

# A Case Report of Mikulicz Syndrome

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## ABSTRACT

Mikulicz Syndrome (MS) is a rare chronic condition characterized by the abnormal enlargement of glandular tissue in the head and neck. Patients usually present with enlarged lacrimal and parotid glands. While this can be a benign self-limiting condition, other complex systemic diseases, such as sarcoidosis, may represent other underlying etiologies. We present a case of MS in a patient with a history of Crohn's disease.

## CASE REPORT

### CASE REPORT

A 43 year-old female presented to the oral surgery clinic for evaluation of 2-3 months of right facial swelling (Fig. 1,2) and dysphagia to dry foods. She reported intermittent episodes of facial swelling precipitated by salty food intake and stress, with each occurrence lasting approximately 24 hours. Swelling was non-painful and alleviated by fluid intake. The patient has a two-decade history of Crohn's disease and reported a flare of inflammatory bowel symptoms associated with a 20-pound weight loss concurrent with her oral and facial symptoms. The patient also reported numbness of the skin overlying the right parotid gland.

Physical exam was notable for moderate swelling of the soft tissues in the right parotid region with a fixed appearance of the parotid tail. She was noted to have weakness in the distribution of the right temporal branch of the facial nerve (CN 7).

Final needle aspiration of the parotid gland, performed by the head and neck surgery service without ultrasound guidance, demonstrated granulomatous inflammation and was

negative for microorganisms. The clinical findings of CN 7 and possibly also CN 5 dysfunction prompted further diagnostic imaging workup with skull base MRI with and without gadolinium.

### Imaging Findings

Magnetic resonance imaging (MRI) of the face demonstrated diffuse enlargement of the entire right parotid gland without evidence of focal lesion or nodularity (Fig. 3-6). The gland demonstrated hypointense T2 signal. No inflammatory stranding or infiltration of the soft tissues or fat surrounding the gland. There was mild asymmetric enlargement of the right sublingual gland, also without surrounding inflammatory changes. The contralateral parotid gland, submandibular glands and lacrimal glands appeared normal. There was no evidence of sialolithiasis or dilatation of the parotid duct. Neither ultrasound nor sialography were ordered by the referring surgeon.

No abnormality was noted involving the major divisions of the cranial nerves; specifically, no imaging correlate was identified to explain the patient's CN 5 or 7 dysfunction.

Management and follow-up

Based on a clinical suspicion for Mikulicz disease, the patient underwent parotid tail biopsy for tissue diagnosis. Final pathology revealed a diagnosis of sarcoid (Fig. 7,8). The patient underwent further diagnostic testing. The patient was referred to the rheumatology service at which time the patient reported complete resolution of symptoms and treatment was therefore withheld.

## DISCUSSION

Etiology & Demographics:

Johann Mikulicz first presented Mikulicz Disease (MD) in 1888 at a meeting of the Society for Scientific Medicine in Königsberg. He later published a report of this sentinel case detailing a 42 year-old man with initial symptoms of lacrimal gland swelling followed by submandibular and parotid swelling [1].

Classic symptoms of MD are xerostomia and parotid enlargement. Dry eyes and lacrimal gland enlargement are also commonly reported symptoms. Parotid and lacrimal gland enlargement has been reported with both bilateral and unilateral distribution, in concurrence, or in isolation [2].

MD has been the subject of considerable debate since it was first proposed. Mikulicz believed MD to be a benign chronic condition secondary to a low-grade infection, refusing to accept other explanations for the physical exam findings [1]. Because of later proposed numerous etiologies, Schaffer and Jacobson have suggested that MD is reserved for cases of parotid and/or lacrimal enlargement of unknown etiology and follows a benign course. They suggest that the term Mikulicz syndrome (MS) be used in cases with some other underlying disorder [3].

Napp described the classic symptoms in the setting of numerous diseases including leukemia, lymphoma, atypical lymphomatosis and tuberculosis [4]. Others have described MD as possibly hereditary in etiology. Additional implicated associated infectious and inflammatory diseases have included syphilis and gout [5].

