Gadophrin-2 enhancement of fatty tissue necroses in rabbits – Can improvement of the differential diagnosis between fatty tissue necrosis and edema in acute pancreatitis be achieved?

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Synopsis:
This study aims to determine if Gadophrin-2, a necrosis-specific contrast agent, accumulates in fatty tissue necroses and can help to differentiate fatty tissue necroses from edema in acute pancreatitis. Fatty tissue necroses were induced in nine rabbits by subcutaneous injection of pancreatic enzymes; Gadophrin-2 enhancement was measured by MRI (T1-w FS FLASH). Histopathologically proven necroses showed a distinctive Gadophrin-2 enhancement one and 24 hours post-contrast (SNR 55.4±16.1 and 52.0±16.4). There was a good correlation in size and shape between contrast-enhancing regions and necroses. Therefore, Gadophrin-2 may improve the differential diagnosis between fatty tissue necroses and edema in acute pancreatitis.

Purpose:
Peripancreatic and retroperitoneal fatty tissue necroses are typical characteristics of severe acute pancreatitis. They significantly affect patient mortality and morbidity. Bacterial infection of these fatty tissue necroses is a severe complication of acute pancreatitis and may change the course of treatment. However, diagnosis of peripancreatic fatty tissue necroses by computed tomography (CT) or magnetic resonance imaging (MRI) is still an unsolved problem. Neither contrast-enhanced CT nor MRI after application of the standard contrast agent Gd-DTPA, can differentiate fatty tissue necroses from innocuous fatty tissue edema. Gadophrin-2 (Bis-gadolinium-mesoporphyrin, Schering, Berlin, Germany) is a new necrosis-specific MRI contrast agent belonging to the group of paramagnetic metalloporphyrins whose accumulation in tumor, myocardial, liver, kidney and skeletal muscle necroses has been proven 1-3. Gadophrin-2 accumulation in fatty tissue necroses has not yet been investigated. The aim of this study is to investigate whether Gadophrin-2 also accumulates in fatty tissue necroses and may therefore help to differentiate peripancreatic fatty tissue necroses from edema.

Material and Methods:
Subcutaneous fatty tissue necroses in the region of the neck were induced in nine White New Zealand rabbits by subcutaneous injection of 1ml of a 3% solution of activated pancreatic enzymes (Pancreatin, Sigma-Aldrich, Munich, Germany). MR imaging (1.5T) (Magnetom Vision, Siemens, Erlangen, Germany) was begun 36h after injection of the pancreatic enzymes with the acquisition of unenhanced axial T1-w fat-saturated FLASH sequences (TR 423.0, TE 10.0). Then 50µmol/kg Gadophrin-2 (100mM) were injected intravenously and axial T1-w fat-saturated FLASH sequences (TR 423.0, TE 10.0) were acquired 1h and 24h after the contrast injection. The rabbits were then sacrificed and tissue samples were taken and processed for histologic examination. The contrast enhancing regions on the MR images were correlated with the presence, size, and shape of the fatty tissue necroses in the histopathologic findings. Signal intensities of the normal fatty tissue and the contrast enhanced fatty tissue regions suspected to be necrotic, as well as the standard deviation of the background signal intensity, were measured on the MR images. Mean values, signal to noise ratios (SNR), and contrast to noise ratios (CNR) were calculated and statistically compared (t-test).

Results:
Histopathology showed circumscribed necroses of the subcutaneous fatty tissue similar to autodigestive peripancreatic fatty tissue necroses in acute pancreatitis in all nine rabbits. The necrotic regions had an irregular shape, a size of about 3 x 3 x 3cm³, and were demarcated by inflammatory cells. Fat cells within the necrotic regions were autolysed. Before contrast injection, the histopathologically proven necrotic regions appeared moderately hyperintense on MRI relative to the surrounding normal fatty tissue (mean SNR 47.6±17.9 vs. 7.3±1.5, mean CNR 36.7±12.0) (Fig. 1A). One hour after intravenous injection of Gadophrin-2, the necrotic regions enhanced distinctively on MRI with a striped enhancement pattern, while the surrounding normal fatty tissue enhanced little (mean SNR 65.7±18.9 vs. 9.2±4.0, mean CNR 55.4±16.1) (Fig. 1B). Twenty-four hours after contrast injection, the necrotic regions still were enhanced on MRI, while no contrast enhancement was measured in the normal fatty tissue (mean SNR 57.6±18.8 vs. 6.2±2.6, mean CNR 52.0±16.4) (Fig. 1C). Differences in pre-contrast and post-contrast (1h and 24hrs) SNRs and CNRs of the necrotic regions were significant at the p<0.02 level. The size and shape of the contrast enhanced regions on MRI correlated well with the histopathologically diagnosed necrotic areas.

Conclusion:
The necrosis-specific contrast agent Gadophrin-2 accumulates in autodigestive necroses of the fatty tissue and may therefore help to differentiate fatty tissue necroses from edema in acute pancreatitis. The Gadophrin-2 contrast enhancement pattern in fatty tissue edema must, however, be investigated further.

References: