Imaging spectrum of Sjögren's syndrome: Glandular manifestations, extraglandular abnormalities, and lymphoproliferative disorders

Poster No.: C-1013
Congress: ECR 2011
Type: Educational Exhibit
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Keywords: Connective tissue disorders, Salivary glands, Head and neck
DOI: 10.1594/ecr2011/C-1013

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Learning objectives

1. To review the clinical features and imaging findings of Sjögren's syndrome.
2. To be familiarized with imaging clues to the diagnosis of various disorders associated with Sjögren's syndrome.
3. To recognize the clinical and imaging characteristics of Mikulicz's disease, which is now considered to be different from Sjögren's syndrome.

Background

A) Introduction [1, 2]

Sjögren's syndrome (SS) is a chronic autoimmune disorder with a distinct predilection for females over 40 years of age. The prevalence of SS in the general population is about 0.5%. In most cases, SS affects the salivary and lacrimal glands as a primary manifestation. The main clinical symptoms are xerostomia (dry mouth) and keratoconjunctivitis sicca (dry eyes) due to impaired glandular function. SS may occur alone (primary SS) or in association with a variety of other connective tissue disorders (secondary SS), most frequently with rheumatoid arthritis.

Two major autoimmune phenomena are observed in SS: periepithelial lymphocytic infiltration of the affected organ and systemic B-cell hyperreactivity. Autoantibodies are commonly detected in SS, of which anti SS-A/Ro and SS-B/La antibodies are relatively disease-specific.

B) Glandular manifestations and diagnostic criteria [1-3]

Xerostomia is a result of diminished saliva production and leads to difficulty in swallowing dry food, changes in the sense of taste, and an increase in oral candidiasis and dental caries. Salivary gland enlargement occurs episodically in many patients. Objective methods for assessing dry mouth include sialometry (measurement of salivary flow rates) and salivary gland imaging such as contrast sialography and salivary scintigraphy.

Keratoconjunctivitis sicca caused by diminished tear production is a characteristic ophthalmological finding in SS. Affected patients usually complain of a sandy or scratchy sensation in their eyes. Objective ways of evaluating dry eyes include Schirmer's test, which measures tear secretion, and Rose-Bengal staining, which assesses conjunctival and corneal epithelial damage.
In 2002, the American-European Consensus Group proposed a new set of classification criteria for SS. Since then, these international classification criteria have been widely used.

1. Ocular symptoms
2. Oral symptoms
3. Objective evidence of ocular involvement
   Schirmer’s test and/or Rose-Bengal score
4. Histopathology
   Minor salivary gland biopsy
5. Objective evidence of salivary gland involvement
   Unstimulated whole salivary flow, parotid sialography, and/or salivary scintigraphy
6. Autoantibodies
   Antibodies to SS-A/SS-B

Diagnosis of primary SS requires four of six criteria, including a positive minor-salivary-gland biopsy sample (item 4) or antibody to SS-A/SS-B (item 6). The presence of any three of four objective criteria (item 3 to 6) is also diagnostic.

C) Extraglandular abnormalities [1, 2, 4]

In addition to the salivary and lacrimal glands, a variety of systemic organs can be affected in SS as a result of either periepithelial lymphocytic invasion or immune-complex mediated processes. The frequency of each extraglandular organ involvement varies widely in the reported literature, partly because of the lack of widely-accepted diagnostic criteria. The commonly affected parts are central/peripheral nervous system, thyroid gland, lungs, gastrointestinal tract, liver, kidneys, vagina, joints, muscles, and skin.

SS patients also present a wide variety of serologic abnormalities including cytopenias and hypergammaglobulinemia.
D) Lymphoproliferative disorders [4, 5]

In SS patients, a broad spectrum of lymphoproliferative disorders may occur both in the exocrine glands and extraglandular sites. The risk of lymphoma in SS patients is 6 to 44 times higher than that in the normal population. The B-cell activation in SS seems to contribute to the development of lymphoma.

