Usefulness of magnetic resonance sialography in patients with juvenile Sjögren’s syndrome

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Abstract

Objective

Sialography is an important means for evaluating parotid gland damage in patients with Sjögren’s syndrome (SS). However, conventional X-ray sialography is invasive and sometimes difficult to perform and repeat, especially for young patients. Recently, magnetic resonance (MR) sialography has been used in adult SS patients. In this study, we investigated the usefulness of MR sialography for evaluating parotid gland damage in juvenile SS.

Methods

Eight young patients suffering from SS were studied. MR sialography and X-ray sialography were performed simultaneously in the same patients. The images obtained by both methods were assessed with Rubin-Holt staging.

Results

MR sialography detected ductal dilatation in 5 of 8 patients, while it was detected in 7 of 8 patients by X-ray sialography. The stages were the same in 4 patients by both methods. In 3 patients, the stages on X-ray sialography were higher than those on MR sialography; in 1 patient, the stage on MR sialography was higher. The correlation between the stages determined by the 2 methods was 0.85. There were no side effects in MR sialography, whereas 3 patients complained of pain during X-ray sialography.

Conclusion

MR sialography can evaluate Stage II ~ III parotid gland damage in juvenile SS. Although MR sialography cannot detect subtle changes in the duct, it has no side effects and can be performed repeatedly in young patients. We propose that MR sialography be chosen as the first tool for diagnosing and during follow-up of the status of the glands in juvenile SS.

Key words

Sjögren’s syndrome, juvenile, MR sialography, X-ray sialography, side effects.
Introduction

SS is a systemic autoimmune disease characterized by chronic exocrinopathy. In patients with SS, the salivary glands are frequently damaged and patients complain of recurrent parotid glands swelling, decreased saliva flow, dental caries and taste abnormalities. To evaluate the damages to the salivary glands, imaging studies (parotid sialography, computed tomography), functional studies (measurement of the rate of saliva flow, parotid scintigraphy) and pathological studies (biopsy) are used. These examinations play important roles in the diagnostic course and follow-up of SS. Parotid X-ray sialography is most frequently used for imaging studies of the parotid glands, and it is included in the revised version of the European criteria (1) and in the revised Japanese criteria (Table I) (2, 3).

There are only less than 30 reports of juvenile SS and it is called a rare disease; moreover, there is a low frequency of complaints of sicca symptoms in children with SS (4-7). However, we have previously described a series of juvenile patients with lip biopsy-proven SS, some with sialographic changes even if they did not present sicca symptoms (8). Since SS is an insidious and chronic disease, it is important to diagnose these patients in early stages and follow up with them for a long time to understand the mechanism of onset and development of the disease. In this sense, evaluation of sialographic changes of juvenile SS may be important. Although ‘conventional’ X-ray sialography is widely used in diagnosing SS, some patients complain of pain on cannulation of the ducts or on injection of the contrast material. Thus, it is difficult to repeat X-ray sialography, especially in young patients; some non-invasive techniques are therefore required.

Recently, magnetic resonance sialography (MR sialography) has been used mainly in adults to evaluate damage to the parotid glands without the injection of contrast material (9-11). In adult SS patients, MR sialography is as useful as conventional methods to reveal damage to the glands and has no side effects (10). In contrast, as far as we know, there are no reports of the use of MR sialography in juvenile SS. It is interesting and important to determine whether MR sialography is useful in patients with juvenile SS, because as previously reported the salivary glands in pediatric SS patients are always less damaged than those of adult patients (5,7). We thus simultaneously performed MR sialography and conventional X-ray sialography in patients with juvenile SS to investigate whether MR sialography is useful for evaluating damage to the parotid glands in patients of this age.

Material and methods

Patients

8 patients with juvenile SS were examined. The diagnosis of SS was based on the revised Japanese criteria for Sjögren’s syndrome defined by the Japanese Ministry of Health and Welfare (1999) (2, 3). Patient data, including pathological findings of minor salivary glands are listed in Table II; also listed are the concentration of serum immunoglobulin G, titer of anti-nuclear-antibody (ANA), rheumatoid factor (RF), anti Ro/SS-A antibody, and anti La/SS-B antibody and symptoms at onset. ANA was measured by an immuno-fluorescent method with Hep2 cells. RF was measured by turbidimetric immunoassay. Anti-Ro/SS-A antibody and anti-La/SS-B antibody were measured by Ouchterlony double immunodiffusion methods. The grading of pathological findings of lip biopsy specimens is based on Greenspan’s grading (12). The mean age was 16.4 (13 to 20 years) and all patients were female. 5 patients had primary SS and 3 had secondary SS, 1 patient had dermatomyositis and 2 patients had systemic lupus erythematosus (SLE). 1 primary SS patient (patient 2) had recurrent parotid gland swelling and sicca complaints, but other patients had neither.

An informed consent was obtained from all patients.

