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CASE REPORT

Childhood neuroblastoma: case presentation and systematic review of the literature

Bernardo Rojo Ochoa[1], Ana Ilian Vielma Gonzalez[1], Jorge Humberto Orduno Hernandez[1], Brenda Gissel Gonzalez Millan[1], Juan Antonio Lugo Machado[1]

[1]"Lic. Luis Donaldo Colosio Murrieta" Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregon, Sonora, Mexico

ABSTRACT

BACKGROUND. Olfactory neuroblastoma (ONB) is a rare tumor in children, with locally aggressive behaviour and difficult surgical access.
OBJECTIVE. To analyze the clinical, therapeutic, and prognostic characteristics of pediatric ONB through a systematic review of published clinical cases and the presentation of a maxillary case.
MATERIAL AND METHODS. A systematic review was carried out in accordance with the PRISMA guidelines. The search was conducted in PubMed, Scopus, ScienceDirect and Mendeley, including studies published in English up to December 2024. The following descriptors were used: ("esthesioneuroblastoma" AND "neuroblastoma") AND ("children" OR "child" OR "pediatric"), applying filters by age (<18 years) and clinical case design or case series. Two authors made the selection blindly using Rayyan. Animal studies with no individual description or duplicates were excluded. Methodological quality was evaluated using the CARE guideline. Additionally, a case of maxillary ONB was documented in a 3-year-old girl.
RESULTS. 76 patients were analyzed. The most effective therapeutic strategies were multimodal, combining chemotherapy, radiotherapy and surgery. The disease-free survival rate was 61.8%. The clinical case showed a favourable evolution after surgical debulking and neoadjuvant chemotherapy.
CONCLUSION. ONB in the pediatric population requires multidisciplinary management. Strengthening collaborative registries and standardising diagnostic and therapeutic protocols is proposed to improve clinical evidence and long-term results.
KEYWORDS: olfactory esthesioneuroblastoma, neuroblastoma, child, sinus neoplasms.

INTRODUCTION

Neuroblastoma is an embryonal neoplasm originating from the sympathetic nervous system and represents the most common extracranial solid tumor in childhood, with an estimated incidence of 107 cases per million children. Although commonly localized to the adrenal gland and paravertebral region, its presentation in the nasal cavity and sinuses, known as olfactory neuroblastoma or esthesioblastoma, is extremely rare but clinically relevant due to its local aggressiveness and potential for intracranial dissemination[1,2].

Olfactory neuroblastoma (ONB) originates in the olfactory neuroepithelium of the lamina cribrosa and can invade adjacent structures such as the skull base, orbits, and frontal lobe, making early diagnosis and radical surgery challenging. Despite representing only 3% to 6% of neoplasms in the sinonasal region, its importance lies in the anatomical complexity of its location, histological variability, and its capacity for recurrence or regional or systemic metastasis[2-4].

In the pediatric population, diagnosis is usually delayed due to the non-specific nature of initial symptoms such as nasal obstruction, epistaxis or anosmia, which frequently mimic benign pathologies. However, recent studies have shown that when diagnosis is made early and multimodal therapy is applied (including surgery, radiotherapy and in some cases chemotherapy), the results can be comparable to those of adults at early stages of disease. Despite these advances, controversies persist regarding the optimal use of chemotherapy, especially in children, given the variability in long-term survival outcomes[2-4].

This article aims to explore the clinical characteristics, diagnosis, treatment and outcomes of olfactory neuroblastoma in the pediatric population, with emphasis on cases located in the nose and paranasal sinuses, through a systematic review of the literature and a comparative analysis of reported clinical cases.

Corresponding author: Juan Antonio Lugo Machado, "Lic. Luis Donaldo Colosio Murrieta" Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. **Address:** Prolongación Hidalgo, Bellavista, Cajeme 85130. Ciudad Obregón, Sonora, Mexico
ORCID: https://orcid.org/0000-0003-4864-8546
E-mail: otorrinox@gmail.com | juan.lugo.imss@gmail.com
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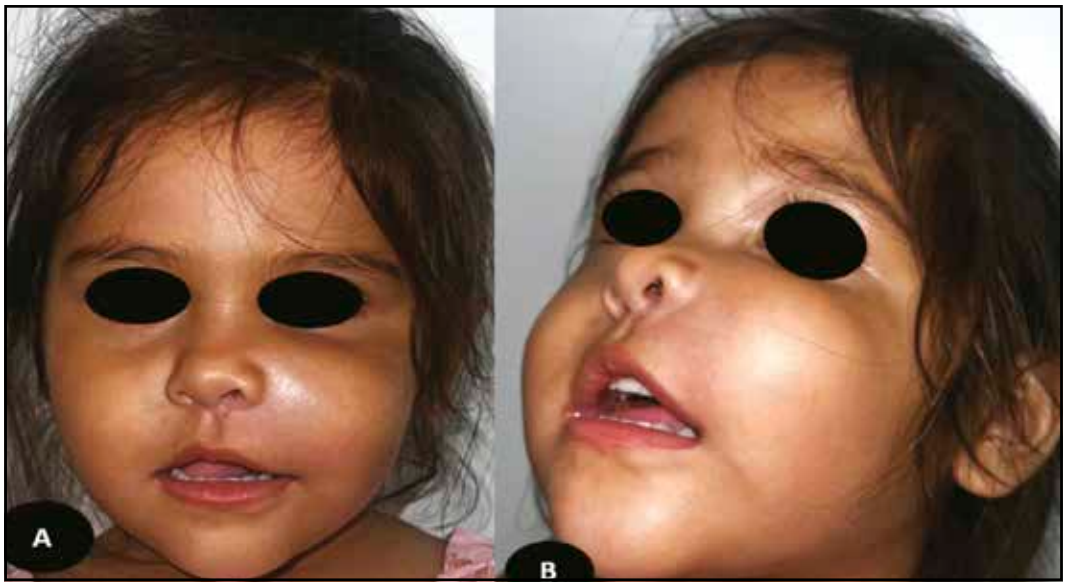

Figure 1. Clinical ENT examination – left maxillary region tumefaction with marked facial asymmetry (**A** – frontal view; **B** – left lateral view).

