Stenosis of the main pancreatic duct in focal form of autoimmune pancreatitis: imaging findings on MR-MRCP and dynamic secretin-enhanced MRCP

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Purpose

Autoimmune pancreatitis is a distinct form of chronic pancreatitis, characterized clinically by frequent presentation with obstructive jaundice with or without a pancreatic mass, histologically by a lymphoplasmacytic infiltrate and fibrosis and therapeutically by a dramatic response to steroids [1]. Although the pathogenesis of AIP remains unclear, an immune-mediated mechanism has been postulated.

This disease typically affects males without a history of alcohol abuse, biliary stone disease, or duodenal wall inflammation. This is supported by the remission of the signs and symptoms related to pancreatic inflammation and the resolution of diagnostic imaging changes after short-term steroid treatment [2-5].

Morphologically AIP has been divided into diffuse and focal form; the first one affects elderly patients and may be misdiagnosed as acute, chronic pancreatitis and lymphoma whereas the focal form is more often associated with obstructive jaundice, abdominal pain, weight loss and must be differentially diagnosed from pancreatic cancer. [6-11] At magnetic resonance, pancreatic imaging findings shows a diffuse or focally enlarged pancreas with hypointense signal of the lesion on T1-weighted images, hyperintense on T2-weighted images and delayed contrast enhancement. [12-18]

The aim of this study was to evaluate the MRI-MRCP findings of focal form of AIP and to describe ductal system involvement at diagnosis and at follow-up.
Methods and Materials

This retrospective study was approved by the investigational review board, and the requirement for informed patient consent was waived. A search of our institution's histopathology, radiology, and medical records for the period between February 2001 and October 2011 revealed 130 patients with AIP. Patient data were included according to the following criteria: (a) clinical diagnosis of AIP based on fulfillment of Italian diagnostic criteria for AIP, (b) histopathologically proved AIP, (c) radiological diagnosis of focal form of PAI and (d) availability of MR examination findings. Exclusion criteria were as follows: (a) there was a lack of available follow-up examination findings because such examinations were performed at other institutions or by using other (not MR) imaging techniques (37 patients), and (b) the diagnosis of the diffuse form of AIP (56 patients).

Thus, the final study population comprised 37 patients with a mean age of 51.8 years (age range, 25-78): 26 men (mean age 52.2 years; age range, 26-78 years) and 11 women (mean age 51.6 years; age range, 25-73 years) (Table 1 on page 5).

All patients underwent contrast material-enhanced MR imaging with MR cholangiopancreatography at diagnosis, after steroid treatment and during the follow-up period (median follow-up period 23.9 months; range 4.1-126.7 months). After the diagnosis was rendered, all patients underwent treatment with high-dose steroid: they received 1 mg per kilogram of body weight for 7-15 days, after which the dose was tapered to 2.5-5.0 mg per week. Steroid treatment was also administered after the first episode of recurrent AIP, whereas after the second episode an immunosuppressive therapy was administered: 2 mg/kg azathioprine per day.

IMAGE ANALYSIS

The MR images were analyzed at a workstation by a radiologist (R.M., 15 year experience in gastrointestinal radiology) who was aware of the diagnosis of AIP. The MR imaging parameters were assessed with qualitative and quantitative image analysis at diagnosis, after steroid treatment, and at follow-up MR imaging.

The qualitative image analysis parameters assessed included:

- Presence of anatomical malformations of the pancreatic ductal system (e.g., pancreas divisum).
- Site (head-uncinate process or body-tail of the pancreas) of pancreatic lesions (Fig. 1 on page 5, Fig. 2 on page 6).
- Signal intensity of the pancreatic parenchyma.
• Contrast enhancement of pancreatic parenchyma during the delayed phase, as compared with the portal venous phase.
• Type of stenosis (complete Fig. 3 on page 8 or thread-like Fig. 4 on page 9) of the MPD.
• Dilation of side branches (Fig. 5 on page 6).
• Presence of the "duct penetrating sign" after administration of secretin (Fig. 6 on page 7).