In 1933, Sjogren described histological similarities between MD and Sjogren Syndrome (SS) and suggested that MD was a subtype of SS [6]. Immunohistological differences have since been described, most notably the absence of Sjogren Syndrome-specific SS-A and SS-B antibodies in MD [7]. MD is now considered part of the IgG4-related autoimmune disease spectrum, which can include inflammatory disorders of the pancreas, thyroid gland, pachymeninges, pituitary gland and infundibulum. Cranial nerve involvement has also been described and there is a postulated association with inflammatory pseudotumor [8].

Multiple etiologies account for Mikulicz syndrome that includes Sjogren syndrome, sarcoidosis, lymphoma, and tuberculosis. The incidence of Mikulicz disease and Mikulicz syndrome is unknown but thought to be quite rare. Females are

affected more commonly than males and patients are typically in their middle years. The etiology, risk factors, treatment, and prognosis are dependent on the underlying cause.

Clinical & Imaging Findings:

Classic symptoms of MD are xerostomia and parotid enlargement. Dry eyes and lacrimal gland enlargement are also commonly reported symptoms. Parotid and lacrimal gland enlargement has been reported with both bilateral and unilateral distribution, in concurrence, or in isolation [2]. In our case, the patient's MRI demonstrated diffuse enlargement of the right parotid gland without nodularity or focal lesion. Sialography can demonstrate abnormal ductal architecture with deficient secondary and tertiary ducts and dye pooling in ectatic terminal ducts [9]. Many cases require tissue sampling in order to complete the diagnosis.

Treatment & Prognosis:

MD is treated with corticosteroid therapy in the acute phase. Surgical excision of the affected gland has also been performed. The long-term prognosis of MD is unknown. Among SS patients, the incidence of non-Hodgkin's lymphoma is 43.8 fold higher than in the general population, although these statistics may be in question given the recently elucidated distinction between MD and SS [10].

Sarcoidosis treatment depends on patient symptoms. Most patients (>75%) require only symptomatic therapy with NSAIDs. Approximately 10% need treatment for extrapulmonary disease and 15% are treated for persistent pulmonary disease. Oral prednisone given daily is the mainstay of treatment for people with chronic disease [11].

Differential Diagnoses:

Many diseases can present with the nonspecific symptoms of lacrimal and salivary gland enlargement. Inflammatory diseases such as Sjogren's syndrome, sarcoid, and gout have been reported. Several diseases such as viral infection and chronic sialadenitis can be diagnosed without imaging, whereas others can be diagnosed on imaging alone.

Sarcoidosis usually presents with painless bilateral parotid enlargement. The imaging features of sarcoidosis are nonspecific but can show multiple non-cavitary masses representing enlarged intra-parotid lymph nodes. Alternatively, affected glandular tissue may be diffusely enlarged with homogenous enhancement.

Imaging in Sjogren's syndrome is typically normal early in disease course. Imaging later on typically demonstrates fatty infiltration with sialectasis and calcification. Patients usually present with dry eyes and mouth. CT findings in Sjogren's syndrome are nonspecific; the gland is usually enlarged, containing nodules and cystic areas with fat deposition. On MRI this has a "salt and pepper" or "honeycomb" appearance on T2 weighted images.

Kimura's disease is an immune mediated inflammatory disease with a classic triad of painless subcutaneous masses in the head or neck region, eosinophilia and elevated IgE levels. Salivary gland enlargement may be unilateral or bilateral. CT or MRI demonstrates ill-defined homogeneously enhancing intra-parotid masses and lymphadenopathy, with rare involvement of the submandibular gland, auricle, scalp, orbit and oral mucosa [12, 13]

Parotid gland enlargement can occur in HIV (human immunodeficiency virus) secondary to enlargement of the intra-parotid lymph nodes. Later in the disease course, benign lymphoepithelial lesion (BLEL) cysts develop [14]. The CT and MRI features of BLEL include multiple cystic and solid masses with tonsillar hypertrophy and reactive cervical adenopathy [15].

Malignancy such as leukemia, lymphoma and salivary gland tumors should also be considered. These lesions can demonstrate replacement of glandular tissue with mass like enhancement.

#### CONCLUSION

We report a case of MS in a 43-year-old female that was found to be secondary to sarcoidosis. MD was first described as painless enlargement of the parotid and/or lacrimal glands. The term MD should be reserved for cases that follow a benign course and lack discernible causative etiology. MS should be used in cases caused by some other disorder. The physical exam and imaging findings can present with a variety of diseases including autoimmune, infectious and neoplastic.