CASE PRESENTATION

We present the case of a previously healthy three-year-old girl who was evaluated for a four-week history of a progressively enlarging facial mass involving the left hemiface. The clinical course was accompanied by intermittent epistaxis from the left nostril, unilateral nasal obstruction on the same side, and difficulty in chewing on the left side.

On physical examination (Figure 1), a localized tumefaction was seen on the left cheek, which slightly displaced the facial midline and distorted the architecture of the upper lip on the same side. The tumor had expansive characteristics, compromising not only the left upper jaw, but also extending towards the zygomatic region and the base of the nose. The nose was deviated to the right, possibly due to the compression by the tumor on the nasal base. The left nostril was elevated, and the facial contour on the affected side was noticeably distended. There were no signs of skin ulceration or superficial inflammatory changes, suggesting a slow growth process, probably of bone or odontogenic origin.

The girl kept her mouth ajar, indicating a functional limitation derived from the growth of the mass.

Neurological examination revealed isochoric and reactive pupils, with integrity of evaluable cranial nerves.

A contrast-enhanced computed tomography (CT) scan of the skull and facial bones revealed a hyperdense mass occupying the left maxillary sinus, with evidence of bone erosion, extension into the periorbital soft tissues, and involvement of the skull base (Figure 2). A hypodense lesion with poorly defined borders was observed completely occupying the left maxillary sinus, with invasion of adjacent bony structures, including erosion of the orbital floor and extension to soft tissues of the midface (Figure 2A).

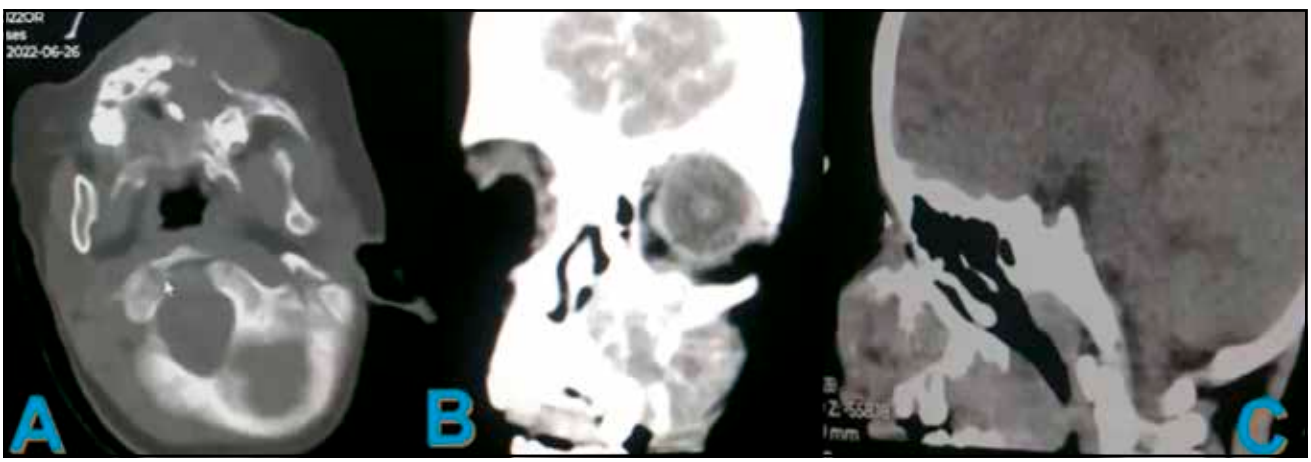

Figure 2. CT scan of the skull and facial structures. The images correspond to tomographic slices in three different windows and planes (**A** – axial section, bone window; **B** – coronal section, soft-tissue window; **C** – sagittal section, bone window) showing an expansive and infiltrative lesion in the left maxillary sinus, compatible with neuroblastoma with a locally advanced destructive pattern.

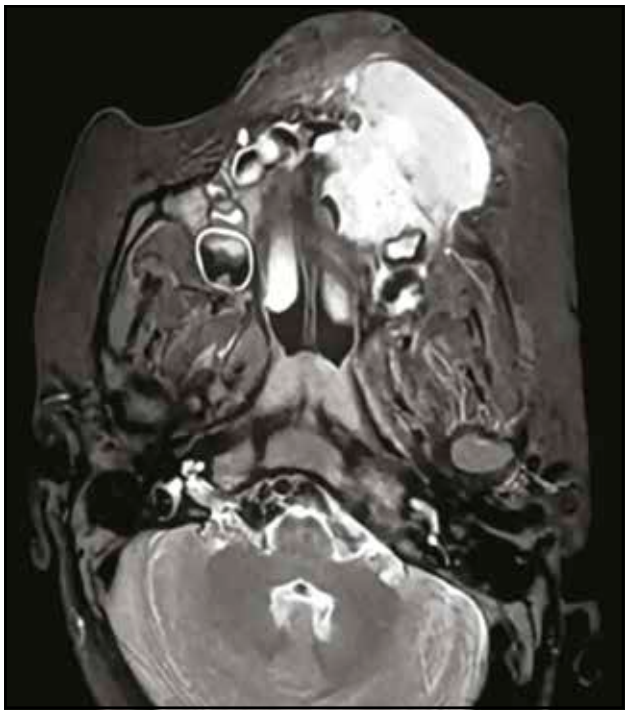

Figure 3. Craniofacial MRI, T1 sequence with contrast and fat suppression, axial plane – expansive lesion located in the left maxillary and/or infratemporal region, with infiltration of the neighbouring structures and displacement of the normal anatomy.

