Rosai-Dorfman as a clinical mimicker of relapsing polychondritis

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INTRODUCTION

Rosai-Dorfman disease is an uncommon non–Langerhans cell histiocytosis. Typical Rosai-Dorfman disease presents with bilateral cervical lymphadenopathy, fever, anemia, and polyclonal hypergammaglobulinemia. Extranodal disease has been reported in 43% of cases, with the skin involved in 10% of such cases.1 We describe an unusual instance of Rosai-Dorfman disease presenting with bilateral ear nodules and airway involvement, mimicking relapsing polychondritis.

CASE REPORT

A 49-year-old woman presented with a 2-year history of pain and swelling of the cartilaginous portion of the ears, swelling of the nasal bridge, and dyspnea. Medications included oral methotrexate 20 mg weekly and mycophenolate mofetil 1 g twice daily for presumed relapsing polychondritis. Examination was notable for bilateral swelling of the ear helices, with overlying red-brown nodules, nasal bridge swelling, and mild stridor (Fig 1). Because of the unusual clinical presentation, a punch biopsy from an ear nodule was obtained, which showed a nodular to diffuse infiltrate of vacuolated S100-positive histiocytes demonstrating emperipolesis with admixed lymphocytes and plasma cells (Fig 2). Stain results for mycobacteria, fungi, and bacteria were negative. Thus, a diagnosis of Rosai-Dorfman disease was rendered. Given the patient’s radiographic findings and respiratory symptoms, a systemic evaluation was pursued. Positron emission tomography—computed tomography demonstrated low-level hypermetabolism of the ears, as well as of pleural-based nodules, periaortic soft tissues, and the right side of the maxillary sinus, suspicious for additional sites of disease involvement. The patient underwent removal of a subglottic nodule of Rosai-Dorfman disease partially obstructing her airway, with significant improvement of her symptoms.
breathing and resolution of inspiratory stridor (Fig 3). In considering further treatment, the UCSF 500 Cancer Gene Panel was completed to assess for any targetable mutations; this was unrevealing. Mycophenolate was discontinued and methotrexate was increased to 25 mg subcutaneous weekly, with resultant decreased swelling of the nasal bridge and pinnae.

DISCUSSION

Although this patient initially presented for further treatment recommendations for a working diagnosis of recalcitrant relapsing polychondritis, the unusual ear morphology of red-brown nodules allowed flexibility in diagnostic reasoning. The differential diagnosis was expanded to include other inflammatory and infiltrative conditions such as sarcoidosis and granulomatosis with polyangiitis; atypical infections such as leprosy, syphilis, tuberculosis, nontuberculous mycobacteria, and deep fungal infections; and neoplastic disease such as leukemia cutis and lymphoma.

Two systems of diagnostic criteria can be used to diagnose relapsing polychondritis.2 The McAdam criteria require 3 or more of the following clinical features: bilateral auricular chondritis, nonerosive, seronegative inflammatory polyarthritis, nasal chondritis, ocular inflammation, respiratory tract chondritis, or cochlear or vestibular dysfunction. Tissue biopsy is recommended if the diagnosis is unclear. The Damiani or modified criteria require all of the following: at least 3 McAdam diagnostic criteria; 1 or more of McAdam clinical criteria, with positive histologic confirmation; and chondritis at 2 or more separate anatomic locations, with a response to glucocorticoids, dapsone, or both. This patient’s cutaneous morphology was not classic for chondritis alone; therefore, a diagnostic skin biopsy was performed, confirming an alternative diagnosis of Rosai-Dorfman disease.

Rosai-Dorfman disease is a rare non–Langerhans cell histiocytosis that classically presents as massive, bilateral, painless cervical lymphadenopathy with or without systemic symptoms.1 Extranodal disease can involve virtually any organ system, including the skin, central nervous system, nasal cavity and

Fig 2. Punch biopsy from right ear. A, A nodular to diffuse infiltrate of histiocytes, lymphocytes, and plasma cells that spanned the entire dermis and extended into the subcutis. B, Pale-staining histiocytes with vacuolated cytoplasm, some with emperipolesis, with admixed lymphocytes and plasma cells. (A and B, Hematoxylin-eosin stain; original magnifications: A, ×2; B, ×40.)

Fig 3. Preoperative laryngoscopy revealing right-sided subglottic nodule (star) and posterior subglottic narrowing (arrows).
Sinuses, gastrointestinal tract, lungs, kidneys, bones, and genitourinary tract. Histopathology reveals infiltration of large pale histiocytes, often with intact intracytoplasmic lymphocytes, or emperipolesis. Emperipolesis is helpful in diagnosing Rosai-Dorfman disease, but not pathognomonic because it can be observed in other conditions such as Erdheim-Chester disease, juvenile xanthogranuloma, and malignant histiocytosis. Rosai-Dorfman disease histiocytes are thought to arise from circulating monocytes rather than tissue-resident macrophages or dendritic cells and display an inflammatory phenotype with constitutive expression of macrophage colony-stimulating factor receptor and the cytokines tumor necrosis factor α, interleukin 1β, and interleukin 6. Various disease states have been associated with Rosai-Dorfman disease, including viral infections such as Epstein-Barr virus, cytomegalovirus, and HIV; hematologic malignancies; autoimmunity; and other forms of immunologic dysfunction. However, a true correlation has not been demonstrated. Results for autoimmune, malignancy, and infectious disease evaluation for our patient were negative.

The prognosis of Rosai-Dorfman disease is not well characterized, but spontaneous remission after a prolonged clinical course often occurs. Patients with multifocal disease, vital organ involvement, or massive tumors with organ compression tend to have a less favorable prognosis. Given the rarity of the disease, a standardized treatment approach is not defined. Treatments range from observation, to systemic treatments with steroids, immunosuppressants, or chemotherapy, to surgical intervention. Recent reports have found a subset of Rosai-Dorfman disease patients with mutations in NRAS, KRAS, PIK3CA, and MAP2K1, offering the potential for targeted therapies. One patient with Rosai-Dorfman disease demonstrating an activating mutation of KRAS was successfully treated with the mitogen-activated protein kinase/extracellular signal-regulated kinase inhibitor cobimetinib. Unfortunately, a targetable mutation was not identified in our patient, and we continue to suppress her disease with methotrexate, with plans for further debulking procedures as needed.

We describe an unusual presentation of Rosai-Dorfman disease with bilateral red-brown nodules of the ear and airway involvement, with likely involvement of the sinuses, nose, pleura, and periaortic tissues as well. We found 3 case reports of similar patients with Rosai-Dorfman disease presenting with multinodular swelling of the pinnae. Like that of our patient, all 3 of these cases were notable for an unusual presentation of “cauliflower ear deformity” of unclear etiology. Two of these patients presented with unilateral ear involvement and 1 had bilateral involvement. Only 1 patient had evidence of extracutaneous disease manifested as lymphadenopathy on computed tomographic scan, but the extent of systemic evaluation was variable among the cases. All 3 patients underwent surgery, with 1 patient undergoing excision of the dermal nodules and 2 undergoing auriculectomy with prosthetic ear placement. In summary, Rosai-Dorfman disease should be included in the differential diagnosis of dermal nodules of the pinna. This case highlights the value of divergent morphology in dermatology; specifically, how attention to an unusual morphology can disrupt the diagnostic script on a case and lead to breakthrough.

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