**Methotrexate as induction of remission therapy for localized manifestations of IgG4-Related Disease.**

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**Objective:**

Medium to high dose glucocorticoids represents the treatment of choice for inducing remission in IgG4-related disease (IgG4-RD) patients. However, clinicians might prefer alternative equally effective drugs in clinical settings where long-term corticosteroids treatment is contraindicated, such as diabetes or osteoporosis. We recently reported the efficacy of methotrexate in maintaining glucocorticoids induced IgG4-RD remission. In the present work we aim to evaluate the efficacy of methotrexate as induction of remission therapy in selected cases of mild and localized IgG4-RD complicated by clinical scenarios that might advice against corticosteroids treatment.

**Methods:**

Five patients with active untreated IgG4-RD were started on oral or subcutaneous methotrexate (up to 15-20 mg/week) without concomitant glucocorticoids. Efficacy of methotrexate in inducing remission was assessed at 6 months by 18F-FDG PET/CT scan and by measuring the IgG4-RD Responder Index (RI) and circulating plasmablasts. Partial response (PR) corresponded to an improvement of the IgG4-RD RI > 2 points. Complete response (CR) corresponded to an IgG4-RD RI score < 3.

**Results:**

All patients were males with a mean age of 67 years (range 53-78). Two had pancreatic involvement; one had lymph node enlargement; one had pancreatic and lymph node involvement; one had pancreatic, aortic, submandibular gland and lymph node involvement. Patients with pancreatic involvement presented with increased serum amylases or abdominal discomfort; none had obstructive jaundice; all had overt diabetes. The mean IgG4-RD RI, serum IgG4 concentration and plasmablasts counts at baseline were 8 (6-15), 483 mg/dL (136-983) and 3336/mL (330-9330/mL), respectively. All patients had increased 18F-FDG uptake on PET/CT scan within the affected organs. After 6 months of methotrexate, Patients 1, 2, and 3 were on CR with improved or normalized PET/CT findings, serum IgG4 and plasmablasts levels. Patient 5 achieved PR, showing improved 18F-FDG-PET/CT findings, normal plasmablasts level, but stable serum IgG4 concentration; after 10 months of methotrexate, persistence of disease activity prompted the introduction of glucocorticoids. Methotrexate was stopped in Patient 4 after 5 months because of nausea and vomiting; at 6 months he showed persistently increased plasmablasts count and 18F-FDG uptake on PET/CT, thus requiring a rescue therapy with glucocorticoids. *(Table 1)*

**Conclusions:**

In localized forms of IgG4-RD with mild manifestations, methotrexate represents a promising alternative strategy for inducing disease remission, especially in the presence of contraindications to glucocorticoids.