Bone remodelling and loss of the maxillary external cortex were observed. The soft-tissue window on coronal CT scan sections (Figure 2B) allowed visualization of the expansive and infiltrative behaviour of the tumor towards the left nostril and the inferior orbital region. The mass displaced the orbital contents superiorly and obliterated the ipsilateral paranasal cavities, in addition to producing a significant mass effect. The posterosuperior extension of the tumor to the base of the anterior skull was also visible on the coronal CT sections (Figure 2C), with alteration of the bony architecture of the lamina papyracea, posterior wall of the maxillary sinus, and probable involvement of the roof of the nasal cavity. The CT scan images also suggested disruption of the palatal plane and extension into the oral cavity, consistent with the clinical findings. Based on the CT scan, differential diagnoses such as Ewing's sarcoma, rhabdomyosarcoma, and ectopic olfactory neuroblastoma were initially considered.

The imaging examination was completed with a contrast-enhanced craniofacial MRI (Figure 3). The technique included suppression of the fat signal (using methods such as FAT-SAT or SPIR), which allowed better visualization of lesion enhancement and vascular structures, by eliminating interference from the bright signal originating from fat tissue. An expansive lesion was identified on the left hemiface, located in the maxillary and/or infratemporal region; it showed heterogeneous enhancement after the administration of contrast, a finding that was compatible with a tumor process. The lesion infiltrated

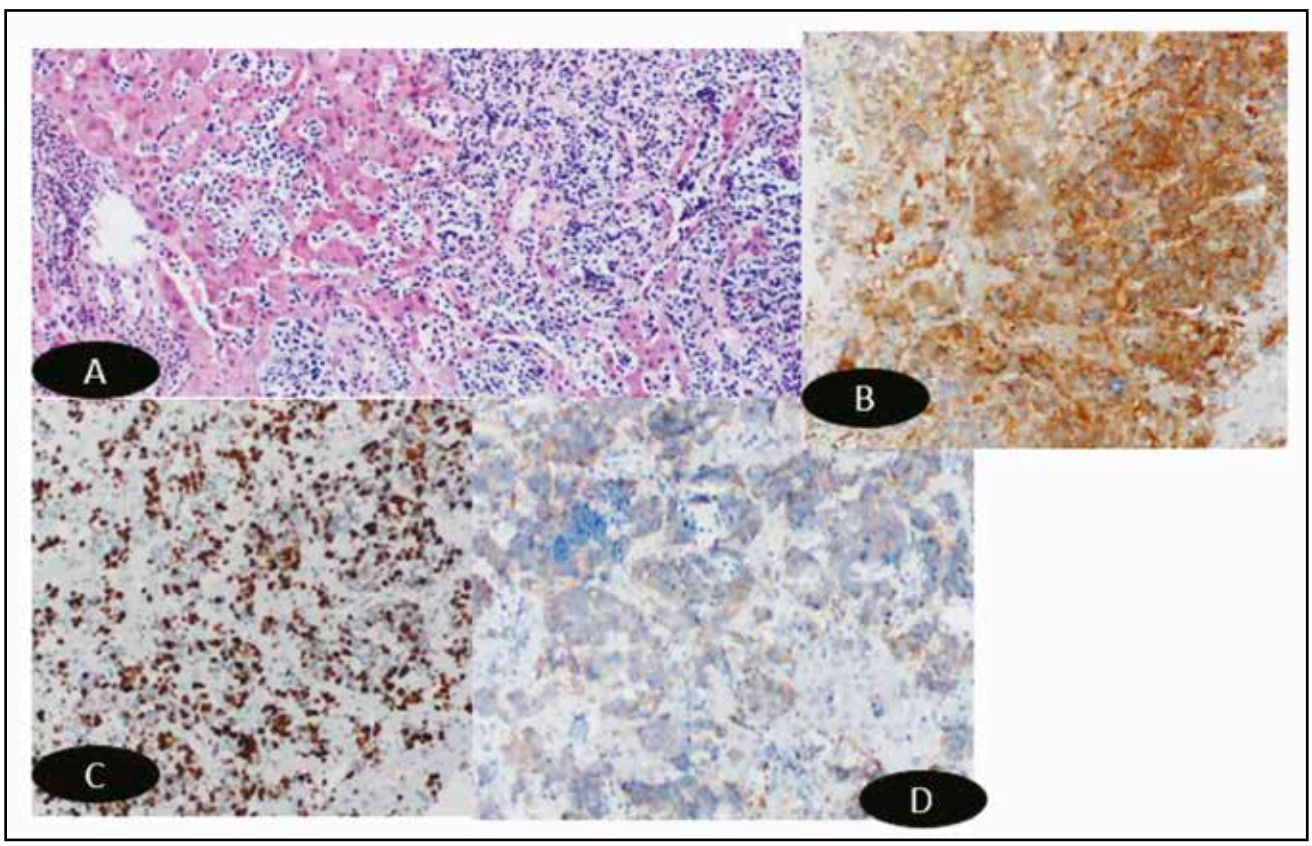

Figure 4. Histopathological results - **A:** neuroblastoma with poor differentiation (Hematoxylin & Eosin); immunohistochemistry results; **B:** positive for enolase; **C:** Ki-67; **D:** weakly positive reaction to synaptophysin.

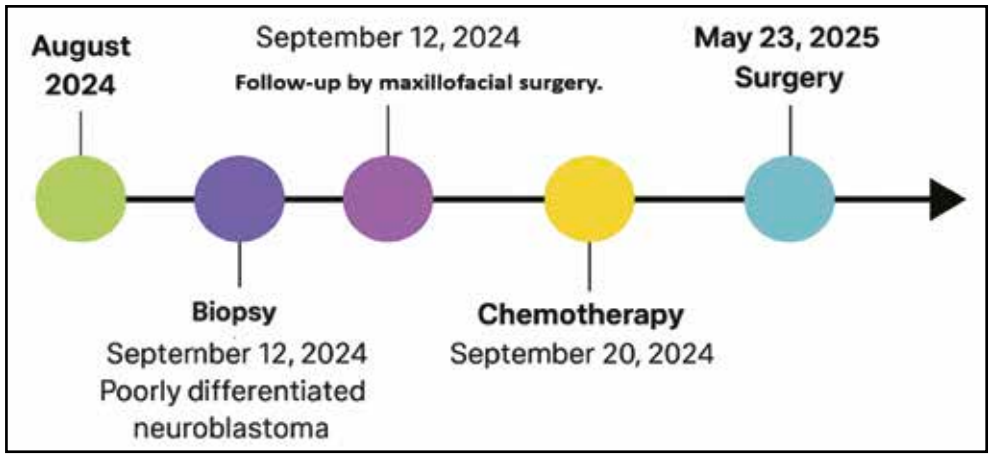

Figure 5. The clinical course of a patient diagnosed with poorly differentiated neuroblastoma.

neighbouring structures and generated displacement of the normal anatomy, with apparent involvement of the left maxillary sinus and possible involvement of the floor of the left orbit.

