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A RETROSPECTIVE ANALYSIS OF NON-ENDEMIC CARCINOMA: OUR EXPERIENCE AT AN INDIAN TERTIARY TEACHING HOSPITAL.

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Abstract

Introduction:

Nasopharyngeal carcinoma (NPC) is a very uncommon malignant tumour in children under the age of 20. The diagnosis of paediatric NPC is challenging due to its relative rarity. This unusual occurrence is frequently linked to delayed diagnosis, which can result in advanced loco-regional illness. Here, we investigate the clinical manifestations, investigations, and treatment of paediatric nasopharyngeal carcinoma in a nonendemic region.

Method:

This study is the retrospective analysis of the data from children and adolescents who had been diagnosed with nasopharyngeal cancer served as the basis for this study, which was carried out at the Cardiology and Pathology Departments of a tertiary teaching hospital Nalanda Medical College and Hospital, Patna, Bihar, India

Result:

In this retrospective analysis, 17 paediatric patients were selected for the study. Between December 2020 and January 2022, they were treated at a tertiary teaching hospital. 17 kids with nasopharyngeal cancer between the ages of 6 and 18 took part in this study. In this study, there were 7 girls (41.1%) and 10 boys (58.8%). NPC diagnosis occurred at a median age of 14 years (interquartile range: 6–18 years). In 15 (88.2%) individuals, neck swelling was the most frequent clinical manifestation, followed by nasal bleeding, nasal block, and hearing impairment in 10 (58.8%), 12 (70.5%), and 11 (64.7%) of cases, respectively.

Conclusion:

With the exception of individuals who have distant metastatic disease, children with NPC have a very good prognosis. NPC in children is typically not clinically suspected until the patient is in a late stage. The most important prognostic factor is the TNM staging. Unfortunately, NPC frequently has distant metastases at the time of diagnosis in the paediatric age range and has a tendency to be locally progressed.

Recommendation :

The clinical manifestation of the nasopharyngeal carcinoma should be detected with accuracy to derive a clinical management plan for it before it progresses to the end stage

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1. Introduction:

Although congenital, inflammatory, and neoplastic lesions are other possible aetiologies, inflammation makes up the bulk of head and neck masses in kids. The presence of swollen lymph nodes in the supraclavicular area or posterior triangle, nodes that are painless, firm and immobile, or a single dominating node that lasts for longer than six weeks all raise concerns about malignancy in the context of persistent adenopathy.[1] Approximately 5% of all juvenile cancers are head and neck neoplasms.[2] .

Trauma is the leading cause of death in children, followed by cancer [2]. Leukaemia and neoplasms of the brain and central nervous system account for more than half of instances of the numerous neoplasms that affect children of all ages [3]. Cancer is the ninth-leading cause of death in children in India between the ages of 5 and 14 [4].

Regarding the precise definition of head and neck tumours, writers and physicians have different views [3,4]. Prior studies of these tumours were either constrained by a criterion that was not physically or histologically unique to the head and neck or were predominately centred on a certain race and tumour site impacted [5–11]. For instance, among newborns, kids, and teenagers, neuroblastomas and lymphomas are the most prevalent head and neck cancers. However, lymphomas are immune system neoplasms, whereas neuroblastomas are often thought of as neuroendocrine neoplasms that are not localised [12,13]. Essentially, there are numerous criteria that overlap, and neither of the cancer kinds is only found in the head and neck. Furthermore, rhabdomyosarcoma, a soft-tissue sarcoma that affects the head and neck in one-third of cases, can be histologically determined to be skeletal muscle tumours that can develop anywhere [14]. Rhabdomyosarcoma cannot therefore be only categorised as a malignancy of the head and neck [15].

The malignant neoplasm known as nasopharyngeal carcinoma (NPC) develops from the epithelial cells that line the nasopharynx. The incidence of NPC, a head and neck cancer, has striking racial and geographic variations. It is an uncommon form of cancer with annual incidence rates of 20 per 100,000 people in high-risk areas and lower rates in paediatric age groups [1]. No matter where you are in the world, NPC is incredibly uncommon in youngsters. While the NPC accounts for about 2% of head and neck malignant neoplasms in children under the age of 18, approximately 5% of primary malignant neoplasms in children originate from the head and neck region [4]. Since this condition is uncommon in children of this age range and has non-specific clinical signs such nasal congestion, lymphadenopathy, and ear problems, the diagnosis is frequently postponed since doctors initially assume benign causes. Radiotherapy is the usual course of treatment for NPC.

2.5% of all paediatric tumours are neoplasms of the head and neck [6]. Due to the possible negative consequences of both the illness process and the treatments used on developing head and neck structures, head and neck neoplasms in children present a challenge. One-fourth of malignant lesions appear in the head and neck area [2] as a result. Here, we investigate the clinical manifestations, investigations, and treatment of paediatric nasopharyngeal carcinoma in a nonendemic region.

2. Materials and methods:

The data from children and adolescents who had been diagnosed with nasopharyngeal cancer served as the basis for this study, which was carried out at the Cardiology and Pathology Departments of a tertiary teaching hospital in the eastern region of India. Pediatric patients with nasopharyngeal carcinoma were selected for the study that occurred between December 2020 and January 2022. The parents of the children taking part in this study provided written consent. A thorough history taking, a thorough head and neck examination, a diagnostic nasal endoscopy,

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and audiological tests were performed on all NPC children.

In all patients of NPC that were diagnosed, standard computed tomography (CT) scans of the neck and nasopharynx were performed. All kids with NPC were given radiotherapy to cover the entire nasopharynx, and some kids also received chemotherapy. Every NPC kid was routinely monitored with physical exams and fiberoptic nasopharyngolaryngoscopies every three months for the first two years, every six months for the following five years, and then once a year after that. The majority of patients underwent hormonal testing following chemoradiation, including thyroid function tests, growth hormone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH).

3. Results:

17 kids with nasopharyngeal cancer between the ages of 6 and 18 took part in this study. In this study, there were 7 girls (41.1%) and 10 boys (58.8%). NPC diagnosis occurred at a median age of 14 years (interquartile range: 6–18 years). In 15 (88.2%) individuals, neck swelling was the most frequent clinical manifestation, followed by nasal bleeding, nasal block, and hearing impairment in 10 (58.8%), 12 (70.5%), and 11 (64.7%) of cases, respectively (Table 1).

Skull base invasion was present in 4cases (23.5%). In 12 cases, neck node hypertrophy was seen (70.5%). According to Table 2, N staging was N1 in 11 instances (64.7%), N2 in 5 cases (29.4%), and N3 in 1 cases (5.8%).

With an overall positive prognosis, radiation was used to treat all the NPC in children. The primary site receives radiation at a rate of 1.8 Gy/day, five days per week, for a total dosage of 40–44 Gy. After completing radiotherapy and/or chemotherapy (if distant metastases were present), 2-3 cycles of cisplatin-based chemotherapy (cisplatin 80–100 mg/m2, 5-fluorouracil 600 mg/m2, bleomycin 15 mg/m2, epirubicin 100 mg/m2, and methotrexate 40 mg/m2) were given to seven children (5 cases of N2 and 1 cases of N3). Therefore, 5 of the 17 patients received adjuvant chemotherapy. After treatment, NPC with neck node metastasis/enlargement displayed a gradual shrinkage. In the instances of our investigation, there was no cranial nerve involvement. One patient was lost to follow-up after completing treatment with radiotherapy and/or chemotherapy (if distant metastases were present), for reasons that are unclear to the treating physician. One patient stopped attending therapy in the middle of the session.

4. Discussion:

In this study, similar greater occurrences of males are observed. A rare tumour, paediatric NPC can occur in both endemic and non-endemic regions. In accordance with earlier research [6–8], the prevalence among boys and girls in the current study is 2.2:1.

NPC is pathologically divided into three groups (WHO classification): undifferentiated carcinoma (WHO type III), non-keratinizing squamous cell carcinoma (WHO type II), and keratinizing squamous cell carcinoma (WHO type I) [9]. The majority of cases are advanced-stage undifferentiated carcinomas (WHO category III) [10]. NPC is typically brought on by environmental carcinogen exposure, genetic predisposition, and Epstein-Barr virus infections.

Markers could be elevated antibody titers to Epstein-Barr virus antigens [11].Nasal haemorrhage, nasal blockage, neck swelling, and ear complaints such headache, tinnitus, and deafness are the clinical manifestations of paediatric NPC. The Rosenmuller Fossa is the most typical location of origin for NPC.

A uncommon malignant tumour that develops in the head and neck area is nasopharyngeal carcinoma. The root causes are multifaceted and include genetic, viral, and environmental factors [5]. NPC is a head and neck cancer that is frequently diagnosed in North Africa, South East Asia, and Southern China [5].

Because NPC incidence rises with age and peaks between the ages of 50 and 59, with a minor peak in late childhood, it has historically been believed to be a disease of the elderly [3]. All around

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Table 1: **Clinical proftle of pediatric nasopharyngeal carcinoma**

Cases	Age (years)	Gender	Neck node swelling (yes/ no)	Nasal bleed-ing (yes/ no)	Nasal block (yes/ no)	Aural symp-toms (otal-gia/hearing loss) (yes/ no)
1	6	M	Y	Y	N	Y
2	7	F	Y	Y	Y	Y
3	7	M	Y	N	Y	Y
4	8	M	Y	Y	N	Y
5	9	F	Y	N	Y	N
6	9	M	Y	N	Y	N
7	10	F	N	Y	Y	N
8	11	M	Y	Y	Y	Y
9	11	M	Y	Y	Y	N
10	12	M	N	Y	Y	Y
11	12	M	Y	N	N	Y
12	13	F	Y	N	N	Y
13	14	M	Y	N	Y	N
14	15	F	Y	Y	Y	N
15	16	F	Y	Y	Y	Y
16	17	M	Y	Y	Y	Y
17	18	F	Y	N	N	Y

Table 2: **Imaging in pediatric NPC**

CT Findings (n = 21)	Number of children	%
Distant metastasis M1 M0	1 16	5.8% 94.1%
Site of lesion Skull base invasion Lateral wall Entire nasopharynx Entire nasopharynx	4 4 6 3	23.5% 23.5% 35.2% 17.6%
Necrotic changes in the neck nodes	12	70.5%
Neck node metastasis N1 N2 N3	11 5 1	64.7% 29.4% 5.8%

the world, particularly in endemic areas, the incidence is higher in men than in women [4].

The patient frequently experiences a protracted period of asymptomatic behaviour in this occult place. Rarely do the traditional clinical manifestations such neck mass, epistaxis, nasal obstruction, and serous otitis media happen near the time of diagnosis, bone erosion near the base of the skull is frequent, whether or not it affects the cranial nerves. In NPC, the cranial nerves III through VI are frequently affected. NPC has a higher propensity for early metastasis than other head and neck malignancies [12]. Bilateral neck node metastases is frequently the initial clinical symptom since the nasopharynx has a robust lymphatic drainage system. Childhood NPC is associated with advanced loco-regional spread and a higher likelihood of distant metastasis since it

is uncommon in children and frequently results in a delayed diagnosis [13]. The cervical lymphadenopathy is frequently diagnosed later because it is thought to have an infectious aetiology. In adult patients with NPC, unilateral serous otitis media is a frequent presentation; in youngsters, this is not an unusual presentation.

In the paediatric age range, otalgia and cervical lymphadenopathy support an infectious aetiology. Further testing is necessary if there is no improvement after taking an antibiotic course. To rule out nasopharyngeal pathology in the presence of persistent unilateral otological symptoms, a flexible nasopharyngolaryngoscopic examination is required. With a male to female ratio of more than 2:1, the highest incidence of NPC in children from non-endemic regions occurs between the ages of 15 and 19 [14]. A higher level of suspicion may be required in children due to the lack of a specific timeline for starting a malignancy workup in the paediatric age group with one-sided otological symptoms.

The preferred form of treatment is radiotherapy, with neoadjuvant chemotherapy administered in more severe instances. For neck nodes, radiation of 50 Gy is frequently preferred. Methotrexate, bleomycin, and cisplatin are all components of the chemotherapy [17]. The radiosensitivity of nasopharyngeal carcinomas is higher [18]. Following radiotherapy and chemotherapy, the patients exhibited a considerable improvement, and they are currently being monitored. Xerostomia is the most common side effect of radiation to the head and neck that patients report. Commonly prescribed chemotherapy drugs like cisplatin cause ototoxicity, which is usually bilateral and irreversible [19]. Early hearing loss can have an impact on a child's social, cognitive, and verbal development. Future treatment must forego the use of such medications. Due to the complicated anatomical placement of the disease, NPC is typically inoperable, and surgery for this primary tumour is limited to biopsy only. If the primary tumour appears to be under control or if there are persisting neck nodes or recurrence in the nodes following chemoradiation or radiation alone, the radical neck dissection is taken into consideration [20]. Paediatric patients under the age of 18 and adult patients both had 5-year survival rates of 77 7.3% and 83 3.9%, respectively, according to Patel et al. [21]. Paediatric NPC patients have a much increased chance of getting a second malignancy after treatment [7]. It is hoped that early detection of NPC in children may prevent locoregional spread and the severity of radiation-related comorbidities. When neoadjuvant chemotherapy is successful in treating a patient with NPC, the radiation dose should be decreased. A breakthrough in the treatment of NPC is intensity-modulated radiotherapy (IMRT), which avoids radiation exposure to healthy tissue while delivering highly conformal dose distributions to the targeted spot [22]. This increases survival and lowers late toxicity. With 5-year disease-specific survival falling between the range of 38 and 51%, the overall prognosis is almost the same between adult and paediatric patients [23]. This result, however, conflicts with research by Sultan et al. [13], who found that NPC patients between the ages of 20 and 45 have a nearly doubled risk of mortality compared to children or adolescents. However, compared to adults, children and adolescents have a higher chance of developing a second cancer, which may be connected to side effects during therapy [13]. For paediatric age groups with NPC, neoadjuvant chemotherapy followed by concurrent chemoradiotherapy has event-free survival rates of about 70–80% [24]. Paediatric patients with recurrent NPC continue to have poor results [25]. The majority of patients with relapsed NPC exhibit distant metastatic disease upon presentation [26]. When treating relapsed NPC, radiation alone is frequently insufficient because the majority of relapses take place at distant sites. Furthermore, the radiotherapy doses needed to treat distant metastatic NPC could be extremely hazardous to various organ systems. In order to treat the majority of paediatric patients, chemotherapy is typically required. Morbidity and death are reduced when paediatric NPC is diagnosed and treated quickly.

5. Conclusion:

Paediatric nasopharyngeal carcinoma is a fairly uncommon clinical condition. If discovered at a late stage, the disease manifests as progressive loco-regional disease. For childhood NPC, treatment must be started as soon as possible. Radiotherapy and chemotherapy are primarily part of the multimodal approach to treating paediatric NPC. High radiation doses have great NPC control, however they come with substantial side effects in the paediatric age group. Along with aiding in local tumour reduction, neoadjuvant or concurrent chemotherapy reduces late toxicity by reducing radiation dosage to the nasopharynx. When a child exhibits neck swelling, nasal obstruction, nasal haemorrhage, unilateral conductive hearing loss caused by middle ear effusion, and growth in the nasopharynx, NPC should be taken into consideration as a differential diagnosis.

6. Limitation:

The study was conducted on a small sample size. A more inclusive large sample size studies are required to understand the pattern of clinical manifestation, the nasopharyngeal cancer.

7. Recommendation.

The clinical manifestation of the nasopharyngeal carcinoma should be detected with accuracy to derive a clinical management plan for it before it progresses to the end stage

8. Acknowledgement:

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9. List of abbreviation.

NPC- Nasopharyngeal Carcinoma
CT- Computed Tomography
FSH- Follicle-Stimulating Hormone
LH- Luteinizing Hormone
WHO- World Health Organization
IMRT- Intensity-Modulated Radiotherapy

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