims to reduce the risk of recurrence, but its benefit after concurrent chemoradiotherapy remains debated, as tolerance often limits the complete administration of the treatment (only 55% of patients in the Al-Sarraf study [36]). The multicenter Chen study [37] compared 508 patients with locally advanced NPC treated with chemoradiotherapy alone or followed by adjuvant chemotherapy, showing no significant benefit in recurrence-free survival (HR=0.88; IC=0.64-1.22; p=0.45) or overall survival (HR=0.83; IC=0.57-1.22; p=0.35), regardless of the subpopulation analyzed, and demonstrated significant acute toxicity (42% Grade 3-4). Furthermore, post-treatment plasma EBV DNA (pEBV) level is identified as an independent prognostic factor for recurrence-free and overall survival according to Hui [38], but the Chan study [37], which randomized patients with detectable pEBV between adjuvant chemotherapy or surveillance, also found no 5-year benefit in terms of recurrence-free or overall survival. These results therefore question the role of adjuvant chemotherapy in preventing relapse in high-risk patients after chemoradiotherapy [36-38].

Re-irradiation for Recurrence

Re-irradiation is a therapeutic option for local recurrences or residual tumors, specifically targeting the tumor volume with

adapted margins based on the technique used. Four approaches are available: Intensity-Modulated Radiation Therapy (IMRT), stereotactic radiotherapy (SRT), brachytherapy, and proton therapy [39]. Two-year survival rates range from 11% to 46% depending on prognostic classes [40,41]. According to Roeder [42], in stereotactic radiotherapy, factors such as rT1 stage, a dose greater than 50 Gy, and associated systemic treatment improve survival in re-irradiation cases, but severe late toxicity is common (29%: hearing loss, dysgeusia, loss of smell, neuropathy, trismus, xerostomia). Furthermore, a fractionated regimen is recommended in SRT for better efficacy and less toxicity than a single session [30]. It is essential to limit the dose per fraction and optimize irradiation to protect the carotid arteries, even in cases of recurrence of cancers with a more favorable prognosis. Given the limited accessibility of brachytherapy in France for these situations, stereotactic radiotherapy currently remains the gold standard for re-irradiation of NPC [30, 40-42].

Palliative Systemic Treatments

Palliative systemic treatments are indicated for patients with locally recurrent NPC inaccessible to local treatment or in a metastatic setting [28,43]. In cases of oligometastases, the choice is debated between local treatment (radiotherapy, surgery, interventional radiology) or systemic treatment. For plurimetastatic progression, first-line chemotherapy may be followed by local treatment on residual lesions if the response is good, to be decided at a multidisciplinary meeting [43]. Treatment choice depends on the histological type: EBV-related non-keratinizing carcinomas follow specific protocols, while keratinizing ones are treated like other UADT cancers [28].

In the first line for metastatic forms, the cisplatin-gemcitabine combination is recommended, as polychemotherapy with more than two agents increases toxicity without additional benefit [28,29]. In case of contraindication, a platinum-taxane or platinum-5FU combination is preferred, or even monotherapy with the usual active cytotoxics for the nasopharynx [28,43]. Treatment usually lasts 6 cycles with re-evaluation at 3 cycles. For the second line, if the last platinum dose was more than 6 months ago, a platinum-containing protocol is again favored, using the same cytotoxic agents as the first line [43-45]. In case of response in metastatic patients after a first line, a locoregional consolidation radiotherapy should be systematically discussed [45].

Special Case: *De Novo* Metastatic Patients

The choice of systemic treatment depends on the NPC subtype [43,46]:

- **Non-keratinizing carcinomas (EBV-related):** Treatment is based on the cisplatin-gemcitabine combination.
- **Keratinizing carcinomas (non-EBV-related):** The proposed chemotherapy protocol is the TPF regimen (Docetaxel 75mg/m² D1, Cisplatin 75mg/m²D1, 5FU 750mg/m² D1-5), 4 to 6 cycles depending on tolerance. In case of a good response, consolidation radiotherapy to the T and N sites will be proposed, as well as possible local treatment of residual metastatic lesions [28,43,47,48].

Targeted Therapies and Immunotherapy in the Metastatic Setting

Nimotuzumab is indicated in combination with concurrent chemoradiotherapy (CCRT) for stage III to IVB as a therapeutic option that improves overall survival [49]. Anti-EGFR agents (Nimotuzumab and Cetuximab) in combination with chemotherapy in the 1st metastatic line improve objective response rates and recurrence-free survival, thus constituting a therapeutic option in this indication [43,50].

In patients with recurrent and/or metastatic NPC, pembrolizumab is not superior to chemotherapy [51]. An open-label, Phase II trial compared the combination of bevacizumab + pembrolizumab versus pembrolizumab alone [52]. In this randomized trial, 48 patients received either pembrolizumab alone or in combination with bevacizumab for 2 years, with crossover potential. The bevacizumab-pembrolizumab combination showed significantly superior results to pembrolizumab alone in terms of objective response rate (58.3% vs. 12.5%), median progression-free survival (13.8 vs. 1.6 months), and a trend toward improved overall survival. Grade 3 adverse events were more frequent in the bevacizumab combination arm (25% vs. 8.3%), with no Grade 4-5 toxicities and a comparable incidence of autoimmune events. The significant decrease in plasma EBV DNA was more frequent in the combination arm (70.8% vs. 21.1%). Translational analyses revealed that bevacizumab rapidly increases immune infiltration, notably B cell density in good responders. In conclusion, the bevacizumab-pembrolizumab combination is well-tolerated and provides superior clinical and immunological benefits compared to pembrolizumab monotherapy.

The international standard for treating R/M NPC is immuno-chemotherapy with an anti-PD1 agent such as toripalimab-tpzi plus cisplatin and gemcitabine [15,28]. After failure, the prognosis is highly unfavorable, and therapeutic options are limited. Becotatug Vedotin, an anti-EGFR antibody-drug conjugate (ADC), demonstrated superior efficacy to standard chemotherapy in this heavily pre-treated population according to a Phase I-II study [53]. In this randomized trial including 173 patients (at least two prior lines of chemotherapy and one anti-PD-(L)1, half exposed to an anti-EGFR), becotatug vedotin significantly increased the objective response rate (30.2% vs. 11.5%) and progression-free survival (median 5.8 vs. 2.8 months, HR = 0.63; p = 0.0146) compared to chemotherapy (capecitabine or docetaxel). Overall survival also tended to improve (17.1 vs. 12 months, HR = 0.73). The rates of Grade 3 adverse events were comparable between groups, maintaining an acceptable safety profile. This study represents a notable advance through the introduction of anti-EGFR antibody-drug conjugates in the treatment of recurrent or metastatic NPC.

Surveillance

Post-therapeutic surveillance relies on imaging modalities (MRI, CT scan, PET-CT), EBV serology, and regular clinical follow-up [10].

The prevention of post-radiation dental complications requires the

Table 2: Prognostic Factors for Nasopharyngeal Carcinoma [54].

Prognostic Factors	Tumor-Related	Patient-Related	Environment/System-Related
Essential	Stage.	Age.	Availability of adequate staging care (MRI, PET Scan).
	Histological Type.	PS (Performance Status).	Access to quality Radiotherapy.
		Comorbidities.	Expertise in Radiation and Chemotherapy.
Complementary	EBV-DNA.	LDH (Lactate Dehydrogenase).	Optimization of Radiotherapy dose fractionation.
	Tumor Volume.		Optimization of Chemotherapy sequences and drugs.
	Location of Metastases.		
New and Promising	Biomarkers.		Progress in diagnostic and therapeutic techniques.
	Genetic Signatures.		

daily use of fluoride gel and systematic dental care.

Prognosis

The prognosis of NPC depends on several factors, which were summarized in Table 2 by O'Sullivan et al. [54]. Some of these factors are classic and long-known, such as age, histological type, and tumor volume. Others are recent or currently under evaluation, such as biomarkers or genetic signatures.

Toh et al. proposed a studied prognostic score based on four parameters [55]:

- Poor performance status (Score 5)
- Hemoglobin < 12g/100 ml (Score 4)
- Disease-free interval < 6 months (Score 10)
- Initial metastases (Score 1)

A cumulative score of 0 to 3 is considered a good prognosis, with a median survival of 19.6 months versus 14.3 months for an intermediate score (4 to 8) and 7.9 months for patients with a high score (≥9). Five-year overall survival rates approach 70–75% with modern combined protocols [56].

Conclusion

Nasopharyngeal Carcinoma (NPC) remains a complex and unique malignancy, strongly linked to the Epstein-Barr virus (EBV) and posing a significant public health challenge in endemic and intermediate-incidence areas like Algeria.

Recent advances in clinical oncology have notably refined its management. The foundation of modern treatment is Intensity-Modulated Radiation Therapy (IMRT), increasingly combined with strategic induction chemotherapy. Furthermore, the implementation of the AJCC 9th edition TNM staging system and the integration of immunotherapy (e.g., anti-PD1 agents) represent major steps forward, optimizing risk stratification and clinical outcomes.

Ultimately, these combined protocols have led to improved survival rates (approaching 70-75% at five years) while new therapeutic avenues, such as antibody-drug conjugates (ADCs), continue to emerge for the refractory disease. Future efforts must focus on personalized treatment selection based on molecular factors and mitigating the long-term toxicities associated with aggressive therapies.

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