A biopsy was performed by the Maxillofacial Surgery specialist, and the histopathological report was compatible with neuroblastoma with poor differentiation. The anatomopathological diagnosis was later confirmed by positive immunohistochemistry for specific neuronal enolase (SNE), synaptophysin, and a high Ki-67 index, indicating high proliferative activity (Figure 4).

At this point, the clinical evolution of the case is important (Figure 5). The timeline highlights key moments in the patient's journey from symptom onset through diagnosis, histological confirmation, and definitive surgical treatment. The patient's symptoms began in August 2024, prompting medical evaluation. On September 12, 2024, a biopsy was performed, establishing the anatomopathological diagnosis of poorly differentiated neuroblastoma. This date marks a pivotal point in the patient's diagnostic process.

The patient was referred to Pediatric Oncology, where she was classified as a case of stage L2 maxillary neuroblastoma according to INRG**,** initiating neoadjuvant chemotherapy was initiated with a schedule based on cyclophosphamide, doxorubicin and vincristine. After the second cycle, an increase in tumor volume was reported.

After the follow-up performed by the maxillofacial surgeon on May 18, 2025, the surgeon requested an otorhinolaryngology evaluation to assess the possibility of surgical tumor reduction, trying to improve the therapeutic response with chemotherapy and radiotherapy.

The ENT physical examination showed a large, firm, expansive tumor involving the left maxillary region, extending to the palate and oral cavity, with blackish superficial ulceration of the oral mucosa and displacement of the ipsilateral eyeball. Tumor growth compromised the masticatory function and facial symmetry, with no clinical signs of systemic spread at this time (Figure 6).

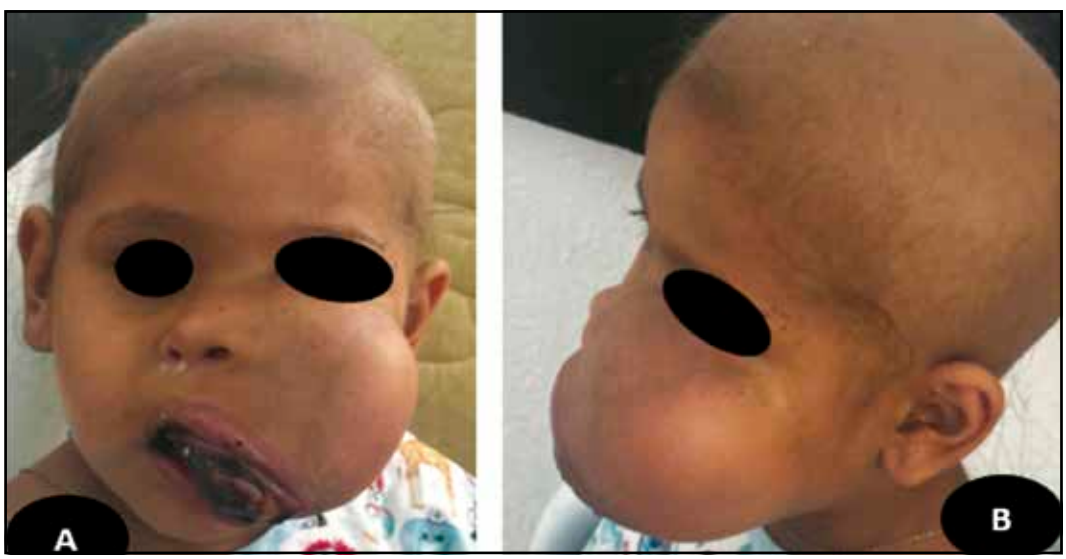

Figure 6. ENT evaluation after two cycles of chemotherapy – growth of the tumor, extension to the palate and oral cavity, with blackish superficial ulceration of the oral mucosa and displacement of the ipsilateral eyeball; facial symmetry (frontal view – **A**; left-side view – **B**).

Figure 7. A. Intraoperative view. **B.** Immediate postoperative view.

The patient underwent surgery on May 23, 2025 for tumor debulking via a transmaxillary approach. A fibro-osseous, infiltrative mass with imprecise borders and poor vascularity was identified, extending to adjacent structures and without a defined cleavage plane, which prevented complete resection (see Figure 7). The procedure was performed without anesthetic or surgical complications. Subsequently, adequate soft-tissue reconstruction was achieved, and the patient was transferred to recovery in a stable state, with conventional postoperative management.

Figure 8. Third postoperative day.

The pediatric patient showed a favourable evolution after partial resection of the left maxillary neuroblastoma. A significant reduction in tumor volume and partial improvement in facial symmetry were observed. The skin remained intact, with no signs of infection or bleeding, and residual swelling was minimal and expected. There were no acute external complications, and the patient remained alert and stable, indicating adequate tolerance of the surgical procedure (Figure 8).

The patient continued her treatment under the care of the Pediatric Oncology Department. She was re-evaluated three weeks after surgery; however, follow-up was subsequently lost, as the Pediatric and Pediatric Oncology services are located in a different hospital within our healthcare network. An attempt was made to contact the treating team to obtain updated clinical information, but no further details were available at the time of this report. The patient's medical record was transferred to the corresponding facility for continued care.

