Case Report

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Extranodal Rosai-Dorfman Disease with Simultaneous Involvement of the Brain, Paranasal Sinus, and the Larynx: A Case Report

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Rosai-Dorfman disease (RDD) is a rare, idiopathic, and nonmalignant histiocytic proliferative disorder involving lymph nodes or extranodal organs. The most common organs involved are skin and subcutaneous tissue, followed by lymph nodes, bone, and head and neck. Some reports have suggested that extranodal involvement is present in approximately 40% of cases. The most frequently affected locations in the head and neck region are nasal cavity, pharynx, and paranasal sinuses. The diagnosis of extranodal RDD is difficult, because its clinical symptom is uncommon or mild. The treatment of symptomatic RDD patients can involve surgical resection, radiotherapy, high-dose steroid, and chemotherapy. Extranodal RDD with simultaneous multifocal involvement is rare and its treatment remains challenging. Therefore, we report a case of extranodal RDD with a simultaneous involvement of the brain, paranasal sinus, and the larynx because it is extremely rare. The clinical, histopathological and immunohistochemical features, and treatment modalities are discussed.

Key words: Rosai-Dorfman disease, non-neoplastic mass, extranodal disease, simultaneous multifocal involvement

Introduction

Rosai-Dorfman disease (RDD), also called sinus histiocytosis, is a rare, idiopathic, and nonmalignant histiocytic proliferative disorder involving the lymph nodes or extranodal organs.[1] The typical clinical manifestations include a painless cervical lymphadenopathy accompanied by a fever, elevated erythrocyte sedimentation rate, weight loss, rhinorrhea, and occasionally hepatosplenomegaly.[1,2] The most common organs involved are the skin and subcutaneous tissue, followed by lymph nodes, bone, and head and neck.[3] Some reports have suggested that extranodal involvement is present in approximately 40% of cases.[4-6] The most frequently affected locations in the head

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and neck region are the nasal cavity, pharynx, and paranasal sinuses.[7] RDD exhibits a distinct histopathologic feature called emperipolesis, in which the nondestructive phagocytosis of lymphocytes or erythrocytes in the cytoplasm of the histiocytes is the hallmark of the disease and required for diagnosis.[1,8] The diagnosis of extranodal RDD without lymphadenopathy is difficult, because its clinical symptom is uncommon and nonobvious. The treatment of symptomatic RDD patients can involve surgical resection, radiotherapy, high-dose steroid, and chemotherapy.[3,6,8,9]

We report a case of extranodal RDD without lymphadenopathy that exhibited synchronous involvement of the brain, paranasal sinus, and the larynx. We discuss the clinical, histopathological, and immunohistochemical features of extranodal RDD and review the literature.

Case Report

A 57-year-old woman sustained a traffic accident with clear consciousness and was sent to an emergency room. She denied having vertigo, blurred vision, epistaxis, dysphagia, dysarthria, hearing impairement, dyspnea, and other neurologic deficits. The noncontrast enhanced computed tomography (CT) scan showed two homogeneously hyperdense masses over the right temporal lobe and the left parietal and occipital lobes with prominent white matter edema suggesting a brain tumor (Fig. 1A & 1B). After a neurosurgeon was consulted, magnetic resonance imaging (MRI) was arranged; on T1-weighted MRI, it revealed dura-based lobulated and hypointense-to-isointense masses over the right temporal and the left parieto-occipital regions, with strong homogeneous enhancement after injection of gadolinium (Fig. 1C & 1D). On T2-weighted images, it revealed hypointense lesion with homogeneous enhancement after injection of gadolinium. Differential diagnoses included metastasis, meningioma, hemangiopericytoma, lymphoma, and RDD. The surgeon performed a tumor excision of the right temporal mass and the left parietal and occipital mass using craniectomy. The pathology revealed clusters of foamy cells admixed with plasma cells, neutrophils, lymphocytes, and eosinophils. Red blood cells and inflammatory cells within the cytoplasm of many large histiocytes have been found, which is a diagnostic feature known as emperipolesis. In an immunohistochemical study, the histiocytes tested positive for CD68 and S-100, and negative for CD1a. RDD was diagnosed (Fig. 2). An enhancing lesion over the left parietal region on the MRI scan in favor of tumor recurrence was observed 10 months after the excision of the brain tumor (Fig. 3A). The patient was referred for stereotactic radiosurgery to treat the recurrent brain tumor using a gamma knife (14 Gy to 50% isodose line) to obtain good tumor control. Two weeks later after radiosurgery, the patient came to our ear, nose, and throat clinic and complained of a husky voice for approximately 2 years. A flexible nasopharyngoscopy showed a mild active bleeding from the orifice of the right sphenoid sinus and smooth polypoid mass lesions over the right glottic area and the bilateral subglottic region, with impending airway compromise (Fig. 3B & 3C), though the patient denied having dyspnea and epistaxis (or blood-tinged sputum). A general examination did not reveal any significant cervical lymph nodes. The chest X-ray showed mild cardiomegaly, and hematological and biochemical parameters were within normal limits. The CT images displayed mild swelling over the right glottic and subglottic regions. Contrast-enhanced CT images also showed radiopacity at the right sphenoid sinus (Fig. 3D) without tumor recurrence in the brain. Under the impression of RDD involving the brain, the right sphenoid sinus, and the larynx causing an airway compromise, a tracheostomy was performed to secure her airway under local anesthesia, and