A second radiologist, who was not involved in the qualitative image analysis, used an electronic caliper to perform quantitative image analysis of the following parameters at a workstation:

• Number of stenoses of the main pancreatic duct (Fig. 7 on page 10).
• Length of the MPD stricture.
• Extent of upstream dilation within the lesion.

MR IMAGING

MR imaging was performed with a 1.5-T MR unit (Magnetom Symphony; Siemens, Erlangen, Germany) by using a four-channel phased array coil. The patients were asked to fast for 4-6 hours before the MR examination and were given 50-150 mL of superparamagnetic iron oxide particles (ferumoxsil, Lumirem; Guerbet, Aulnay-sous-Bois, France) orally just before the examination to prevent the overlap of fluid-containing organs on the MR images.

The MR imaging pulse sequences and parameters used are reported in Table 2. Dynamic contrast-enhanced MR imaging involved a quadriphasic study after the injection of 0.1 mmol of a gadolinium chelate gadobenate dimeglumine (Multi-Hance; Bracco, Milan, Italy) or gadoterate meglumine (Dotarem, Guerbet, Aulnay-sous-Bois, France) per kilogram of body weight, administered at 2.0-2.5 ml/sec by using a power injector (Medrad, Pittsburgh, Pa). Images were obtained before the contrast material administration and during the late arterial pancreatic, portal venous, and delayed phases (35-45, 75-80, and >180 seconds after contrast material administration, respectively).
Images for this section:

Table 1: Focal form of autoimmune pancreatitis: distribution of patients by age.

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**Fig. 1:** Focal form of autoimmune pancreatitis: MR-MRCP features. Axial T2-weighted image with Rapid Acquisition with Relaxation Enhancement (RARE) (TR/TE 1600/100 ms) sequence, shows a focal enlargement in the head of pancreas.

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**Fig. 2:** Focal form of autoimmune pancreatitis: MR-MRCP features. Axial T1-weighted image with Gradient eco (GRE) "in fase" (TR/TE 108/5,1 ms) sequence, shows a focal enlargement localized in the body-tail of pancreas.

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Fig. 5: Focal form of autoimmune pancreatitis: RM-MRCP features. Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show the presence of side branches dilated, localized in the body-tail of pancreas.

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**Fig. 6:** Focal form of autoimmune pancreatitis: RM-MRCP features. a,b: Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show the "duct penetrating sign": a single stenosis is located at the head of the pancreas (a) that undergoes resolution after pharmacological stimulation with secretin (b).

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Fig. 3: Focal form of autoimmune pancreatitis: RM-MRCP features. Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show a complete stenosis of the main pancreatic duct.

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Fig. 4: Focal form of autoimmune pancreatitis: RM-MRCP features. Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show a thread-like stenosis of the main pancreatic duct.

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Fig. 7: Focal form of autoimmune pancreatitis: RM-MRCP features. Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show multiple stenoses of the main pancreatic duct.

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Results

OBSERVATIONS AT DIAGNOSIS

Qualitative image analysis

- **Anatomical malformations of the pancreatic ductal system**: the presence of pancreas divisum was observed in 2/37 (5.4%) patients.
- **Site of pancreatic lesions and signal intensity of the parenchima**: signal intensity abnormalities and focal enlargement of pancreatic parenchyma was localized in the head in 18/37 (48.6%) cases and in the body-tail in 19/37 (51.4%) patients (Table 2 on page 14).
- **Contrast enhancement of pancreatic parenchyma**: the lesion appeared hypointense in T1-weighted images and lightly hyperintense in T2-weighted images in all cases; thus, after contrast fluid administration, the lesion showed poor enhancement during pancreatic phase and delayed contrast enhancement during portal venous and delayed phases.
- **Type of stenosis of the MPD**: MRCP sequences showed a complete stenosis in 30/37 (81%) patients and a thread-like narrowing in 7/37 (19%) cases.
- **Dilation of the side branches**: dilation of side branches was observed in 17/37 (46%) patients, whereas in the remaining 20/37 (54%) patients the caliber of the MPD was normal.
- **"Duct penetrating sign"**: after secretin administration the duct penetrating sign was observed in 15/37 (40.5%) patients.

