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CASE REPORT

Rosai-Dorfman disease presenting as laryngeal masses

Larenks kitleleri olarak kendini gösteren Rosai-Dorfman hastalığı

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Extranodal lesions may be the sole manifestation of Rosai-Dorfman disease (RDD). Although the head and neck region is one of the most common extranodal sites, laryngeal involvement is very rare. A 44-year-old woman presented with a complaint of progressive dyspnea. She had a three-year history of treatment for asthma and a history of operation for a nasal mass that afflicted her for 15 years and was diagnosed as rhinoscleroma. On physical examination, she had three subcutaneous lesions, in the left lower eyelid, right epicanthal area, and left forearm, respectively. No lymphadenopathy was present. Laryngoscopic examination revealed three solid, polypoid masses in the subglottic region, 1 cm in diameter. With a two-staged operation, the laryngeal masses were excised totally together with the subcutaneous lesions. Histological examination of all the specimens showed proliferation of histiocytes. Immunohistochemical staining revealed typical S-100 protein-positive histiocytes and emperipolesis. Both laryngeal and subcutaneous lesions were diagnosed as RDD. A re-evaluation of sections from the previous operation specimen of the nasal mass showed the same morphological features. The patient was healthy without recurrence, nine months following surgery.

Key Words: Diagnosis, differential; histiocytosis, sinus/pathology; laryngeal diseases/pathology.

Ekstranodal lezyonlar Rosai-Dorfman hastalığının (RDH) tek bulgusu olabilir. Baş-boyun bölgesi RDH'de en sık tutulan bölgelerden biri olmasına karşın, hastalığın larengeal tutulumu çok nadirdir. Kırk dört yaşında bir kadın hasta ilerleyici nefes darlığı yakınmasıyla başvurdu. Öyküsünden, astım için üç yıldır tedavi gördüğü ve kendisini 15 yıldır etkileyen bir burun kitlesi nedeniyle ameliyat geçirdiği, bu lezyona da rinoskleroma tanısı konduğu öğrenildi. Fizik muayenede, sol alt gözkapağında, sağ epikantal bölgede ve sol önkolda üç adet subkutan lezyon görüldü. Lenfadenopatiye rastlanmadı. Larengoskopik incelemede, subglottik bölgede, 1 cm çapında üç adet solid polipoid kitle gözlendi. Larenksteki kitleler ve subkutan lezyonlar iki aşamalı bir ameliyatla çıkarıldı. Histolojik incelemede örneklerin hepsinde histiosit proliferasyonu görüldü. İmmünhistokimyasal boyamada tipik S-100 proteini için pozitiflik gösteren histiositler ve emperipolez gözlendi. Larenks kitleleri ve subkutan lezyonların tanısı RDH şeklinde kondu. Hastanın daha önce geçirmiş olduğu ameliyatta çıkarılan burun kitlesine ait kesitlerin yeniden incelenmesi aynı morfolojik özellikleri gösterdi. Ameliyattan dokuz ay sonra hasta sağlıklıydı ve nüks yoktu.

Anahtar Sözcükler: Tanı, ayırıcı; histiositozis, sinüs/patoloji; larenks hastalıkları.

Rosai-Dorfman disease (RDD) is a histiocytic proliferative disorder of unknown origin that was first described by Rosai and Dorfman. "Sinus histiocytosis with massive lymphadenopathy" is the eponymous of RDD because it is classically characterized by painless cervical lymphadenopathy. However, in

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about one-third of cases, RDD may present extranodal manifestations. The head and neck region is one of the most frequent localizations of extranodal involvement; the most common sites being the nasal cavity, paranasal sinuses, orbit, eyelids, skin, and upper respiratory tract.[1-4] Laryngeal involvement has been reported in only 14 cases in the literature, and among these, presenting symptoms due to a laryngeal mass are even rarer.[1-3,5-9]

We herein described an unusual case of RDD that involved the subglottic region of the larynx and clinically presented as an occlusive laryngeal mass.

