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CASE REPORT

IgG4-related systemic disease – a rare indication for multi-visceral transplantation

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Summary

Multivisceral transplantations (MVT) are rarely performed procedures. In this case report, we present a 37-year-old male patient with a large retroperitoneal tumor. After exclusion of malignancy, we performed MVT (distal stomach, liver, pancreas, and small bowel). After a follow-up of 1 year, the patient is in good clinical condition. Histologic examination revealed a chronic sclerosing IgG4-associated disease. Our case shows that MVT can be successfully performed in this rare disease.

Background

Multivisceral transplantations (MVT) are rarely performed procedures with only a few indications [1]. In this report, we describe a MVT performed because of a large, nonmalignant retroperitoneal tumor which later turned out to be a chronic sclerosing IgG4-associated disease.

Case report

A 37-year-old male patient was admitted to our hospital with progressive weight loss of more than 20 kg within 2 months and steady increasing back pain, which had aggravated during 1 year. Furthermore, the patient complained about increasing discomfort and decreased food intake. Total parenteral nutrition was already required for 2 months before admission to our department. Clinically, he showed signs of portal hypertension (ascites and esophaeal varices).

Abdominal CT-scan showed a large tumor in the mesenteric root (Fig. 1) with encasement of the suprarenal inferior vena cava as well as extended portal and mesenteric vein thrombosis. The tumor mass showed liquid areas in the fluoro-18-desoxyglucose-positron emission tomography (FDG-PET), whereby only one had a moderately increased glucose metabolism. CA 19-9 was negative.

We decided to perform an explorative laparotomy for suspected malignant tumor. Hereby, we confirmed the large tumor mass. As a result of infiltration of the inferior vena cava and extensive mesenteric and portal vein thrombosis, the tumor was considered to be technically not resectable. We took several biopsies from different

locations of the tumor. Hereby, a retroperitoneal fibrosis, the so-called Morbus Ormond, was diagnosed. A leiomyoma was ruled out by anti-smooth muscle antibodies (ASMA) staining. Furthermore, the histologic examination of several biopsies ruled out a malignant disease.

We started a treatment with corticosteroids, but because of the large (nonmalignant) tumor, the patient's condition deteriorated further, especially because of treatment-refractory back pain (despite elaborate pain management) and progressive ascites. Thus, the patient's quality of life was severely impaired and his physical activity was limited because of the considerable weight loss and need of total parenteral nutrition. We performed a follow-up computer tomography, whereby a large aneurysm of the superior mesenteric artery was diagnosed. This aneurysm was fed by branches of the inferior pancreaticoduodenal artery and middle colic artery. A planned coiling of this rupture-prone finding was cancelled because of a high risk for ischemia of small bowel segments.

We reviewed all diagnostic findings and decided to list the patient for MVT, especially for the aforementioned deterioration of the patient's condition despite corticosteroid therapy and the aneurysm.

After a waiting time of 3 months, a suitable organ became available. The 20-year-old donor had died after 2 days in the intensive care unit after a severe head injury. For additional donor characteristics see Table 1.

The multi-visceral transplantation (liver, small intestine, pancreas, stomach) was performed with replacement of the retrohepatic vena cava. Arterial reconstruction of the celiac trunk and the mesenteric artery was performed with a patch on the branching of the recipient's superior mesenteric artery. The recipient's antrum was anastomosed end-to-end with the donor antrum, and the terminal ileum was drained as an ileostoma in right lower abdomen (Fig. 2). Cold ischemia time was 3 h; warm ischemia time was 30 min.

Immunosuppression was initially performed as quadruple therapy with anti-thymocyte globulin, tacrolimus,

Table 1. Donor characteristics.

Age (years)	20
Weight (kg)	72
Height (m)	1.85
Body mass index	21
Noradrenaline (μg/kg/min)	0.6
Resuscitation	No
Sodium (mM)	142
Lipase (U/l)	10
Amylase (U/l)	17

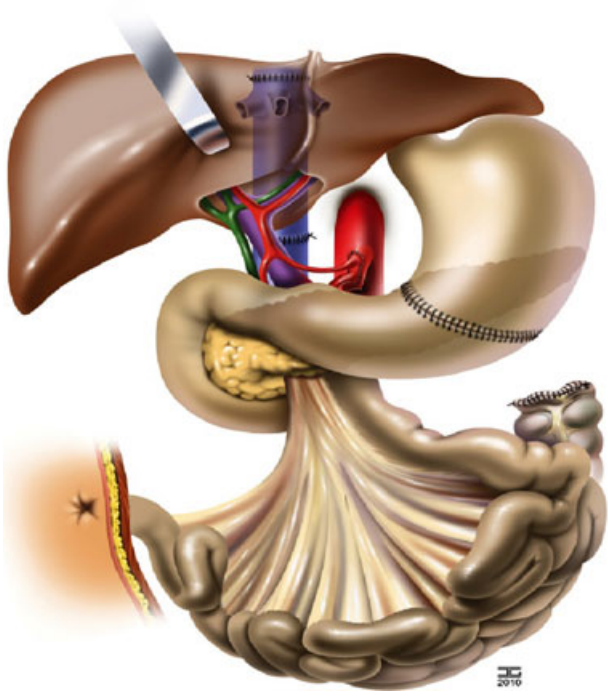

Figure 2 Schematic image of the situs after multivisceral transplantation. Illustration performed by Jens Geiling, Institute of Anatomy, University Hospital Jena.