Quantitative image analysis

- **Number of stenoses of the MPD**: a single stenosis was observed in 27/37 (73%) patients, 2 stenoses in 8/37 (21.6%), 3 in 1/37 (2.7%) and 4 in 1/37 (2.7%) cases.
- **Length of the MPD stricture**: the mean length of the MPD narrowing was 13.5 mm (median 13mm; range 4.5-30 mm).
- **Upstream dilation**: the caliber of the MPD upstream the lesion was 3.9 mm (median 3.7 mm; range 0-7.5 mm).

OBSERVATIONS AFTER STEROID TREATMENT

Qualitative image analysis
Image analysis showed a complete return to the normal size of the gland in 12/37 (32.5%) patients, a reduction/atrophy of the parenchyma in 16/37 (43.2%) patients, a recurrence of the disease in 5/37 (13.5%) cases and finally 4/37 (10.8%) patients underwent surgery (Fig. 8 on page 17).

33 patients were treated with corticosteroid; 21/33 (63.6%) of these showed a normalization of T1-weighted images, whereas only 12/33 (36.4%) patients showed a signal inhomogeneity due to the fibrosis of the parenchyma. After contrast fluid administration 25/33 (75.8%) cases showed a normal vascularization while in 8/33 (24.2%) patients the parenchyma was hypo-vascular.

MRCP images showed a complete resolution of the stricture in 20/33 (60.6%) patients. This result compared with the findings at time of diagnosis was statistically significant (p<0.01) (Fig. 9 on page 18).

In MRCP images we found that 8/37 (21.6%) patients showed a thread-like stenosis, 5/37 (13.5%) a complete stricture and 24/37 (64.9%) showed no narrowing of the MPD. The difference between these values and the findings at time of diagnosis was not statistically significant (Table 3 on page 14).

Dilation of the side branches was observed in only 5/37 (13.5%) patients, showing a reduction statistically significant (p<0.01).

The duct penetrating sign was observed in 7/37 (19%) patients. This data was not statistically significant.

Qualitative imaging findings are summarized in Table 4 on page 15.

Quantitative image analysis

- After steroid treatment the mean number of the stenoses of the MPD was 0.43 (median 0; range 0-3), showing a reduction statistically significant (p<0.01).
- The mean length of the MPD stricture was 3 mm (median 0 mm; range 0-25 mm); again, the difference resulted significant (p<0.01).
- The mean diameter of the upstream dilation of the MPD was 1 mm (median 0 mm; range 0-4.6 mm); this reduction was statistically significant (p<0.01) (Table 5 on page 19).

Quantitative imaging findings are summarized in Table 6 on page 15, Table 7 on page 16.

Eventually we focused on the 13 patients in which at least 1 stenosis remained after steroid treatment. In these patients the mean number of the stenoses of the MPD was 1.23 (median 1; range 1-3), the mean length of the MPD stricture was 8.4 mm (median 8 mm; range 1.5-25 mm) and the mean diameter of the upstream dilation of the MPD
was 3 mm (median 3 mm; range 1,2-4,6 mm). The difference between this data and the findings at time of diagnosis was statistically significant only in the reduction of the length of the stenosis (p=0,018) (Table 8 on page 16, Table 9 on page 17).
Table 2: Prevalence of autoimmune pancreatitis in different locations.

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Table 3: Focal form of autoimmune pancreatitis: variations of the type of stenosis of the MPD between the diagnosis and the post-treatment control.

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<table>
<thead>
<tr>
<th>Patterns</th>
<th>Diagnosis</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Presence divisum of pancreas MPD</td>
<td>2/37 (5,4%)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>2 Complete stenosis of the MPD</td>
<td>30/37 (81%)</td>
<td>5/13 (38,5%)</td>
<td>NS</td>
</tr>
<tr>
<td>3 Thread-like stenosis of the MPD</td>
<td>7/37 (19%)</td>
<td>8/13 (61,5%)</td>
<td>NS</td>
</tr>
<tr>
<td>4 Dilation of the side branches</td>
<td>17/37 (46%)</td>
<td>5/37 (13,5%)</td>
<td>&lt;0,01</td>
</tr>
<tr>
<td>5 Duct penetrating sign</td>
<td>15/37 (40,5%)</td>
<td>7/37 (19%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 4: Focal form of autoimmune pancreatitis: characteristics at diagnosis and at follow-up. Qualitative Analysis

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<table>
<thead>
<tr>
<th>Patterns</th>
<th>Diagnosis</th>
<th>Control</th>
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<tbody>
<tr>
<td>1 Mean number of stenoses of the MPD</td>
<td>1,35</td>
<td>0,43</td>
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<td>2 Mean length of the stricture</td>
<td>13,7 mm</td>
<td>3,0 mm</td>
<td>&lt;0,01</td>
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<tr>
<td>3 Mean caliber of upstream dilation</td>
<td>3,9 mm</td>
<td>1,0 mm</td>
<td>&lt;0,01</td>
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</tbody>
</table>

**Table 6:** Focal form of autoimmune pancreatitis: characteristics at diagnosis and at follow-up. Quantitative Analysis.

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**Table 7:** Focal form of autoimmune pancreatitis: changes in the mean number of stenosis, the mean length of the stenotic tract and the mean caliber of the DPP between the diagnosis and the control post-treatment. Quantitative analysis performed on all patients.

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Table 8: Focal form of autoimmune pancreatitis: characteristics at diagnosis and at follow-up of 13/37 patients in which a narrowing remained. Quantitative Analysis.

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<table>
<thead>
<tr>
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<th>Diagnosis</th>
<th>Control</th>
<th>p-value</th>
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<tbody>
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<td>Mean number of stenoses of the MPD</td>
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<td>1.23</td>
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<td>Mean length of the stricture</td>
<td>14.5 mm</td>
<td>8.4 mm</td>
<td>0.018</td>
</tr>
<tr>
<td>Mean caliber of upstream dilation</td>
<td>4 mm</td>
<td>3 mm</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 9: Focal form of autoimmune pancreatitis: changes in the mean number of stenosis, the mean length of the stenotic tract and the mean caliber of the DPP between the diagnosis and the control post-treatment. Quantitative analysis performed on 13/37 patients in which a narrowing remained.

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Fig. 8: Focal form of autoimmune pancreatitis: MRI characteristics of the reduction of parenchymal volume after steroid therapy. a: axial T2-weighted image, with Half Fourier Single-Shot Turbo Spin Echo (HASTE) (TR/TE 1000/100 ms) sequence shows a local enlargement in the body-tail of pancreas. b: axial T1-weighted image, with Rapid Acquisition with Relaxation Enhancement (RARE) (TR/TE 1600/100 ms) sequence shows the same patient after a short-term steroid treatment.

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Fig. 9: Focal form of autoimmune pancreatitis: RM-MRCP features. a,b: Coronal T2-weighted MRCP image, obtained using Half-Fourier single-shot turbo spin-echo (HASTE) TR/TE #/1100 ms, sequences show a single stenosis of the MPD in the head of the pancreas with upstream dilation and side branches dilated (a); the complete resolution of these alterations after a short-term steroid treatment (b).

Table 5: Focal form of autoimmune pancreatitis: prevalence of normal or dilated side branches at diagnosis and at control post-treatment.

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Conclusion

The focal form of autoimmune pancreatitis is an emerging disease, diagnosed more frequently in response to a request for an in-depth radiological analysis in patients with acute pancreatitis or abdominal pain not well characterized.

All patients in our study showed significant response to steroid treatment, evaluated with the remission of symptoms and improvement or complete resolution of radiological patterns.

MRI, thanks to its elevated high contrast resolution, shows pancreatic abnormalities suggestive of AIP and allows to evaluate the response to treatment and the presence of early recurrence even before the disease is clinically evident.

In conclusion we consider MRI-MRCP an useful technique in the diagnosis, in monitoring response to therapy and evaluation of the presence of relapse of the disease during follow-up period. We find it useful to submit patients with AIP to repeated follow-ups with an interval of at least 6 months.

Finally it represents a problem-solving tool in the differential diagnosis between focal AIP and ductal pancreatic adenocarcinoma.
References