MATERIAL AND METHODS

A systematic review of the literature was carried out with the aim of describing the case reports and case series published on neuroblastoma of the nasal and paranasal sinus region in the pediatric population. Two researchers independently performed the search and selection of the studies, following the

appropriate methodological guidelines for studies of this type. The search strategy was guided by the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and focused on studies published in English from 1970 to 2024[5].

The search was carried out in the electronic databases PubMed, ScienceDirect, Scopus and Mendeley, using the following descriptors as combined search terms: ("esthesioneuroblastoma" AND "neuroblastoma") AND ("children" OR "child" OR "pediatric"). Rayyan software was used as a tool for reference management and to facilitate blind review and resolution of discrepancies between reviewers[6].

The inclusion criteria considered studies with a case report or case series design, including patients under 18 years of age diagnosed with olfactory neuroblastoma or neuroblastoma in the nasal or paranasal sinus region. We excluded duplicate articles, reviews without individual case descriptions, animal studies, and articles without access to the full text. In addition, the CARE checklist (CAse REport Guidelines) was applied as an instrument to evaluate the methodological quality and transparency in the reporting of the included cases[7]. Discrepancies among researchers were resolved through joint discussion or, if necessary, with the participation of a third reviewer.

RESULTS

In our review, 1,449 records were identified, of which 160 were evaluated in full text. Only 24 articles met the inclusion criteria by providing consistent clinical and therapeutic information on olfactory neuroblastoma in the pediatric and juvenile population, despite notable methodological heterogeneity. We included 24 studies comprising a total of 76 pediatric and adolescent patients, aged between 0.9 and 18 years, diagnosed with olfactory neuroblastoma (ONB), also known as esthesioneuroblastoma (ENB). Most studies were case reports (n = 17), followed by case series (n = 5) and two cohort studies, one retrospective and one prospective[8-31] (Table 1).

Regarding age distribution, 77.6% of the studies did not specify the exact age of all patients or included a wide range; however, subgroups were identified, with a predominance in adolescents (13–18 years: 7.9%) and children under 6 years of age (9.2%). The clinical presentation was varied, with the most common symptoms being epistaxis, rhinorrhea, exophthalmos, and olfactory masses with intracranial extension, although detailed symptoms were not specified in 80% of the studies[11,12,15,17,20,22].

The most frequent therapeutic strategies were multimodal combinations, in which the triad of surgery, radiotherapy (RT) and chemotherapy (CHT) was used in 42.1% of cases. Likewise, the use of proton therapy as a primary or adjuvant treatment was documented in 31.6% of patients. Other approaches included surgery alone (6.6%), isolated RT or CHT (3.9% each), and hybrid protocols to a lesser extent. Regarding prognosis, most patients (61.8%) achieved disease-free or overall survival in the medium–long term, being more frequent in cohorts treated with combined strategies and prolonged follow-up. Only three perioperative or disease-progression-related deaths were recorded, while in 21.1% of cases the results were unspecified or limited by brief follow-up. Multimodal treatment was associated with higher rates of local control and survival, especially in studies with larger sample sizes and structured protocols[8,15,17-19,25-27].

In individual cases, surgical resection was the initial treatment, followed by radiotherapy and adjuvant or neoadjuvant chemotherapy, depending on the stage and extent of the tumour. To a lesser extent, the use of isolated surgery, RT or CHT was reported as the only management, and mixed protocols such as biopsy followed by RT. Others reported the use of proton therapy with promising results in survival and reduced toxicity[13,19,20,25,28].

In terms of prognosis, disease-free or overall survival was reported in 61.8% of patients, especially in studies with multi-

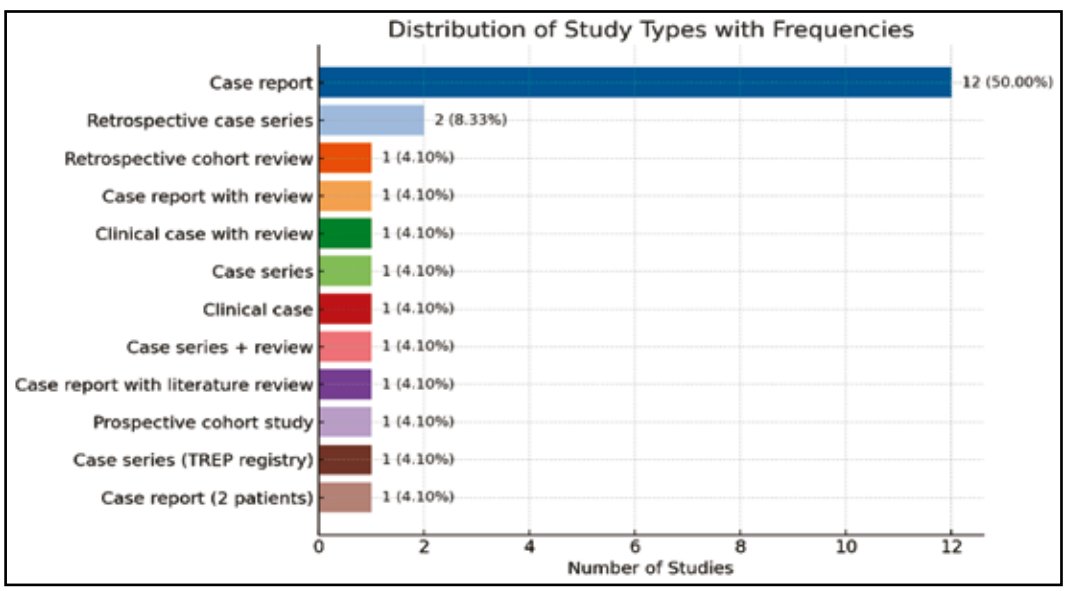

Figure 9. Types of items included in the review.

modal treatments and adequate follow-up. Three deaths related to perioperative complications or disease progression were recorded. Complete remission was documented in some cases, while a significant percentage (21.1%) had unspecified outcomes or insufficient follow-up[8,9,11,14,17,18,21,24,27,31].