Various histological subtypes of non-Hodgkin lymphoma have been described in SS patients. Extranodal marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT) is the predominant histological subtype, followed by diffuse large B-cell lymphoma. MALT lymphoma is usually indolent and remains localized in the affected organ for a long time. However, MALT lymphoma can sometimes progress to high-grade large B-cell lymphoma. The progression from polyclonal to oligoclonal lymphoproliferation, to monoclonal lymphoproliferative disorder, to MALT lymphoma, and finally to high-grade B-cell lymphoma is considered to be a multi-step process.

E) Sjögren’s syndrome vs. Mikulicz’s disease [6, 7]

Mikulicz’s disease (MD) is a disorder clinically characterized by persistent swelling of the salivary and lacrimal glands. Although MD has long been categorized into a subtype of primary SS, there are several clinical and pathological differences between these two entities. The distinct features of MD are as follows:

• Symmetrical and persistent swelling of the exocrine glands
• Mild sicca syndrome
• Good responsiveness to steroid therapy
• No positivity of antibodies to SS-A or SS-B
• Elevated level of serum IgG4
• Prominent infiltration of IgG4-positive plasma cells in the exocrine glands

MD often coexists with other IgG4-related disorders such as autoimmune pancreatitis and retroperitoneal fibrosis. Therefore, MD is now considered to be salivary and lacrimal gland involvement of IgG4-related sclerosing disease. It is important to distinguish MD from SS because the natural history, complications, and response to glucocorticoid therapy are considerably different. Thus, imaging features of MD are also discussed in this presentation.
Chronic sclerosing sialadenitis (Küttner tumor) is a tumorlike fibroinflammatory condition of the submandibular glands. Küttner tumor also appears to be part of IgG4-related sclerosing disease.

**Imaging findings OR Procedure details**

**A) Salivary glands**

A variety of imaging modalities can visualize the affected salivary glands although imaging findings change with the stage of the disease. US, CT and MRI do not directly contribute to the diagnosis of SS according to the international classification criteria (2002); the knowledge of glandular imaging features, however, is valuable both in proper diagnosis and management of SS and related disorders. For instance, the recognition of these typical imaging findings may provide a clue to the proper diagnosis in subclinical SS patients, and the awareness of underlying SS will be helpful in diagnosing coexisting extraglandular abnormalities and lymphoproliferative disorders.

1) **Contrast sialography** [8] (Fig. 1 on page 12)

Contrast sialography has been widely used to directly assess architectural changes in the salivary duct system despite its invasiveness and technical difficulties. The sialographic changes are classified as punctate, globular, cavitary, and destructive dilatation (sialectasia) of the acinar system. Sialectasia slowly worsens with the progression of the disease.

2) **Salivary scintigraphy** [9] (Fig. 2 on page 13)

Salivary scintigraphy using $^{99m}$Tc-pertechnectate can evaluate the function of the salivary glands noninvasively. Salivary gland function is usually classified into four grades based on visual quality of glandular uptake and excretion into the oral cavity after administration of the excretory stimulus, being grade 1 the normalcy and grade 4 the total absence of uptake and excretion.

3) **US** [10] (Fig. 3 on page 14)

US features of the major salivary glands in SS include parenchymal inhomogeneity, hypoechoic foci with hyperechoic bands, cysts, calcifications, and irregular contour of the gland.

Slightly inhomogeneous parenchyma with normal or increased glandular volume can be observed in early stages of SS, while multiple hypoechoic areas with echogenic bands
become evident as the disease progresses. Marked inhomogeneous glands with irregular contour and parenchymal atrophy are characteristic in patients with advanced SS.

4) CT [11, 12] (Fig. 4 on page 15 and fig. 5 on page 16)

Salivary gland enlargement with hyperdense parenchyma relative to the normal glands may be observed on CT in early stages of SS. CT shows increasing areas of fat density in the salivary glands in parallel with the continuation of disease progression, reflecting fat deposition caused by glandular destruction. Diffusely scattered fat density areas or almost complete fatty replacement with parenchymal atrophy is characteristic of the salivary glands in advanced SS. Multiple punctate calcifications or microliths may also be present in advanced cases.