CASE REPORT

A 44-year-old woman with a three-year history of treatment for asthma presented to our clinic with a complaint of progressive dyspnea. She also had a history of a solitary cervical mass excision at another hospital 15 years before, which was diagnosed as benign reactive lymphadenopathy. She had been suffering from nasal obstruction for the past 15 years, for which she underwent surgery at an outside hospital six months before, and the excisional biopsy of the nasal mass was interpreted as consistent with rhinoscleroma, although gram-negative bacterium, *Klebsiella rhinoscleromatis,* was not identified by the Giemsa stain.

On physical examination, she had three subcutaneous lesions, each 0.5 to 1 cm in diameter, in the left lower eyelid, right epicanthal area, and left forearm, respectively. They were pale, firm, mobile, and nontender. No lymphadenopathy was present. Laryngoscopic examination revealed three solid, round-oval, polypoid laryngeal masses, circumferentially localized in the subglottic region of the larynx, each 1 cm in diameter (Fig. 1). Laryngeal mucosa covering the lesions was intact without ulceration. Routine laboratory work-up of the patient showed an elevated erythrocyte sedimentation rate (31 mm/hr) and increased lipid values. Hypergammaglobulinemia was detected. IgG values were slightly increased; other immunoglobulins and protein electrophoresis were normal. Computed tomography (CT) of the larynx showed one subglottic mass lying anteriorly and two bilateral masses inferior to this, all narrowing the laryngeal lumen (Fig. 2). Abdominal ultrasonography, thorax and cranial CT images, and technetium-99 bone scans showed normal findings.

A tracheotomy was needed for excision of the laryngeal masses. A staged operation was planned and three submucosal masses were excised totally at two stages interspersed with four months. Operation field was cauterized afterwards with silver nitrate ($AgNO_3$). There was no cartilage involvement. Bilateral vocal cord edema which developed intraoperatively following cauterization disappeared at the postoperative sixth hour. The subcutaneous lesions in the left lower eyelid and right epicanthal area, which were suspected to be related with the laryngeal masses were also excised. The patient was decannulated 24 hours following operation without

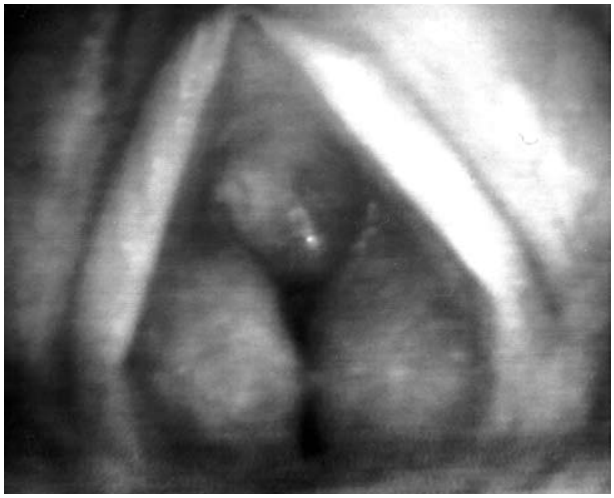

Fig. 1. *Videolaryngoscopic view of the larynx showing subglottic masses.*

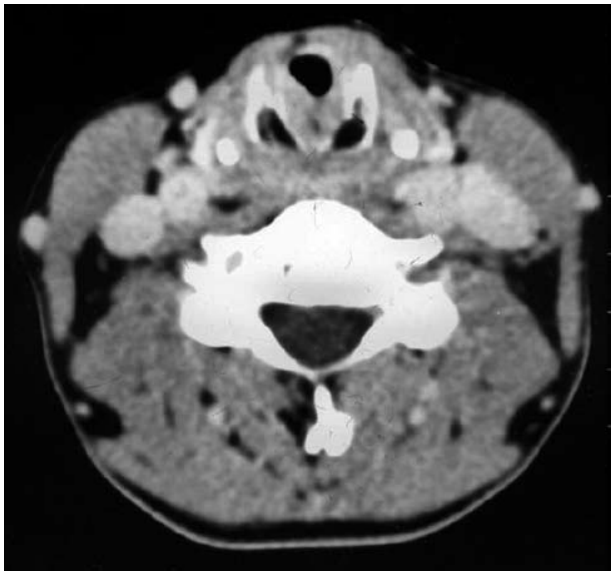

Fig. 2. *Axial tomographic scan of the larynx showing uniformly dense soft tissue masses at the subglottic level.*

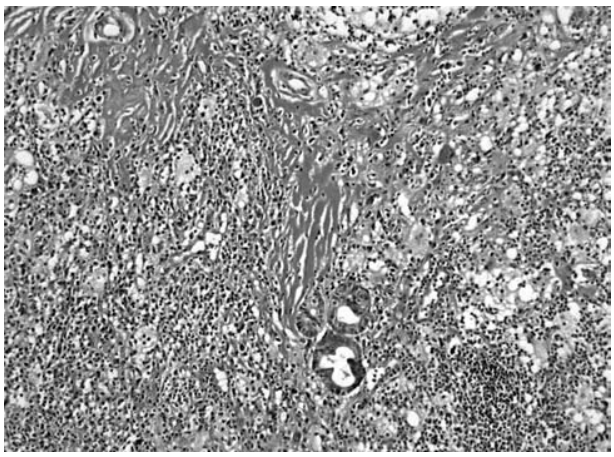

Fig. 3. *Proliferation of histiocytic cells in the background of abundant plasma cells and lymphocytes. Residual laryngeal glands are observed in the center (H-E x 50).*

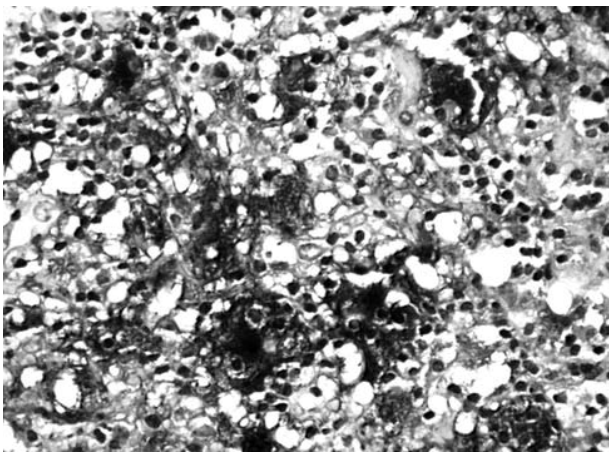

Fig. 4. *S-100 positive histiocytes showing emperipolesis (S-100 x 200).*

any complications. The patient was healthy without recurrence, nine months following excision.

Macroscopically, the laryngeal biopsy specimen consisted of multiple gray-white tissue fragments and two nodular specimens partially covered by mucosa, measuring 9 mm in diameter. Biopsy specimens of the two subcutaneous lesions were 18 mm and 7 mm in diameter, respectively, and had a yellow-white cut surface. Histological examination of the larynx specimens by hematoxylin-eosin showed a cellular proliferation composed of a mixture of histiocytes, lymphocytes, and plasma cells (Fig. 3). Scattered multinucleated cells and neutrophils were also present. This cellular infiltration was observed beneath the epithelium involving the whole thickness of the subepithelial tissue. Granuloma formation was not identified. Histiocytic cells were easily identified and characterized by round to oval vesicular nuclei and abundant eosinophilic to clear cytoplasm. However, cellular borders of histiocytes were not well defined and cellular pleomorphism was not observed. Immunohistochemical staining revealed the typical S-100 protein-positive histiocytes and also facilitated the observation of emperipolesis (Fig. 4). The histiocytes were negative for CD1a and histochemical stains for bacterial, mycobacterial, and fungal microorganisms were also negative. Similar histological findings were observed for subcutaneous lesions. Both laryngeal and subcutaneous lesions were diagnosed as RDD. We also examined the hematoxylin-eosin stained sections from the previous operation specimen of the nasal mass and found the same morphological features. We did not have the chance to review the slides of the lymph node specimen.