This set of studies demonstrates the clinical and therapeutic heterogeneity of pediatric ONB and highlights the need to standardise diagnostic and treatment schemes to improve comparison between cohorts and the quality of long-term follow-up.

Common limitations included small sample sizes, therapeutic heterogeneity, and poor long-term follow-up, which make it difficult to extrapolate generalised results.

Figure 9 illustrates the distribution of study types included in the dataset. It is evident that case reports are the most common type, representing half of all studies (50%), with a total of 12 reports. This suggests a strong reliance on individual clinical observations within the available literature.

Retrospective case series account for 8.33% of the total, corresponding to 2 studies. All other study types appear with equal frequency, each represented by a single study (4.10%). These included retrospective cohort studies, prospective cohort studies, case reports (some accompanied by literature reviews), individual clinical cases, case series (with or without integrated reviews), case reports involving two patients, and a multicentre case series from the Italian TREP registry (Tumori Rari in Età Pediatrica, an acronym in Italian), which focuses on rare pediatric tumors.

Overall, the data reflect a predominance of descriptive and observational designs, particularly case-based studies, likely due to the rarity or complexity of the condition or topic under investigation.

The methodological quality of the included studies was assessed using the CARE (CAse REport) Guidelines, focusing on key elements such as the clinical course, confirmed diagnosis, intervention performed, clinical outcome, and academic reflection. Among the 24 studies analysed, 11 (44%) were classified as high quality, 8 (32%) as moderate quality, and 6 (24%) as low quality.

The highest-quality studies were distinguished by comprehensive clinical descriptions, the use of diagnostic imaging and histopathological techniques, and documented patient follow-up after the intervention. In contrast, the lower-quality reports exhibited notable limitations, including the absence of long-term follow-up, unclear clinical chronology, and insufficient contextualisation of the case within the existing literature.

Although the predominance of case reports and small series constrains the generalizability of the findings, the systematic application of the CARE guidelines enabled the identification of studies with greater narrative rigour and clinical relevance for the management of nasal and paranasal neuroblastoma in the pediatric population.

DISCUSSIONS

Olfactory neuroblastoma (ONB) is an extremely rare neoplasm in the pediatric population, particularly when it is located in the paranasal sinuses or maxillary region. Its low frequency has been documented in retrospective series such as that of Alvi et al.[32], who identified only one case of esthesioneuroblastoma among 118 pediatric neuroblastomas in a tertiary hospital over 15 years. Similarly, Chung et al.[33], analysing 210 cases of pediatric sinonasal malignancies in the SEER database, reported that ONB accounted for only 17.6% of tumors in this location, confirming its rarity. In Yi et al.'s Korean series[34], only three of 20 sinonasal malignancies corresponded to ONB, and it was also noteworthy that most were in advanced stages at the time of diagnosis.

In terms of therapeutic patterns, the most commonly adopted strategy is multimodality: surgery, chemotherapy and radiotherapy. However, the ideal sequence of treatment remains a matter of debate. In Chung et al.'s study[33], patients treated with surgery alone had longer long-term survival, which could reflect less tumor aggressiveness or earlier stages. In our case, the ONB showed initial resistance to chemotherapy, which led to an early debulking surgical intervention, confirming that the therapeutic approach must be adapted to individual clinical behaviour. In this context, new strategies such as proton therapy are being explored as promising options to improve locoregional control and minimise toxicity in adjacent tissues.

The prognosis of pediatric ONB is closely linked to histologic grade, locoregional extent, and proliferation markers. Grade IV tumors, such as that of our patient (elevated Ki-67 index), have been associated with lower survival rates at 5, 10, and 20 years[33]. On the other hand, Yi et al.[34] reported an overall five-year survival of 52% in their cohort, with ONB being one of the tumors with the best prognosis compared with lymphomas, although still limited by late diagnosis. In addition, metastatic presentations such as the one documented by Kalaskar et al.[35], with oral manifestations in a three-year-old child, reflect the infiltrative capacity and clinical aggressiveness of some ONBs, even when their primary origin is not sinonasal.

Overall, our clinical case coincides with the literature regarding the low frequency of ONB in children under five years of age, its nonspecific presentation, and its aggressive behaviour in anatomically complex locations. The need for personalised treatments, close monitoring of response, and the incorporation of emerging therapies reinforce the importance of establishing multicentre registries and developing standardised therapeutic protocols to optimise the management of this rare and challenging entity.

The prognosis of these cases is generally poor, both in terms of survival and functional outcomes in the short term.

CONCLUSIONS

Pediatric olfactory neuroblastoma, particularly in nasal and paranasal locations, represents an infrequent but clinically challenging oncological entity due to its nonspecific presentation, locally aggressive behaviour, and difficult surgical access. The clinical case presented, corresponding to a three-year-old girl with infiltrating maxillary neuroblastoma refractory to initial chemotherapy, illustrates the main diagnostic and therapeutic challenges associated with this neoplasm at an early age. The histopathological findings of high proliferative activity (elevated

Table 1. Articles on neuroblastoma of the nose and paranasal sinuses in pediatric patients.