then glottic and subglottic polypoid lesions were excised using a CO_2 laser (microscopic laryngeal surgery) under general anesthesia. Active bleeding from the right sphenoid sinus worsened after the orifice was widened during the endoscopic sinus surgery. Therefore, only hemostasis was performed without a biopsy at the right sphenoid sinus lesion in consideration of massive tumor bleeding. Ten days after surgical intervention, the patient was referred to an oncologist for adjuvant treatment with high-dose prednisolone (50 mg per day) for 1 month (tapered thereafter in the following 3 months). Regression of the right sphenoid sinus lesion was found after consecutive treatment with a high dose of prednisolone for 2 months (Fig. 4A). After combined surgical and medical treatment, glottic and subglottic polypoid mass lesions fully subsided and no epistaxis was found. However, 13 months after the completion of medical treatment, mild subglottic tumor recurrence was observed (Fig. 4B), and prednisolone (30 mg per day) was used to control the disease for 2 months. No glottic and subglottic lesion was noted after completion of medical treatment using a half dose of prednisolone (Fig. 4C). A regular brain MRI was performed every 3 months after radiosurgery

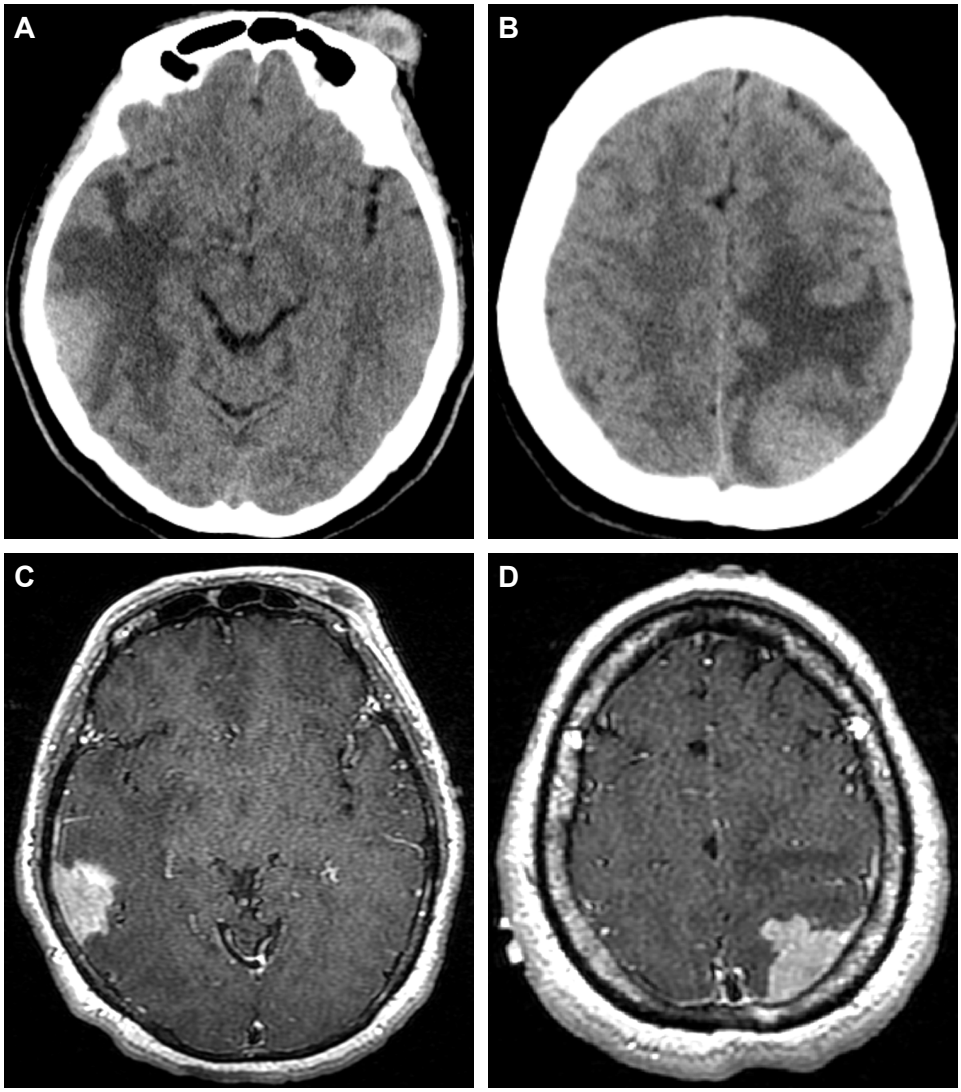

Fig. 1 Computed tomography of the brain indicating two homogeneously hyperdense masses over the right temporal lobe (A) and the left parieto-occipital region with obvious white matter edema (B). T1-weighted contrast-enhanced magnetic resonance imaging of the brain showing dura-based masses over the right temporal (C) and the left parieto-occipital regions (D).

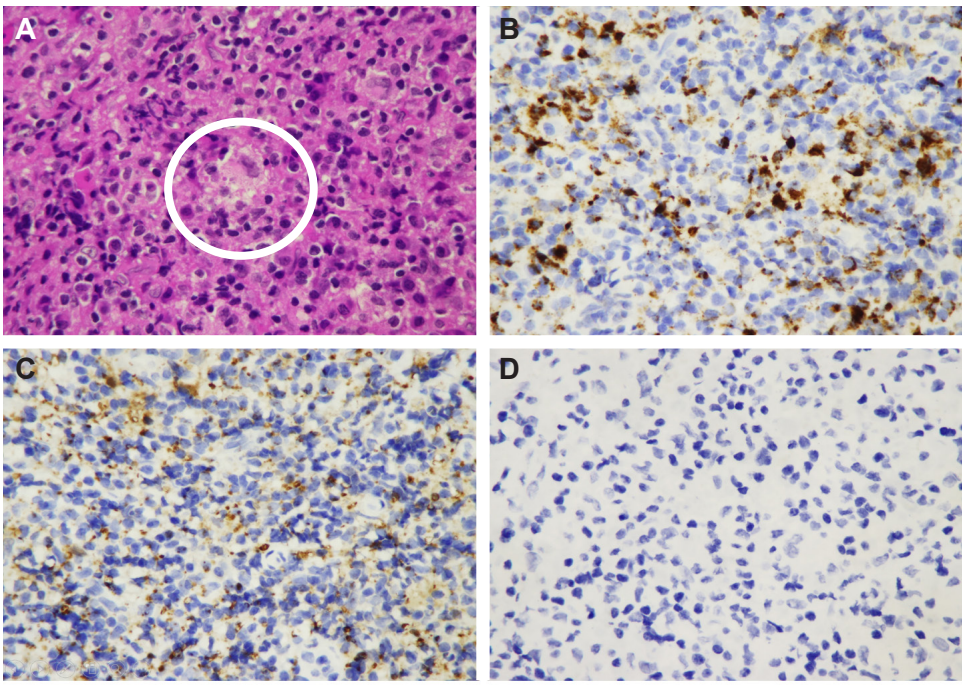

Fig. 2 Hematoxylin-eosin staining revealing large histiocytes with red blood cells and inflammatory cells within cytoplasm known as emperipolesis (original magnification × 400, circle) (A). Immunohistochemical staining revealing that histiocytes are positive for S-100 (B) and CD68 (C) but negative for CD1a (E) (original magnification × 400).