Modern immunohistological analysis suggests that MD is part of a spectrum of IgG4-related autoimmune diseases that are associated with end organ manifestations in the abdomen, brain, head and neck.

MD or MS should be considered by neuroradiologists in patients with a clinical history of oral or facial swelling and xerostomia in whom diffuse unilateral or bilateral enlargement of the parotid and/or lacrimal glands is identified, as further clinical and diagnostic testing may be required for definitive diagnosis and treatment.

#### TEACHING POINT

The term Mikulicz Disease should be reserved for cases that follow a benign course and are of unknown etiology. Mikulicz Syndrome should be used in cases with concomitant disorders. Unilateral or bilateral enlargement of the parotid and lacrimal glands on imaging should prompt radiologists to discuss the possibility of these two disease entities.

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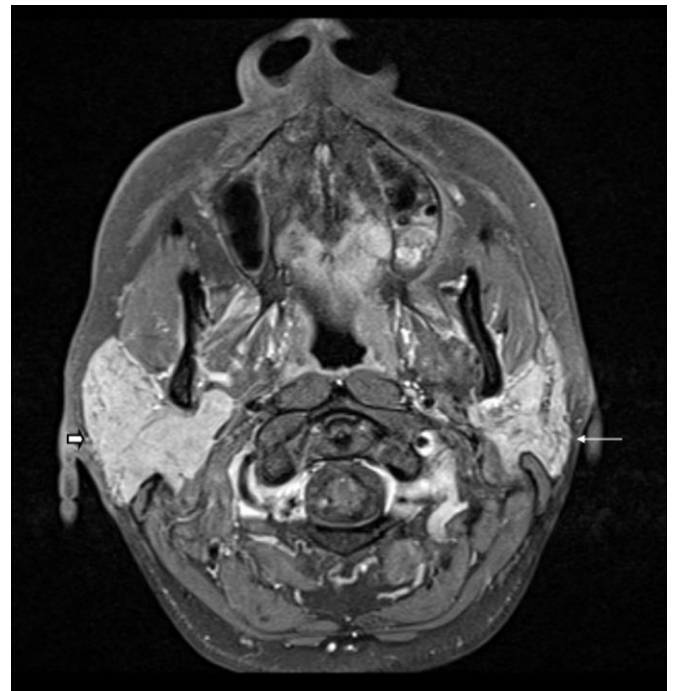
FIGURES



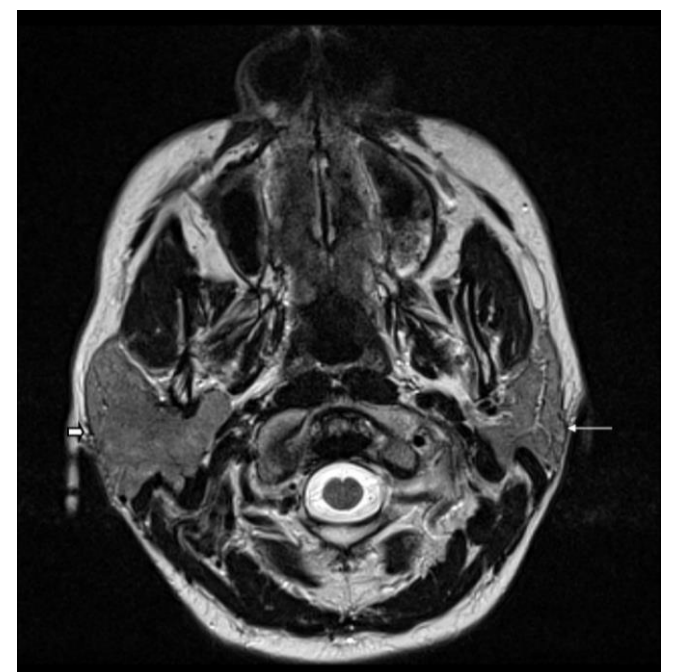
**Figure 1:** A 43-year-old female with Mikulicz Syndrome. Findings: A frontal picture of the patient demonstrates asymmetric facial swelling in the right parotid region (short thick arrow). The left face and parotid region is normal (thin arrow).