Author; year	Type of study	Population (n)	Inclusion criteria	Intervention / Exhibition	Variables / Outcomes	Main results	Methodological Quality CARE Guidelines	Limitations
Gull et al.[8] (1997)	Case report	A 2-year-old boy	Exophthalmos, epistaxis, rhinorrhea Olfactory mass with intracranial extension	Transnasal resection (frontal craniotomy)	Clinical presentation, imaging findings, pathology	Complete resection; intraoperative cardiac arrest and death 3 h later	High	Only one case High perioperative mortality
Thompson et al.[9] (2012)	Case report	A 12-year-old girl	Kadish C T3N0M0 esthesioneuroblastoma with extensive calcifications	Assisted endoscopic resection + RT	Surgical technique, margins, recurrence, survival	Recurrence-free disease at 18 months	High	Only one case Limited tracking
El Kababri et al.[10] (2014)	Retrospective review of a single-centre cohort	11 pediatric patients	Kadish B–C esthesioneuroblastoma	Neoadjuvant CHT (cyclophosphamide, doxorubicin, vincristine, ± carboplatin/ etoposide) + surgery + RT	Neoadjuvant response rate; Overall and disease-free survival	The multimodal approach achieved a 5-year survival rate of 91%, with high treatment response and only one fatal relapse.	According to JBI Checklist for Case Series, it is classified as high quality	Small sample size Heterogeneous treatment
Zateska-Czepko et al.[11] (1996)	Case report	An 8-year-old child	Kadish C ONB confirmed by biopsy and CT	Alternate multidrug CHT (vincristine + cyclophosphamide or cisplatin + daunorubicin; 4 weeks) + RT	Complete remission, follow-up imaging	Complete remission maintained at 40 months	High	A single patient No control group
Ferlito et al.[12] (1979)	Case report	A 3-year-old girl	Children's ENB Review of 2 previous cases	RT (4,500 rads) + CHT with weekly vincristine (x11)	Clinical-pathological characteristics	Initial improvement High levels of catecholamines Unfavourable prognosis	Moderate	Difficult diagnosis No initial surgery
Maggiore et al.[13] (2018)	Case report	A 13-year-old patient	ENB Kadish B without cribriform lamina invasion	Unilateral endoscopic resection + septal flip flap (SFF) reconstruction	Quality of life, preservation of smell, negative margins	Preserved smell Free margins Quick recovery	High	Only one case Short-term follow-up
Yadav et al.[14] (2024)	Case report	A 16-year-old girl	Pediatric ENB with SIADH detected during primary CHT	CHT with cisplatin (3 cycles); water restriction for SIADH	Emergence of SIADH, radiological progression	SIADH as a marker of clinical progression	Moderate	Only one case Very rare event
Pacino et al.[15] (2020)	Case report	A 16-year-old female	Patient with ONB confirmed by biopsy and local smear	Craniofacial resection (bifrontal + transfacial), reconstruction + RT 56 Gy	Surgical technique, reconstruction, locoregional control	Resection with negative margins and good reconstruction Locoregional control after 56 Gy of RT (follow-up not specified)	High	Only one case There is a lack of detail of long-term follow-up No comparator or quality assessment
Wormald et al.[16] (2011)	Case series	4 pediatric patients	ONB in locations outside the usual olfactory region (the anterior ethmoidal sinuses, the nasopharynx, the lateral nasal wall, the floor of the nose)	Surgery with/without adjuvant RT	Anatomical location, surgical and radiation management	Description of 4 forms of ectopic ONB Forecast according to length	Low	Very small series Poor clinical follow-up No quantitative survival data
Yaris et al.[17] (2003)	Case report	A 2-year-old girl	Stage IV neuroblastoma with involvement of the sphenoid sinus	Intensive chemotherapy according to neuroblastoma protocol	Clinical, laboratory, MRI/CT, survival	Sphenoid infiltration Died at 5 months after diagnosis	Low	Single case Without local surgical managemen Fatal prognosis Not applicable to primary ONB
Gu et al.[18] (2024)	Case series	5 pediatric patients	ONB modified Kadish stage B (one case), C (two cases) and D (two cases)	Surgery + chemotherapy + radiotherapy	Baseline symptoms, histology, Kaddish stage, survival, recurrence	4 survivors, 1 death Mean follow-up 22.3 months Without recurrence	Good quality study according to STROBE	Very small size No control group Retrospective data
Lucas et al.[19] (2015)	Case series	8 patients (4 children, 4 adolescents; ≤21 years)	ENB Kadish stage B (three cases), C (one case), D (four cases)	Proton radiation therapy + surgery ± chemotherapy	Global survival, local and regional control, RT toxicity	High survival (87.5%) and good local control, with distant relapses and limited visual toxicity in a few cases.	Moderate	Small number of cases No comparator with photons Heterogeneity in adjuvant treatments