MR sialography

MR sialography was performed on a 1.5-T MR system (Signa Horizon, GE Medical Systems, Milwaukee, Wis), using the 5-inch phased-array coils. T1
weighted images were obtained for localization of MR sialographic images and volume measurement of the parotid gland. Then MR sialographic images were obtained with a heavily T2-weighted 3D-Fast spin echo sequence as hydrographic imaging. The parameters were as follows: repetition time (TR), 5000 to 6000 msec; echo time (TE), 200 msec; field of view, 140 mm; Sagittal plane; matrix: 512*192 pixels (apparent spatial resolution was increased to 512*384 using Zerofill Interpolation Processing); slice thickness, 1.5 mm; gapless images; number of slices, 20 images. The echo train length was 32 or 64 and correspondingly the acquisition time was 12 min 24 sec or 6 min 12 sec. It does not require contrast material. In all patients, MR sialographic images were sent to an image processing workstation (Advantage Windows 2.0, GE Medical Systems). Maximum intensity projection (MIP) reconstruction was used, and lateral and frontal views were obtained for evaluation. We performed MR sialography before X-ray sialography in all patients.

Table I. Revised Japanese criteria for Sjögren’s syndrome (1999) (from ref. 2).

<table>
<thead>
<tr>
<th>Criteria Name</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histopathology</td>
<td>Positive for at least one of A) or B):</td>
</tr>
<tr>
<td>A)</td>
<td>Focus score ≥ 1 (periductal lymphoid cell infiltration ≥ 50) in a 4 mm² minor salivary gland biopsy;</td>
</tr>
<tr>
<td>B)</td>
<td>Focus score ≥ 1 (periductal lymphoid cell infiltration ≥ 50) in a 4 mm² minor lacrimal gland biopsy.</td>
</tr>
<tr>
<td>Oral Examination</td>
<td>Positive for at least one of A) or B):</td>
</tr>
<tr>
<td>A)</td>
<td>Abnormal findings in sialography ≥ Stage 1 (diffuse punctate shadows of less than 1 mm);</td>
</tr>
<tr>
<td>B)</td>
<td>Decreased salivary secretion (flow rate ≤ 10 ml/10 minutes according to chewing gum test or ≤ 2 gram/2 minutes according to the Saxon test) and decreased salivary function according to salivary scintigraphy.</td>
</tr>
<tr>
<td>Ocular Examination</td>
<td>Positive for at least one of A) or B):</td>
</tr>
<tr>
<td>A)</td>
<td>Schirmer’s test ≤ 5 mm/5 minutes and rose bengal test ≥ 3 according to the van Bijsterveld score;</td>
</tr>
<tr>
<td>B)</td>
<td>Schirmer’s test ≤ 5 mm/5 minutes and positive fluorescein staining test.</td>
</tr>
</tbody>
</table>

4. Serologic Examination

Definition. Positive for at least one of A) or B):

A) Anti-Ro/SS-A antibody;
B) Anti-La/SS-B antibody.

Diagnostic criteria:
Diagnosis of Sjögren’s syndrome can be made when the patient meets at least 2 of the above 4 criteria.

Table II. Profiles of patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Symptoms at onset</th>
<th>Grade of lip biopsy</th>
<th>ANA (1: )</th>
<th>RF (IU/ml)</th>
<th>IgG (mg/dl)</th>
<th>Anti-Ro antibody (1: )</th>
<th>Anti-La antibody (1: )</th>
<th>Other collagen diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>14</td>
<td>erythema</td>
<td>4</td>
<td>&gt; 1280</td>
<td>59</td>
<td>2450</td>
<td>64</td>
<td>32</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>17</td>
<td>recurrent parotid glands swelling</td>
<td>NT 1</td>
<td>&gt; 1280</td>
<td>63</td>
<td>3150</td>
<td>&gt; 256</td>
<td>32</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>13</td>
<td>erythema</td>
<td>4</td>
<td>&gt; 1280</td>
<td>222</td>
<td>2920</td>
<td>16</td>
<td>2</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>15</td>
<td>fever, erythema</td>
<td>2</td>
<td>&gt; 1280</td>
<td>22</td>
<td>1620</td>
<td>&gt; 256</td>
<td>(-)</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>17</td>
<td>hyperγ-globulinemia</td>
<td>4</td>
<td>&gt; 1280</td>
<td>35</td>
<td>2120</td>
<td>64</td>
<td>(-)</td>
<td>none</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>18</td>
<td>muscle weakness</td>
<td>4</td>
<td>&gt; 1280</td>
<td>38.6</td>
<td>2637</td>
<td>(-)</td>
<td>(-)</td>
<td>dermatomyositis</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>17</td>
<td>fever, erythema</td>
<td>4</td>
<td>320</td>
<td>&lt; 11</td>
<td>2490</td>
<td>1</td>
<td>(-)</td>
<td>SLE</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>20</td>
<td>erythema, arthralgia</td>
<td>4</td>
<td>320</td>
<td>&lt; 10</td>
<td>1020</td>
<td>&gt; 256</td>
<td>2</td>
<td>none</td>
</tr>
</tbody>
</table>

Ages shown here are those at the examination.
1 NT: not tested, the stage of previous X-ray sialography was III.
measured with a caliper on the original images. In the diagnosis criteria of SS, finding of Stage I or above are defined positive for sialography.