**Figure 2:** A 43-year-old female with Mikulicz Syndrome. Findings: A preoperative photo from the operating room demonstrates the right facial and parotid swelling (thick arrow).

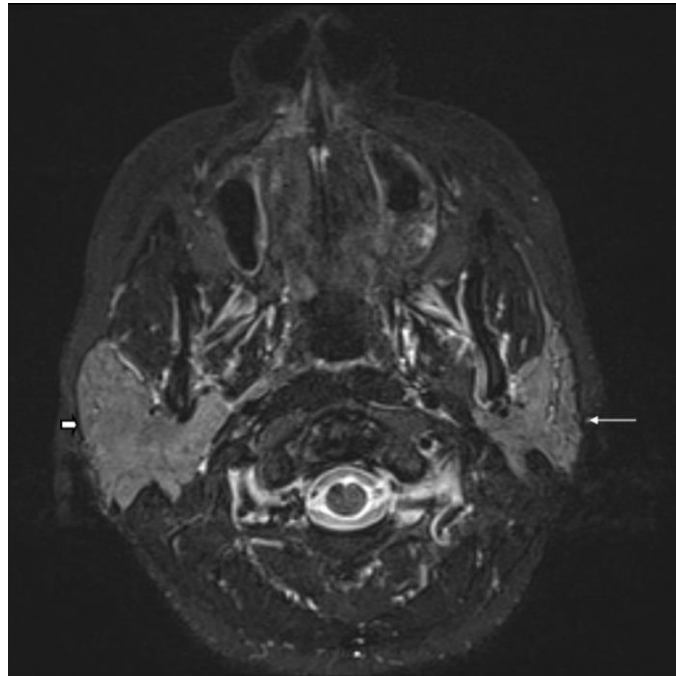


**Figure 3:** A 43-year-old female with Mikulicz Syndrome. Findings: Axial T1 fat saturated sequence with intravenous contrast demonstrating diffuse enlargement of the right parotid gland (thick short arrow) with homogeneous and normal signal intensity in the right parotid gland without a focal parotid lesion. The left parotid gland is normal in size and signal intensity (thin long arrow). Cranial nerves 5 and 7 were unremarkable (not shown). Technique: 1.5 Tesla magnet, Axial T1 fat saturated sequence with intravenous contrast in venous phase, TR 768ms TE 11ms, gadodiamide 11 mL.

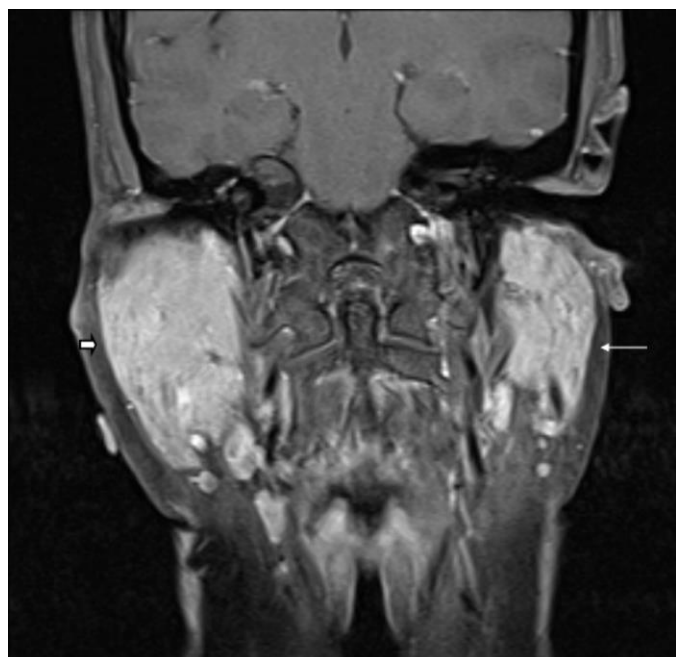


**Figure 4:** A 43-year-old female with Mikulicz Syndrome. Findings: Axial T2 sequence without contrast demonstrating slightly hypointense T2 signal in the right parotid gland with diffuse enlargement of the right parotid gland (thick short arrow).