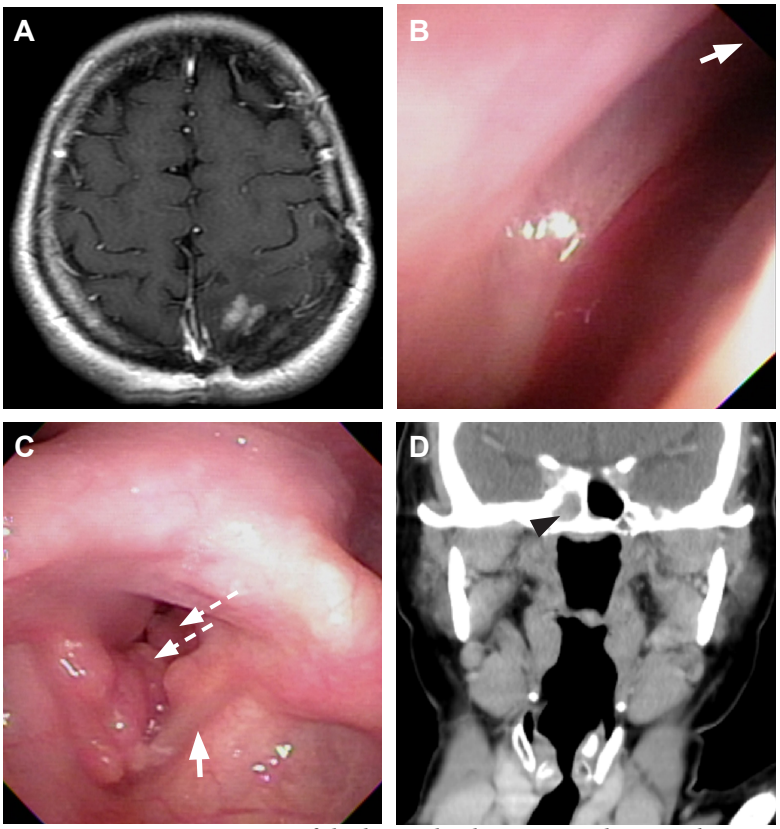

Fig. 3 T1-weighted magnetic resonance imaging of the brain displaying an enhancing lesion over the left parietal region 10 months after tumor excision (A). Nasopharyngoscopic examination showing mild active bleeding from the orifice of the right sphenoid sinus (B, white arrow) and smooth polypoid mass lesions over the right glottic area and bilateral subglottic region (white dashed arrow) with impending airway compromise (C). Left vocal cord not involved (white arrow). Contrast-enhanced computed tomography showing the right sphenoid sinus radiopacity (D, black arrowhead).