Author; year	Type of study	Population (n)	Inclusion criteria	Intervention / Exhibition	Variables / Outcomes	Main results	Methodological Quality CARE Guidelines	Limitations
Kakar al.[20] (1972)	Case report	A 3-year-old child	Histologically documented primary neuroblastoma of the maxilla	Single supervoltage radiation therapy	Clinical presentation, radiological and histological findings, response to RT	There was no response Persistent tumor	Low	Only one case No alternative options Limited tracking
Kumar et al.[21] (2002)	Case series	5 pediatric patients (≤18 years)	ENB	Neoadjuvant/adjuvant CHT + RT ± resection	Clinical presentation, multimodal treatment, 5-year survival	Three patients responded well, but three died due to relapse. Two remained disease-free at short-term follow-up. Neoadjuvant chemotherapy achieved good tumor reduction.	Moderate	Retrospective Small sample Heterogeneity in schemes
Shahriari et al.[22] (2017)	Case report	A 21-month-old girl	Bilateral proptosis, blindness, and sphenoidal/ethmoid mass confirmed on imaging as ENB	Surgery + VAC protocol (vincristine, actinomycin-D, cyclophosphamide)	Ocular symptomatology, imaging findings, IHC, response to CHT	Improved vision and proptosis after 4 cycles Ongoing follow-up	High	A single patient Brief follow-up No long-term recurrence data
Mims et al.[23] (2020)	Case report	A 13-year-old boy	Ectopic ENB (nasal lateral wall)	Endoscopic resection + proton beam therapy	Ectopic origin, surgical margin, 6-month status	No evidence of disease at 6 months Complete excision and adjuvant RT	Moderate	Single case Short follow-up Few paediatric data
McDowell et al.[24] (2020)	Case report	A 15-year-old girl	ENB Kadish C with cranial extension (biopsy and IHC)	Neoadjuvant CHT (cisplatin + etoposide) + transfrontal resection	Tumor reduction, post-CHT calcification, surgical margins	Great reduction and calcification after 3 cycles Resection with negative margins Good evolution	High	Only one case Anecdotal finding Limited tracking
Drescher et al.[25] (2024)	Cohort study	15 patients (≤21 years old)	ENB Kadish stage B (n = 2), C (n = 9), D (n = 4)	Proton radiation therapy after CHT ± resection	All patients achieved long-term complete disease control, with 100% overall survival and disease-free survival. No locoregional or distant recurrences were observed. Both acute and late toxicities were minimal or not reported.	All patients survived without relapse, achieving long-term complete disease control.	High	No photonic control group Variable doses Significant toxicity
Bisogno et al.[26] (2012)	Case series	9 patients (0.9–18 years)	ENB with bone erosion (7 patients) and intracranial (4 patients) or intraorbital (4 patients) extension	CHT + difficult resection + RT (48.5–60 Gy)	Tumor control, CHT response, endocrine and growth sequelae	8/9 long-term controlled Endocrine and craniofacial sequelae	High	Small sample Heterogeneity protocols Unquantified sequelae
Kupeli et al.27 (2011)	Case report	2 pediatric patients	ONB	Partial resection + RT (48 Gy) + CHT (cisplatin/etoposide)	Diagnostic stage, response to CHT/RT, survival	Patient 1 stable at 3 years Patient 2 died at 9 months	Moderate	Only 2 cases Without a comparator Brief follow-up
Thakur et al.[28] (2013)	Case report	A 12-year-old male	ENB grade I	Excision via lateral rhinotomy	Clinical presentation, histology	Resected tumor Referral to RT with no reported recurrence	Low	No follow-up No data evolution
Wei et al.[29] (2002)	Case report	A 15-year-old girl	NB isolated from the maxillary sinus without systemic disease	Craniofacial resection	Imaging, genetics (1p deletion, gain of 17, N-myc not amplified)	No recurrence at 2 years Genetic characteristics described	Moderate	Only one case Limited tracking
Das[30] (1971)	Case report	A 11-year-old girl	ENB originating in the nasal cavity and infiltrating the cheek	Excisional biopsy; referred to RT	Histological findings (rosettes, neurofibrils)	Histological diagnosis No data evolution	Low	Loss of follow-up No detailed adjuvant treatment
Woerner et al.[31] (1986)	Case report	A 2-year-old boy	ONB with sudden blindness and intracranial extension	RT 2600 rads + CHT (cyclophosphamide, vincristine, DTIC, adriamycin)	Clinical signs, CHT/RT response, cognitive development	Complete remission to 3 years Preserved cognitive function	Moderate	Single case Undocumented long-term effects

RT – radiotherapy; CHT – chemotherapy; ONB – olfactory neuroblastoma; ENB – esthesioneuroblastoma; SIADH - syndrome of inappropriate ADH secretion; IHC – immunohistochemistry; NB – neuroblastoma

Ki-67 index), the need for an aggressive surgical approach and the initiation of multimodal treatment are consistent with the emerging recommendations of the international literature.

The systematic review, although limited in methodological quality and sample size, agrees that the optimal therapeutic approach to pediatric ONB should be multidisciplinary, combining surgery, radiotherapy, and chemotherapy. Disease-free survival rates reach up to 61.8% with these strategies, although there is still great heterogeneity in the protocols applied. It also highlights the low proportion of studies with prolonged follow-up, as well as the low frequency of prospective or cohort studies, which restricts the possibility of issuing standardised recommendations.

The present paper underscores the urgent need to establish international multicentre registries and consensus guidelines for the diagnosis, staging, and management of olfactory neuroblastoma in childhood. The systematic implementation of tools such as the CARE guide and databases such as TREP can strengthen the quality of case reporting and facilitate the consolidation of robust clinical evidence. Likewise, the use of emerging therapies such as proton therapy could improve the toxicity profile without compromising effectiveness, opening up new therapeutic opportunities in pediatric patients with tumors located in anatomically complex regions.

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Limitations: The review only included articles in the English language, we did not have access to all the articles found.

Ethical aspects: Written informed consent was obtained from the patient's mother for the publication of this clinical case, including medical data and diagnostic images. The confidentiality of the information was guaranteed, ensuring that the identity of the minor was not revealed at any time. Consent was granted voluntarily, after the objectives of the publication and the scope of the information presented were clearly explained.

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Authors' information

Bernardo Rojo Ochoa, Resident Physician in Otolaryngology – Head and Neck Surgery, "Lic. Luis Donaldo Colosio Murrieta", Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. E-mail: otorrinox@gmail.com. ORCID: https://orcid.org/0009-0006-6842-1970.

Ana Ilian Vielma Gonzalez, Resident Physician in Otolaryngology – Head and Neck Surgery, "Lic. Luis Donaldo Colosio Murrieta", Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. E-mail: otorrinox@gmail.com. ORCID: https://orcid.org/0009-0002-7080-0153.

Jorge Humberto Orduno Hernandez, Resident Physician in Otolaryngology – Head and Neck Surgery, "Lic. Luis Donaldo Colosio Murrieta", Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. E-mail: otorrinox@gmail.com. ORCID: https://orcid.org/0009-0001-5461-7730.

Brenda Gissel Gonzalez Millan, Resident Physician in Otolaryngology – Head and Neck Surgery, "Lic. Luis Donaldo Colosio Murrieta", Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. E-mail: otorrinox@gmail.com. ORCID: https://orcid.org/0009-0001-7405-2159.

Juan Antonio Lugo Machado, Attending Physician in Otolaryngology – Head and Neck Surgery, "Lic. Luis Donaldo Colosio Murrieta", Specialties Hospital No. 2, National Medical Center of the Northwest, Mexican Institute of Social Security, Ciudad Obregón, Sonora, Mexico. E-mail: otorrinox@gmail.com. ORCID: https://orcid.org/0000-0003-4864-8546.

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