5) MRI [12-15] (Fig. 6 on page 17 and fig. 7 on page 17)

In early stages of SS, glandular enlargement can be demonstrated. As the disease progresses, the salivary glands develop various degrees of fat deposition and lobular destruction, finally resulting in inhomogeneous parenchyma consisted of hypo- and hyperintense areas simultaneously on T1WI (so-called salt-and-pepper appearance). On T2WI with fat suppression, hyperintense spotty cores relative to the remaining gland lobules are also characteristic for SS, which probably represents mononuclear cell aggregations.

Bilateral multiple parotid cysts can rarely occur in SS. These cysts may represent diffuse cystic changes in the benign lymphoepithelial lesions.

Diffusion-weighted MR imaging has revealed that the apparent diffusion coefficients (ADCs) of the parotid glands in SS patients correlate with the severity of gland damage.

MR sialography using a heavily T2-weighted sequence is a promising alternative technique to contrast sialography, although there is a discrepancy in the sialographic findings between these two techniques at later stages of SS.

6) Plain radiographs (Fig. 8 on page 18)

Punctate calcifications in the parotid glands are rarely visualized on radiographs.

Xerostomia may bring on extensive dental caries, which is visible on panoramic radiographs. Radiograph or CT can visualize oral prostheses used to treat caries.

7) Imaging features of MD [16]
The affected salivary glands in MD have fairly characteristic imaging findings, which are quite different from SS. The recognition of imaging characteristic of MD is important for radiologists to avoid misdiagnosis.

• **US (Fig. 9 on page 19)**

Bilateral nodal hypoechoic areas with hypervascularity are seen more dominantly in the submandibular glands than in the parotid glands. Unlike in SS, adjacent gland parenchyma has a normal echo pattern.

• **CT**

CT demonstrates bilateral glandular enlargement although nodal areas on US cannot be distinguished from adjacent normal glandular tissue. Fat deposition or glandular atrophy is an atypical finding in MD.

• **MRI (Fig. 10 on page 20)**

In addition to enlargement of the involved glands, nodal areas on US may be visualized as hypointense masses on T2WI. In some cases, however, the nodal lesions are unclear on MRI.

• **Contrast sialography**

Parenchymal defect can be seen in accordance with nodal areas on US. In contrast to SS, sialogram shows no dilatation of the acinar system in MD.

**B) Lacrimal glands [17, 18] (Fig. 11 on page 21)**

Lacrimal gland hypertrophy can be observed in early stages of SS. As in the salivary glands, volume reduction of the lacrimal glands and parenchymal fat deposition progress with the advancement of the disease. Diffusion-weighted MR imaging has shown that the ADCs of the lacrimal glands in SS patients are significantly lower than those of the normal lacrimal glands.

**C) Extraglandular abnormalities**

Imaging studies can also depict a variety of extraglandular manifestations.

1) **Central nervous system (CNS)**

CNS findings in SS include white matter lesions, aseptic meningitis, optic neuritis, and myelopathy [19].
White matter lesions (Fig. 12 on page 22)

In SS patients, multiple hyperintense lesions, generally smaller and less prominent than those in multiple sclerosis, may be seen in the periventricular and subcortical white matter on T2WI [20]. These lesions may represent gliosis or demyelination.

Hypertrophic pachymeningitis (Fig. 13 on page 23)

Hypertrophic pachymeningitis is characterized by localized or diffuse dural thickening and is associated with various autoimmune/vasculitic, infectious, or neoplastic disorders [21].

Myelopathy (Fig. 14 on page 24)

Extensive spinal cord involvement can be seen in SS patients. Recent studies indicate that myelopathy in SS might be a manifestation of neuromyelitis optica (NMO) [22]. NMO is a CNS demyelinating disease characterized by optic neuritis and myelopathy extending more than three vertebral segments [23]. Serum aquaporin (AQP)-4 autoantibody is highly specific for NMO.

2) Thyroid gland

Autoimmune thyroid disease, especially in the form of Hashimoto’s thyroiditis, seems to be commonly associated with SS [24]. Hypothyroidism is clinically-apparent in 10-15% of SS patients, but subclinical autoimmune thyroid disease may be more frequent.

Hashimoto’s thyroiditis (Fig. 15 on page 24)

Hashimoto’s thyroiditis is characterized by painless diffuse enlargement of the thyroid gland accompanied by thyroid autoantibodies and occasional hypothyroidism. On US the gland is diffusely enlarged and the parenchyma is coarsened and hypoechoic, while symmetrical enlargement and diffusely decreased density of the gland is typical on CT.