**Statistical analysis**
The MR sialographic stages and X-ray sialographic stages were compared with Pearson’s correlation coefficient.

**Results**
The staging of the parotid glands of each patient by X-ray sialography and MR sialography are shown in Figure 1. In 7 patients, there were some abnormal findings in the parotid ducts, while 1 patient had normal findings (patient 7). Using X-ray sialography, 2 were classified as Stage I (patients 1, 4), 4 as Stage II (patients 2, 5, 6, 8), and 1 as Stage III (patient 3). In all patients, the right and left parotid glands had same grade of ductal change as determined by MR sialography. 3 patients were classified as Stage 0 (patients 1, 4, 7), 1 as Stage I (patient 8), 2 as Stage II (patients 2, 5), and 2 as Stage III (patients 3, 6). There were no patients classified as Stage IV by either method. For 4 patients (patients 2, 3, 5, 7), the stages determined by MR sialography and X-ray sialography were the same. Among these 4 patients, patient 3 was classified as Stage III by both methods (Fig. 2, a, b), 2 patients (patients 2, 5) were classified as Stage II, and patient 7 as Stage 0. For the remaining patients, the stage determined by X-ray sialography for 3 (patients 1, 4, 8) was higher than that determined by MR sialography, whereas the stage determined by MR sialography was higher in 1 patient (patient 3). For patients 1 and 4, who were classified as Stage I by X-ray sialography, whereas the stage determined by MR sialography was Stage 0. For these patients, there were few high intensity areas on individual source images obtained by MR sialography. For patient 8, whose stage was determined by X-ray sialography to be Stage II, the stage determined by MR sialography was Stage I. For the remaining patient (patient 6), the stage determined by X-ray sialography was Stage II, whereas the stage determined by MR sialography was Stage III. The association between the MR sialographic stage and the X-ray sialographic stage was statistically significant (p=0.005) and Pearson’s correlation coefficient was 0.85 (Fig. 1).

There were no side effects for MR sialography, while 3 of 8 patients complained of pain after X-ray sialography.

**Discussion**
In this study, we investigated the usefulness of MR sialography, a new tool...
for the evaluation of salivary gland damage in juvenile SS. We compared the stages determined from the MR sialographic images with those determined by X-ray sialography, which is used most frequently to evaluate changes in parotid gland damage.

There are 2 possibilities to explain the lower stage of damage on the MR sialographic images compared with the X-ray sialographic images. One is the level of damage to the glands. The damage in these patients was Stage I or Stage II by X-ray sialography, stages that are considered to reflect mild destruction of the glands. These mild changes could be detected more readily by X-ray sialography. Mildly dilated areas of the ducts may be magnified by the injection of the contrast material in the conventional method (9, 10). In contrast, MR sialography does not need contrast material, so ductal changes are never magnified; thus the images obtained by MR sialography show a more “natural” status of parotid glands damage. This may cause negative results on MR sialography when the damage to the parotid glands is mild.

The other possibility is the characteristics of MR sialography. As previously reported, individual MR sialographic source images may be lost when a whole volume is displayed (10, 14). Even though some small high intensity areas may be present in some of the source images, those spots are not detected in the whole MIP images. Thus, whole MIP images were not defined as Stage I.

In patient 6, the stage determined by MR sialography was higher than that determined by X-ray sialography. This discrepancy can be explained by the window setting of MR sialography and the effects of MIP reconstruction in MR sialography (10).

The finding of the present study suggest that the overall sensitivity of MR sialography is less than that of X-ray sialography under the current staging protocol, especially when damages to the gland is subtle. The consideration of individual source images should be discussed when MR sialography is used for the diagnosis of SS.

MR sialography has no adverse effects and none of the patients complained of pain, whereas 3 patients complained of pain in the parotid glands after X-ray sialography. MR sialography also does not require well-trained operators; thus the results are independent of manual skills and highly reproducible (10). MR sialography also has further advantages. It can detect the natural status of the ducts, evaluate both sides of the parotid glands at the same time, it is not contraindicated by infection and it can be used repeatedly in young patients so that the progression of damage to the parotid glands can be followed. This reveals how fast the damage progresses and whether there are individual differences in the progression by follow-up study with MR sialography.

Although MR sialography requires a longer time to obtain images, sometimes it has motion artifacts and is expensive, these technical and economical problems can be resolved in the near future. Thus, despite several problems, we propose that MR sialography may be chosen for the first tool for the evaluation of salivary glands by image analysis in patients with juvenile SS. If the patients have moderate or severe damages in parotid glands (up to Stage II), we may be able to define the damage by only one step and not use invasive technique. In the diagnostic course, X-ray sialography could be performed after MR sialography if patients have less severe damages.

In conclusion, MR sialography is useful for examination of the parotid glands in juvenile SS patients, has no adverse effects and can be repeated in young patients. MR sialography makes it easy to diagnose juvenile SS in some patients that have moderate or severe damages in parotid glands and to follow up the natural disease course in all juvenile patients.

References