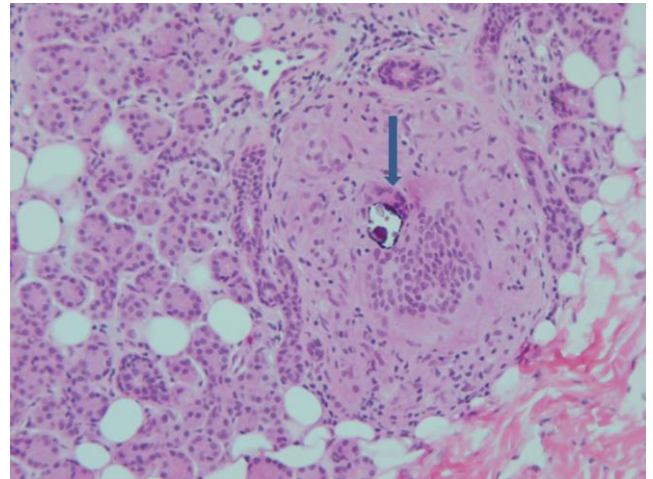
arrow) without a focal parotid lesion. The left parotid gland is normal in size and signal intensity (thin long arrow). Cranial nerves 5 and 7 were unremarkable (not shown).  
 Technique: 1.5 Tesla magnet, Axial T2 sequence without contrast, TR 4340ms TE 113ms.



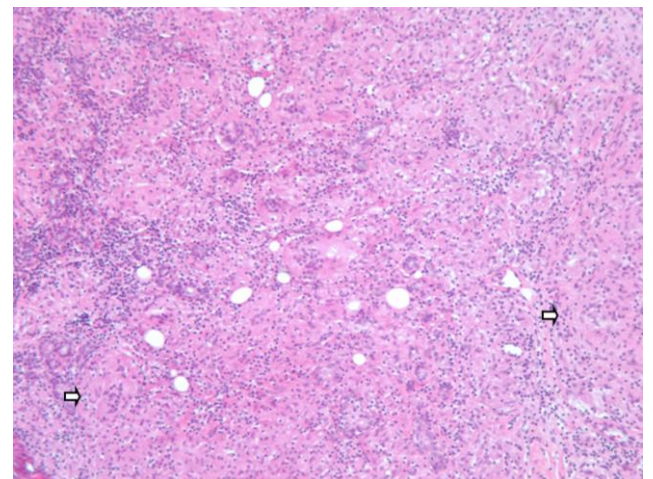
**Figure 5:** A 43-year-old female with Mikulicz Syndrome. Findings: Axial STIR sequence without contrast demonstrating diffuse enlargement of the right parotid gland (thick short arrow) with normal and homogeneous signal intensity without a focal parotid lesion. The left parotid gland is normal in size and signal intensity (thin long arrow). Cranial nerves 5 and 7 were unremarkable (not shown).  
 Technique: 1.5 Tesla magnet, Axial STIR sequence without contrast, TR 5930ms TE 87ms TI 140ms.



**Figure 6 (left):** A 43-year-old female with Mikulicz Syndrome. Findings: Coronal T1 fat saturated sequence with IV contrast demonstrating diffuse enlargement of the right parotid gland (short thick arrow) with homogeneous and normal signal intensity without a focal parotid lesion. The left parotid gland is normal in size and signal intensity (thin long arrow). Cranial nerves 5 and 7 were unremarkable (not shown).  
 Technique: 1.5 Tesla magnet, Coronal T1 fat saturated sequence with IV contrast in venous phase, TR 673ms TE 10ms, gadodiamide 11mL.



**Figure 7:** A 43-year-old female with Mikulicz Syndrome. Findings: Hematoxylin and eosin stained pathology section (50x magnification) demonstrates a multinucleated giant cell of the granuloma with a Schaumann body. Schaumann bodies, although not diagnostic, characterize sarcoidosis and are easily seen in the multinucleated giant cells of the granuloma (arrow).



**Figure 8:** A 43-year-old female with Mikulicz Syndrome. Findings: The hematoxylin and eosin stained pathology section (100x magnification) shows atrophic parotid gland infiltrated sparsely with lymphocytes. Most prominently is the presence of non-necrotizing granulomatosis that are dispersed extensively throughout, predominantly in a micronodular configuration (arrows). Focal confluence of the nodules is evident, which features the sarcoidosis essence of the lesion. Special stains for fungal organisms and mycobacteria were negative (not shown).