3) Lungs

Pulmonary involvement of SS includes interstitial pneumonia and small airway disease (tracheobronchial sicca). Nonspecific interstitial pneumonia (NSIP) appears to be more common than lymphoid interstitial pneumonia (LIP) [25]. SS patients may also develop a wide spectrum of lymphoproliferative disorders of the lung.

Nonspecific interstitial pneumonia (NSIP) (Fig. 16 on page 25)
NSIP is characterized by lower lobe peripherally predominant ground-glass opacity with reticular abnormality and traction bronchiectasis [26].

**Small airway disease** *(Fig. 17 on page 26)*

Bronchiectasis, bronchial or bronchiolar wall thickening, centrilobular branching opacity and nodules can be observed in SS patients [27]. Centrilobular abnormalities mainly reflect follicular bronchiolitis.

**Lymphoid interstitial pneumonia (LIP)** *(Fig. 18 on page 27)*

LIP is histologically characterized by diffuse interstitial infiltration of lymphoid cells, although the distinction between LIP and lymphoproliferative disorder is still controversial. Previously reported CT findings of LIP include ground-glass opacity, centrilobular and subpleural nodules, thickening of the bronchovascular bundle and interlobular septa, and thin-walled cysts [28]. However, CT characteristics of LIP diagnosed by recent criteria have not been well-established. Lower lobe predominant diffuse ground-glass opacity with scattered thin-walled cysts can be seen in some patients [29]. Check valve phenomenon in peripheral airway appears to contribute to cyst formation.

4) **Gastrointestinal tract**

Gastrointestinal manifestations of SS include dysphagia, which may be caused by xerostomia and/or esophageal dysmotility [30]. Chronic atrophic gastritis with lymphocytic infiltration is occasionally seen in SS patients. In the lower gastrointestinal tract, protein-losing enteropathy and celiac disease have been reported to be associated with SS.

**Chronic gastritis** *(Fig. 19 on page 28)*

On double-contrast barium examination, chronic gastritis is characterized by thickened folds, mucosal nodularity, erosions, and enlarged areae gastricae. Increased $^{18}$F-FDG uptake in the stomach can be observed in patients with gastritis [31].

5) **Hepato-biliary-pancreatic system**

Primary biliary cirrhosis (PBC) can occur in SS at times, although pathological changes of the liver appears to be mild with a propensity for slow progression [32]. Autoimmune hepatitis (AIH) has also been reported to be associated with SS [33].

Chronic pancreatitis was once considered to be a common extraglandular manifestation of SS; however, recent recognition of IgG4-related systemic disease suggests that most cases reported as pancreatitis associated with SS were probably cases of IgG4-related disease.
related sclerosing disease, involving both the pancreas (autoimmune pancreatitis) and the salivary/lacrimal glands (MD) [34].

Primary biliary cirrhosis (PBC) (Fig. 20 on page 29)

PBC is an autoimmune hepatic disorder characterized by progressive destruction of the small intrahepatic bile ducts, and resulting cholestasis causes cirrhosis. Antimitochondrial antibodies can be detected in 90% of PBC patients.

CT and MRI demonstrate hepatic cirrhotic changes, extrahepatic findings of portal hypertension, and abdominal lymphadenopathy. Periportal halo sign (halos of low signal intensity around portal venous branches on T1W and T2W images) was reported to be a specific MR sign for PBC [35].

Autoimmune hepatitis (AIH) (Fig. 21 on page 29)

AIH is a chronic autoimmune disease of the liver characterized by the presence of autoantibodies, hyperglobulinemia, and histological findings of periportal inflammation and piecemeal necrosis (interface hepatitis).

Extensive fibrosis and global atrophy of the liver without enlargement of the caudate lobe and/or left lateral segment are common findings on CT and MRI [36].

6) Kidneys

Renal involvement is common in SS and can be primarily attributed to tubulointerstitial nephritis although the patients frequently have minimal clinical symptoms. Laboratory-evident renal dysfunction can be seen in one-fourth of SS patients [37], and some of them present with hypokalemic paralysis, medullary nephrocalcinosis, and/or renal calculi due to distal renal tubular acidosis.

Medullary nephrocalcinosis (Fig. 22 on page 30)

Medullary nephrocalcinosis means radiologically demonstrable deposition of calcium in the renal medulla. On US, the pyramids are echogenic and may have acoustic shadowing. CT clearly shows calcifications in the medulla.

7) Musculoskeletal system

Arthropathy is frequent in SS patients, but arthralgia and arthritis are usually mild and intermittent [38]. Rheumatoid factor is positive in a large number of SS patients, while anti-cyclic citrullinated peptide (CCP) antibodies (highly specific for rheumatoid arthritis) are much less common.
Myalgia and muscle weakness sometimes occur in SS; however, elevations of muscle enzymes are usually mild in inflammatory myopathy associated with primary SS. Polymyositis and inclusion-body myositis have been reported to be associated with SS. Myalgia attributable to fibromyalgia, which is frequently associated with SS, is also common.

**Arthritis (Fig. 23 on page 31)**

Arthritis in SS is typically nonerosive on radiographs. Synovitis, tenosynovitis, bone edema and erosion can be seen on MR, but these imaging findings are nonspecific [39].

**D) Lymphoproliferative disorders**

Malignant lymphoma may arise not only in the exocrine glands but also in diverse nodal and/or extranodal sites in SS patients. The majority of lymphomas associated with SS initially involve the neck organs [40], including:

- **Salivary glands** (Fig. 24 on page 31, fig. 25 on page 32 and fig. 26 on page 33)
- **Ocular adnexa** (Fig. 27 on page 34)
- **Thyroid gland** (Fig. 28 on page 34)
- **Cervical lymph nodes** (Fig. 29 on page 35)

In some cases, lymphoproliferative disease primarily involves the thoracoabdominal organs or lymph nodes. The commonly affected sites are as follows:

- **Thymus** (Fig. 30 on page 35)
- **Lungs** (Fig. 31 on page 36)
- **Heart** (Fig. 32 on page 36)
- **Stomach**
- **Adrenal glands**
- **Lymph nodes** (Fig. 33 on page 37)

Imaging features of lymphoma associated with SS are not substantially different from those in patients without SS [40], although MALT lymphomas (the predominant histopathological subtype) sometimes show characteristic imaging findings in a variety
of organs [41]. The typical imaging feature of MALT lymphoma of the parotid gland (Fig. 24 on page 31 and fig. 25 on page 32) is multiple solid nodules with or without cystic lesions. Cysts are believed to arise from compression of terminal parotid ducts by lymphoid tissue. Thymic MALT lymphoma (Fig. 30 on page 35) is a rare disorder usually associated with autoimmune diseases. A well-demarcated anterior mediastinal mass with multilocular cysts is a typical imaging finding [42]. The imaging findings of pulmonary MALT lymphoma (Fig. 31 on page 36) include nodules, localized areas of consolidation with air bronchogram, and peribronchial infiltrates. CT angiogram sign may be seen within the lesions.

E) Others
Amyloidosis associated with SS, especially in the form of pulmonary nodular amyloidosis, could be sometimes visualized on imaging studies.

Pulmonary amyloidosis (Fig. 34 on page 38)
Pulmonary nodular amyloidosis in SS manifests as multiple irregularly-shaped nodules along with thin-walled cysts, parenchymal opacity, and bronchiectasis [43]. These nodules may contain nodular calcifications and abut cyst walls. Extensive amyloid deposition and lymphoid cell infiltration in the bronchiolar wall seem to cause check valve phenomenon and lead to cyst formation.