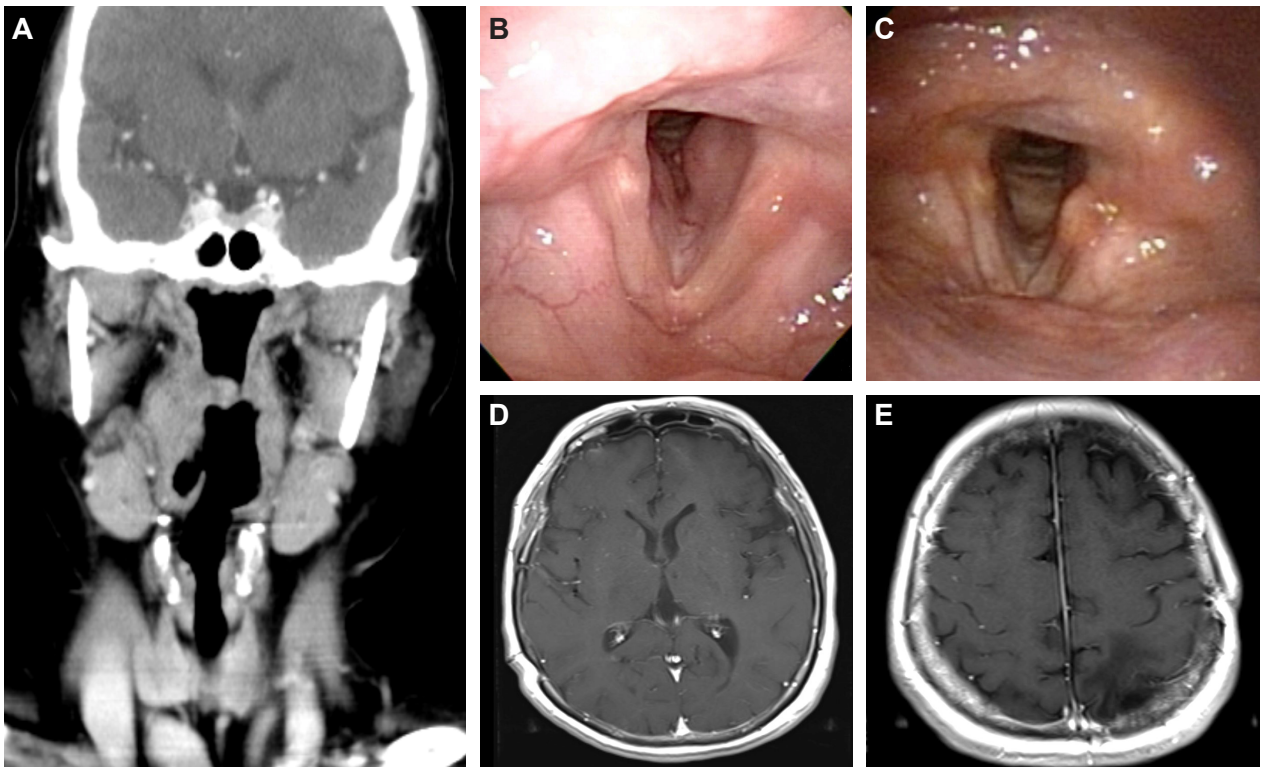

Fig. 4 Contrast-enhanced computed tomography showing regression of the right sphenoid sinus lesion after consecutive treatment with a high dose of prednisolone for 2 months (A). Mild recurrence of the left subglottic polypoid lesion was observed 13 months after the completion of steroid treatment (B). No glottic and subglottic lesion noted after completion of steroid treatment using a half dose of prednisolone (C). T1-weighted contrast-enhanced magnetic resonance imaging of the brain showing no enhancing mass lesion over the right temporal (D) and the left parieto-occipital regions (E) 20 months after the completion of radiosurgery.

and revealed no recurrence or progression (Fig. 4D & 4E). The intracranial lesion is stable without recurrence for 24 months after surgery and radiosurgery. However, the glottic and subglottic lesion is stable for 3 months after the completion of the steroid treatment using approximately a half dose of prednisolone for the recurrent disease in the larynx. The patient has a stable disease without recurrence so far and is under follow-up (Fig. 4C). Figure 5 presents a timeline of the case, which describes the history in detail.

Discussion

Because the clinical symptoms are uncommon and mild, it is not easy to diagnose extranodal RDD without lymphadenopathy. Extranodal disease is seen in approximately 40% of cases and rarely occurs in the absence of nodal disease.[6] Common areas of extranodal involvement include the skin, bone, head and neck, kidney, and central nervous system.[3] Laboratory studies may indicate an elevated erythrocyte sedimentation rate, leucocytosis, hypergammaglobulinaemia, and autoimmune hemolytic anemia.[6] In the present case, no related abnormal laboratory data has been found. Patients with central nervous system involvement are often free of the general symptoms and may manifest with only neurological symptoms related to lesion location.[10] In this case, the extranodal RDD was accidentally found when the patient received brain CT scans following a traffic accident with a mild head injury. Although the patient had extranodal RDD with severe intracranial and laryngeal involvement (impending airway compromise),

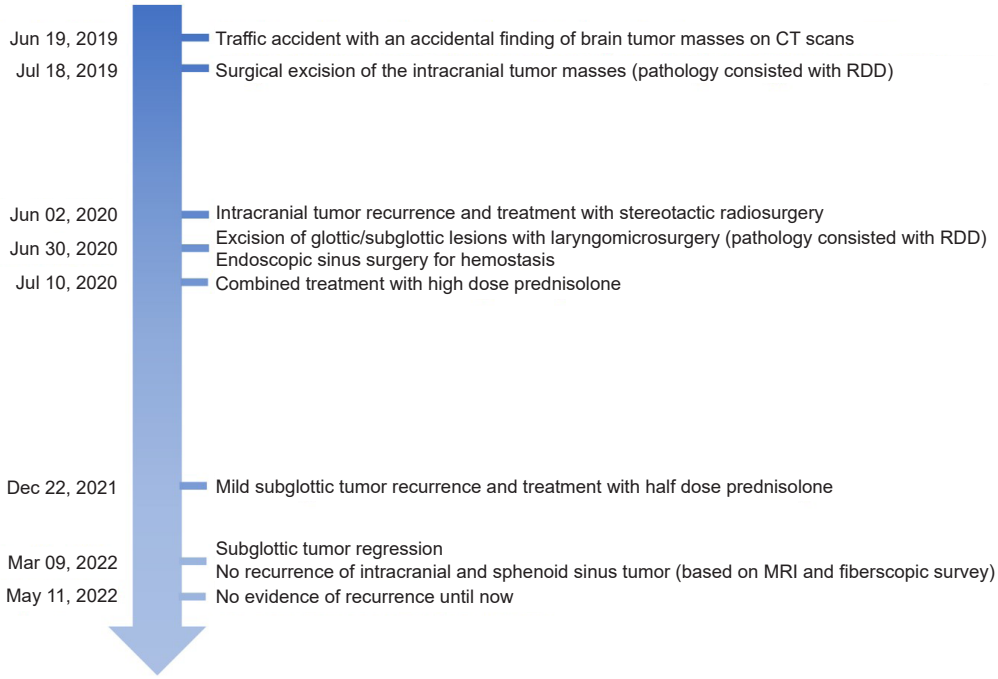

Fig. 5 Timeline of the case presentation.

she only complained of a mild husky voice for about 2 years and denied dyspnea. RDD is typically benign with no obvious symptoms or signs, but multiorgan involvement is a poor prognostic indicator. Extranodal RDD with a simultaneous involvement of the brain, paranasal sinus, and the larynx is an extremely rare case and its treatment remains challenging. Histopathologic findings are used to diagnose extranodal RDD, but it remains difficult to identify the disease by imaging studies. RDD with intracranial involvement presents as a dural-based lesion that mimics meningioma. It is usually an isodense lesion on a CT scan and isointense-to-hypointense lesion on a MRI scan, with marked perilesional edema on the contiguous structures and, similar to meningioma, exhibits homogeneous contrast enhancement.[10] Without treatment, relapsing-remitting RDD occurs in 70% of cases, spontaneous regression occurs in 20% of cases, and disease progression occurs in 10%. Surgery is an appropriate option for diseases that can be excised, including those with central nervous system involvement and head and neck involvement (for maintaining airway patency).[8] In this case, the specimen was obtained from the intracranial tumor mass, and exhibited the hallmark of RDD: emperipolesis. The immunohistochemical stain results were positive for S-100 and CD68 and negative for CD1a, confirming the diagnosis.[1-3,8] The intracranial lesions are stable without recurrence following surgical resection through craniectomy and subsequent adjuvant radiosurgery using a gamma knife. However, although the lesions at the glottic and subglottic region have been excised and vaporized using a CO_2 laser alongside adjuvant corticosteroid use, the subglottic lesion recurs 13 months after the completion of medical treatment. No ideal treatment exists for the management of RDD. Corticosteroids are frequently used, with approximately one-third of patients achieving a complete or partial response to treatment.[9] Prednisolone (30 mg per day) for 2 months has been used to control the recurrent disease, and the disease is stable without recurrence after a 3-month follow-up. Surgical excision may be used for symptomatic airway, cranial, spinal, or sinus disease.

Patients with multifocal irresectable extranodal disease may require systemic therapy.[6] Due to the limitations of the operative field and the nearby vital organs and tissues, it is difficult to perform a radical surgical resection of the disease (intracranial and subglottic lesions in this case). In this case, radiosurgery using a gamma knife (14 Gy to 50% isodose line) seemed to have better control of the recurrent intracranial RDD, and no complications were observed. In contrast to radiosurgery, corticosteroids exhibit no long-term control of the recurrent laryngeal RDD. A multidisciplinary approach to managing primary and recurrent RDD lesions is required to provide good local control and functional results for individual patients.[3,9] Close follow-up for the larynx and the brain is necessary. If subglottic or glottic lesion recurs causing respiratory distress, surgical intervention, radiotherapy, steroids, or chemotherapy may be used in a combined treatment modality in the future.

In conclusion, we report a case of extranodal RDD with simultaneous involvement of the brain, paranasal sinus, and larynx. When encountering dura-based intracranial mass lesions, the sinonasal, subglottic, and tracheal areas (even neck lymph nodes) should be examined. Likewise, when encountering smooth polypoid mass lesions in the subglottic area, the sinonasal and intracranial areas should be further surveyed. Management for extranodal RDD with intracranial, sinonasal, and laryngeal involvement may benefit from a combination of surgical resection, radiosurgery, and steroids.

Author Contributions

Conception and design of study (CC Chen, CC Hsieh, SN Pei, CF Lien); Acquisition of data (CC Hsieh, YD Tsai, SN Pei, CF Lien); Drafting the manuscript (CC Chen, SN Pei, CF Lien); Approval of the version of the manuscript (CC Chen, CC Hsieh, YD Tsai, SN Pei, CF Lien).

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Data Availability Statement

Not applicable.

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Conflicts of Interest

The authors declare no conflict of interest.

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