**Figure 6 (left):** A 43-year-old female with Mikulicz Syndrome. Findings: Coronal T1 fat saturated sequence with IV contrast demonstrating diffuse enlargement of the right parotid gland (short thick arrow) with homogeneous and normal signal intensity without a focal parotid lesion. The left parotid gland is normal in size and signal intensity (thin long arrow). Cranial nerves 5 and 7 were unremarkable (not shown).  
 Technique: 1.5 Tesla magnet, Coronal T1 fat saturated sequence with IV contrast in venous phase, TR 673ms TE 10ms, gadodiamide 11mL.

<b>Etiology</b>	Multiple including Sjogren Syndrome, Sarcoidosis, Tuberculosis, Lymphoma
<b>Incidence</b>	Unknown
<b>Gender Ratio</b>	Females > Males
<b>Age predilection</b>	Middle years
<b>Classification</b>	Autoimmune
<b>Risk factors</b>	Unknown beyond concomitant disorder
<b>Treatment</b>	Dependent on underlying cause.
<b>Prognosis</b>	Dependent on underlying cause.
<b>Findings on Imaging</b>	Lacrimal or salivary gland swelling, bilateral or unilateral

**Table 1:** Summary table of Mikulicz Syndrome.

<b>Differential Diagnosis</b>	<b>Clinical presentation</b>	<b>CT</b>	<b>MRI</b>
<b>Mikulicz Disease</b>	Parotid and lacrimal gland swelling with xerostomia	Enlargement of bilateral lacrimal and salivary glands with no discrete lesion and homogenous enhancement	Enlargement of bilateral lacrimal and salivary glands with no discrete lesion and homogenous enhancement. Hypointense T2 and Isointense T1 signal of the gland.
<b>Mikulicz Syndrome</b>	Parotid and lacrimal gland swelling with xerostomia	Enlargement of bilateral lacrimal and salivary glands with no discrete lesion and homogenous enhancement	Enlargement of bilateral lacrimal and salivary glands. Specific Imaging features depend on underlying pathology, i.e.: see below
<b>Sarcoid</b>	Painless parotid enlargement usually bilateral	Either multiple noncavitary enlarged intraparotid lymph nodes or diffuse homogenous glandular enlargement	Either multiple noncavitary enlarged intraparotid lymph nodes or diffuse homogenous glandular enlargement
<b>Sjogren's Syndrome</b>	Dry eyes and mouth	Nonspecific; usually enlarged, dense nodules and cysts, calcification	"Salt and pepper" or "honeycomb" appearance (particularly on T2 weighted images) with fat deposition.
<b>Kimura's Disease</b>	Triad of painless subcutaneous masses in head and neck, eosinophilia, and elevated IgE levels.	Ill-defined homogeneously enhancing parotid masses and lymphadenopathy	Ill-defined homogeneously enhancing parotid masses and lymphadenopathy
<b>HIV</b>	Bilateral parotid swelling	Multiple cystic and solid masses in the parotid glands	Multiple cystic and solid masses in the parotid glands
<b>Sialadenitis</b>	Asymmetric salivary gland enlargement and pain	Asymmetric enlargement with or without obstructive stone. Inflammatory stranding. Ductal dilation.	Asymmetric enlargement with or without obstructive stone. Inflammatory stranding. Ductal dilation.
<b>Primary malignancy</b>	Palpable nodule, or asymmetric glandular enlargement with possible weight loss	Discrete lesion with enhancement.	Discrete lesion with enhancement. Isointense T1 and hypo-hyperintense T2 of lesion.

**Table 2:** Differential diagnosis table for Mikulicz Syndrome.

## ABBREVIATIONS

MD = Mikulicz Disease  
MRI = Magnetic Resonance Imaging  
MS = Mikulicz Syndrome

## KEYWORDS

Mikulicz' Disease; Sjögren-Mikulicz syndrome; Sjogren's Syndrome; Immunoglobulin G; Xerostomia; Salivary Gland Diseases

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