Images for this section:
Fig. 1: Contrast sialograms in a 36-year-old woman with Sjögren’s syndrome (case courtesy of Dr. Katsumi Hayakawa, Kyoto City Hospital). (a, b) Frontal parotid sialograms show multiple coalescing collections of contrast material throughout the glands, indicating destructive sialectasia.
**Fig. 2:** Salivary scintigraphic images in a 37-year-old woman with Sjögren's syndrome. Note almost no uptakes in the salivary glands and absence of excretion into the oral cavity, classified as grade 4 functional impairment.
Fig. 3: US images in a 66-year-old woman with Sjögren's syndrome. (a, b) The right parotid gland shows parenchymal inhomogeneity and hypoechoic areas with echogenic bands (yellow arrows). (c, d) The submandibular glands are slightly atrophic with irregular echogenicity (green arrows), suggesting fat deposition.
Fig. 4: CT images in a 66-year-old woman with Sjögren's syndrome (the same patient as in fig. 3). (a) Non-enhanced CT image shows mild fatty infiltration in both parotid glands (yellow arrows). Note that punctate calcifications are also seen in the glands (blue arrows). (b) Non-enhanced CT image shows fat deposition and slight parenchymal atrophy of both submandibular glands (green arrows).
**Fig. 5:** CT images in a 54-year-old woman with Sjögren's syndrome. (a, b) Non-enhanced CT images show diffuse fatty replacement of the salivary glands (yellow and green arrows).

![CT images](image_url)

**Fig. 6:** MR images in a 37-year-old woman with Sjögren's syndrome (the same patient as in fig. 2). Both T1W (a) and T2W (b) images show diffusely increased intensity with several low signal spots (so-called salt-and-pepper appearance) in the parotid glands bilaterally (yellow arrows), indicating parenchymal atrophy and severe fatty infiltration of the parotid glands. T1W (c) and T2W (d) images also demonstrate diffuse atrophy of both submandibular glands with fat deposition (green arrows).

![MR images](image_url)
Fig. 7: MR images in a 63-year-old woman with Sjögren’s syndrome (case courtesy of Dr. Toshihide Yamaoka, Kyoto Katsura Hospital). T2WI (a) and contrast-enhanced T1WI with fat suppression (b) show diffuse cystic changes in the enlarged parotid glands, suggestive of cystic lymphoepithelial lesions. (c, d) MR sialograms of the parotid glands clearly visualize multiple cystic lesions. The Stensen ducts are barely visible (yellow arrows).
Fig. 8: Plain radiograph in a 61-year-old woman with Sjögren's syndrome. Note oral prostheses, suggesting a history of rampant dental caries due to xerostomia.
**Fig. 9:** US images in a 73-year-old man with Mikulicz’s disease (IgG4-related sclerosing disease). (a-d) US images show multiple nodular hypoechoic lesions in the salivary glands, which are more prominent in the submandibular glands (green arrows) than parotid glands (yellow arrows). Note normal echo pattern of adjacent glandular parenchyma.
Fig. 10: MR images in a 73-year-old man with Mikulicz's disease (IgG4-related sclerosing disease) (the same patient as in fig. 9). T1W (a) and T2W (b) images show patchy hypointense lesions in both parotid glands (yellow arrows). T1W (c) and T2W (d) images visualize enlargement of the submandibular glands (green arrows), but nodular masses observed on US (see fig. 9) are unclear.
Fig. 11: MR images in a 65-year-old woman with Sjögren's syndrome. T1WI (a) and contrast-enhanced T1WI with fat suppression (b) show the atrophic lacrimal glands with fat deposition (yellow arrows). Note diffuse dura-arachnoid enhancement (green arrows), which is suggestive of coexisting hypertrophic pachymeningitis (see fig. 13).
Fig. 12: White matter lesions in a 59-year-old woman with Sjögren’s syndrome. (a) FLAIR image shows occipital-predominant hyperintensity in the white matter. The corpus callosum is also involved (yellow arrow). (b, c) T2W images clearly depict a hyperintense lesion in the body of the corpus callosum (green arrows) with splenial atrophy. (d) Contrast-enhanced T1WI shows peripheral enhancement of the lesion (green arrow).
Fig. 13: Hypertrophic pachymeningitis in a 65-year-old woman with Sjögren's syndrome (the same patient as in fig. 11). (a, b) Contrast-enhanced T1W images with fat suppression show diffuse dura-arachnoid enhancement. Note that both parotid glands have coarse nodular internal structure caused by parenchymal atrophy and fatty infiltration (yellow arrows).

Fig. 14: Myelopathy in a 45-year-old woman with Sjögren's syndrome. This patient showed positive results for serum aquaporin (AQP)-4 antibody, suggesting the diagnosis of neuromyelitis optica. (a, b) T2W images show extensive hyperintense intramedullary lesion with cord swelling. Note the atrophic submandibular glands (yellow arrows). (c) Contrast-enhanced T1WI demonstrates enhancement of the lesion (green arrow).
Fig. 15: (a) Hashimoto’s thyroiditis in a 56-year-old woman with Sjögren’s syndrome. US image shows enlargement of the thyroid gland with coarse hypoechoic parenchyma. (b) Hashimoto’s thyroiditis in a 61-year-old woman with Sjögren’s syndrome. Contrast-enhanced CT image demonstrates the slightly enlarged thyroid gland with relatively hypodense parenchyma.
Fig. 16: Nonspecific interstitial pneumonia (NSIP) in a 77-year-old woman with Sjögren’s syndrome. (a, b) High-resolution CT images show subpleural ground-glass opacity with reticulation. Note a subpleural line (yellow arrow). (c) Coronal CT image clearly visualizes peripheral and lower lung zone predominance.
Fig. 17: Small airway disease in a 67-year-old woman with Sjögren's syndrome. (a) High-resolution CT image shows mild bronchiectasis in the right upper lobe (yellow arrows). (b) High-resolution CT image shows mild bronchial wall thickening and small centrilobular nodules (green arrow) in the left lower lobe.
Fig. 18: Lymphoid interstitial pneumonia (LIP) in a 42-year-old man with Sjögren's syndrome. (a, b) High-resolution CT images show thin-walled cystic lesions with centrilobular nodules and interlobular septal thickening (blue arrow). (c) Coronal CT image clearly demonstrates multiple cystic lesions in both lungs.
**Fig. 19:** Chronic gastritis in a 51-year-old woman with Sjögren's syndrome. (a) FDG-PET/CT fused image shows focal FDG uptake in the gastric antrum (yellow arrow). (b) Endoscopic image reveals chronic atrophic gastritis with mild erosions.

**Fig. 20:** Primary biliary cirrhosis (PBC) in a 77-year-old woman with Sjögren's syndrome (the same patient as in fig. 16). (a, b) Contrast-enhanced CT images show cirrhotic liver with minimal ascites around the spleen (yellow arrow).
Fig. 21: Autoimmune hepatitis (AIH) in a 61-year-old woman with Sjögren's syndrome (the same patient as in fig. 15b). (a) Contrast-enhanced CT image (arterial phase) shows an exophytic hepatocellular carcinoma after transarterial embolization therapy (yellow arrows). Note esophageal varices (blue arrow). (b) Contrast-enhanced CT image (portal venous phase) visualizes hepatic deformation and tumor thrombus in the umbilical portion of the left portal vein (green arrow).
Fig. 22: (a, b) Medullary nephrocalcinosis in a 63-year-old woman with Sjögren's syndrome. US image of the right kidney (a) shows echogenic renal pyramids (yellow arrow). Non-enhanced CT image (b) demonstrates faint calcifications in the medulla of both kidneys. (c) Medullary nephrocalcinosis in a 54-year-old woman with Sjögren's syndrome (the same patient as in fig. 5). Coronal non-enhanced CT image shows dense calcifications in the renal medulla.

Fig. 23: Arthritis in a 60-year-old woman with Sjögren's syndrome. (a-c) Contrast-enhanced VIBE images show mild synovial enhancement in the PIP (yellow arrows) and wrist joints (green arrows) bilaterally.
Fig. 24: MALT lymphoma of the left parotid gland in a 66-year-old woman with Sjögren’s syndrome (the same patient as in fig. 3 and 4). (a, b) Contrast-enhanced CT images show a lobulated mass with tiny calcifications in the left parotid gland (yellow arrows). Note mild fatty deposition and punctate calcifications (green arrows) in both parotid glands. (c) US image demonstrates a hypoechoic mass in the left parotid gland (yellow arrow).
Fig. 25: MALT lymphoma of the parotid glands in a 61-year-old man with Sjögren’s syndrome (case courtesy of Dr. Toshihide Yamaoka, Kyoto Katsura Hospital). (a) Contrast-enhanced CT image shows masses with cyst formation in the parotid glands bilaterally (yellow arrows). (b) Contrast-enhanced CT image visualizes the atrophic submandibular glands (blue arrows).