DISCUSSION

Rosai-Dorfman disease is a clinicopathological entity usually seen in children and young adults.[10] The disease may present only nodal involvement as a cervical mass or may only exhibit extranodal involvement. The head and neck region is one of the most common extranodal sites. In the literature, 30% to 43% of the cases show extranodal head and neck involvement. The most common sites of involvement in this region in decreasing frequency include the nasal cavity, paranasal sinuses, orbit, eyelids, skin, upper respiratory tract, salivary glands, oral cavity and cranium.[1-3,11-13] In RDD of the head and neck region, clinical findings may consist of nasal obstruction, epistaxis, exophthalmos, ptosis, stridor or dyspnea, depending upon the involvement site. Patients with multiple sites of involvement may present with overlapping signs and symptoms.[1,5,8] Common systemic manifestations of the disease include fever, leucocytosis, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia. In extranodal cases, immune dysfunction may be seen; thus, it is suggested that patients with extranodal disease have a diagnostic work-up for immune abnormalities.[1,13-16]

Laryngeal involvement has been described in only 14 patients in the literature.[1-3,5-9] The ages of the patients with laryngeal involvement varied from 8 to 81 years, with males outnumbering females (10:4). Subglottic involvement was the most common (6 cases),[2,3,5-8] although glottic (4 cases),[1,9] and supra-

glottic (1 case),[1,5] lesions were also defined. In three cases, involvement was at more than one laryngeal site.[1,5] Only one case had isolated laryngeal involvement.[9] Eleven patients had associated lymphadenopathy, and 12 patients had extranodal involvement, most commonly being in the nasal cavity, as in the present case. Due to the rarity of laryngeal form of the disease, clinicians do not suspect RDD. In the presence of submucosal multiple masses particularly in the subglottic area, RDD should be considered in the differential diagnosis. A prolonged clinical history, associated lymphadenopathy or a history of lymph node excision, as in the present case, should raise the suspicion of laryngeal RDD.

The characteristic histopathological feature of the disease is proliferation of histiocytic cells that manifest emperipolesis in the background of abundant plasma cells and lymphocytes.[1,8,11,12,14] Some multinucleated cells and neutrophils may also be observed. Despite this rather characteristic histological appearance, diagnosis of the disease may present difficulties at extranodal sites. As in this case, RDD may be misdiagnosed as rhinoscleroma; however, lack of emperipolesis and documentation of the microorganism by silver and Giemsa stains in rhinoscleroma are helpful in the differential diagnosis. Rosai-Dorfman disease can also be misinterpreted as Wegener's granulomatosis, eosinophilic granuloma or Hodgkin's disease, although well formed granulomas, vasculitis, CD-1a positive Langerhans cells and Reed-Sternberg cells are absent in RDD.[14,16] The diagnostic problem at extranodal sites is partly due to the fact that RDD is generally expected as a lymph node disease and, in the absence of a diagnostic lymph node, it is not considered in the differential diagnosis. An additional problem at extranodal sites is the relative paucity of histiocytes showing emperipolesis.[1] We feel that S-100 protein immunohistochemical staining is particularly helpful in demonstrating the cytoplasmic borders of the histiocytes and the lymphocytes within.

The disease generally has a long-term clinical course characterized by exacerbations and remissions. The treatment protocol should be altered according to the clinical presentation. Rosai-Dorfman disease usually has a self-limiting course, but in cases with organ dysfunction or mechanical obstruction, surgical resection of the mass might be necessary. In the literature, all masses located in the larynx were treated by surgical or CO_2 laser excision because of mechanical obstruction caused by the lesions, except for one case in which laryngectomy was necessary due to organ dysfunction. No recurrences were observed at laryngeal involvement sites, although follow-up time was short and variable in the reported cases.[1-3,5-9] Besides surgery, adjuvant therapies (systemic chemotherapy or radiotherapy) were used in RDD, but their efficacy was limited to case reports.[3,16] Vinca alkaloids, alkylating agents (vinblastine sulfate, chlorambucil, cyclophosphamide), and corticosteroids may be of therapeutic value.

Since RDD is a rare clinicopathological entity, the diagnosis could only be made with suspicion of the disease in extranodal cases. Ear-throat-nose examination of the patient should be performed carefully and, in the presence of submucosal multiple masses particularly in the subglottic area, RDD should be considered in the differential diagnosis. On histopathologic examination, emperipolesis in S-100 positive histiocytes will enable the diagnosis. Although the disease generally has a benign clinical course, surgical intervention due to mechanical obstruction may be necessary.

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