Fig. 26: Diffuse large B-cell lymphoma of the gingiva and right submandibular gland in a 72-year-old woman with Sjögren’s syndrome. (a) Contrast-enhanced CT image shows a right submandibular mass (yellow arrow). Note severe fat deposition in the left
submandibular gland (green arrow). (b) Coronal contrast-enhanced CT image shows a right gingival mass (blue arrow) probably arising from a minor salivary gland.

**Fig. 27:** Orbital MALT lymphoma in a 75-year-old woman with Sjögren's syndrome. (a) Contrast-enhanced CT image shows a homogeneously enhancing mass in the right orbit (green arrows). (b) Coronal contrast-enhanced CT image demonstrates the right optic nerve (yellow arrow) surrounded by the tumor (green arrow).

**Fig. 28:** Diffuse large B-cell lymphoma of the thyroid gland in a 73-year-old man with Sjögren's syndrome. (a, b) Contrast-enhanced CT images show a huge tumor replacing the left thyroid lobe (yellow arrows). Cervical lymphadenopathy is also visualized (green arrow). Note fatty deposition in the left parotid gland (blue arrow). (c) FDG-PET/CT fused image shows intense FDG uptake in the tumor and lymph nodes. (d) T2WI demonstrates
relatively homogenous signal intensity of the tumor for its size. (e) Diffusion-weighted image visualizes the tumor and enlarged lymph node (orange arrow) of hyperintensity.

**Fig. 29:** Diffuse large B-cell lymphoma of the cervical lymph nodes in a 48-year-old man with Sjögren's syndrome. (a, b) T2W images show enlarged right cervical lymph nodes (yellow arrows). Note mild atrophy and fat infiltration of the submandibular glands bilaterally (green arrows).

**Fig. 30:** Thymic MALT lymphoma in a 37-year-old woman with Sjögren's syndrome (the same patient as in fig. 2 and 6). (a, b) Contrast-enhanced CT images show an
anterior mediastinal tumor with multilocular cysts (yellow arrows). (c) MIP PET image demonstrates mild FDG uptake in the tumor (yellow arrow).

**Fig. 31:** Pulmonary MALT lymphoma in a 69-year-old woman with Sjögren's syndrome. (a, b) High-resolution CT images show multiple areas of consolidation with air bronchogram (yellow and green arrow). Thin-walled cystic lesions are also visible (blue arrows). (c) Coronal CT image clearly demonstrates peribronchial location of the right upper lobe lesion (yellow arrow).
Fig. 32: Cardiac diffuse large B-cell lymphoma in a 66-year-old woman with Sjögren's syndrome. Contrast-enhanced short-axis (a) and four-chamber-view (b) CT images (arterial phase) show hypovascular tumors lying in the right and left atrioventricular groove (yellow arrows). The right coronary artery (blue arrows) and left circumflex coronary artery (orange arrows) run through the tumors without luminal narrowing. (c) Short-axis HASTE image shows the tumors of relatively homogenous signal intensity (yellow arrows). (d) MIP PET image demonstrates intense FDG uptake in the tumors (yellow arrows).
Fig. 33: Polyclonal lymphoproliferative disorder in a 57-year-old woman with Sjögren's syndrome. (a-e) MIP PET image and FDG-PET/CT fused images show FDG uptakes in the left parotid gland (orange arrows), axillary lymph nodes (yellow arrows), common iliac lymph nodes (blue arrows), and external iliac lymph nodes (green arrows). Note fat deposition in the right parotid gland (white arrow).

Fig. 34: Pulmonary nodular amyloidosis in a 40-year-old woman with Sjögren's syndrome (case courtesy of Dr. Norihisa Nitta, Shiga University of Medical Science). (a-c) High-resolution CT images show multiple well-demarcated nodules (yellow arrows) with adjacent cystic spaces (green arrows).
Conclusion

Recognition of the glandular and extraglandular radiological features is important for the diagnosis of SS, and is helpful in detecting additional abnormalities including malignant lymphoma.

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References