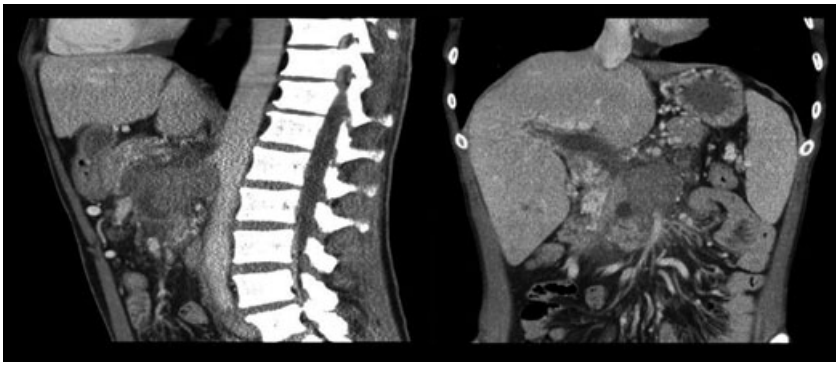

Figure 1 Computer tomographic scan showing the tumor mass in the mesenteric root. Left side: sagittal view. Right side: coronar view.

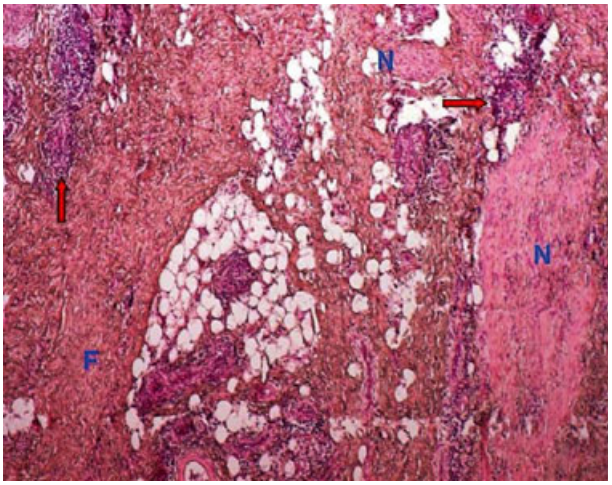

Figure 3 Histologic examination of the explanted multivisceral block from the patient. H&E staining, 40× magnification; fibrosis (F) with lymphoplasmacellular infiltrates (→) and nerves (N).

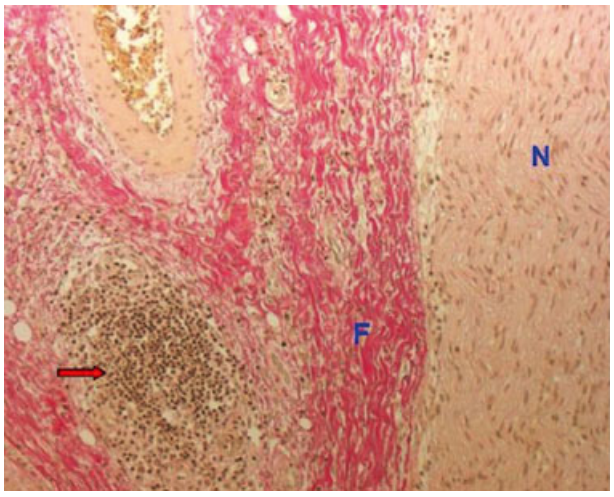

Figure 4 Histologic examination of the explanted multivisceral block from the patient. van Gieson staining 100× magnification; fibrosis (F) with lymphoplasmacellular infiltration (→) and nerve (N).

mycophenolatemofetil, and prednisolone. Immunosuppressive maintenance was managed with tacrolimus (target level 10 μg/l) and prednisolone.

During the early postoperative course, there were two gastric perforations that required surgical repair. There were no further postoperative complications, in particular, no episodes of rejections or infections and no impairment of the renal function.

Definitive histologic examination yielded the diagnosis of a chronic sclerosing IgG4-associated disease (see Figs 3–5). The histologic analysis demonstrated (various degrees of) fibrosis, intense inflammatory cell infiltration with lymphocytes, plasma cells, scattered neutrophils, and

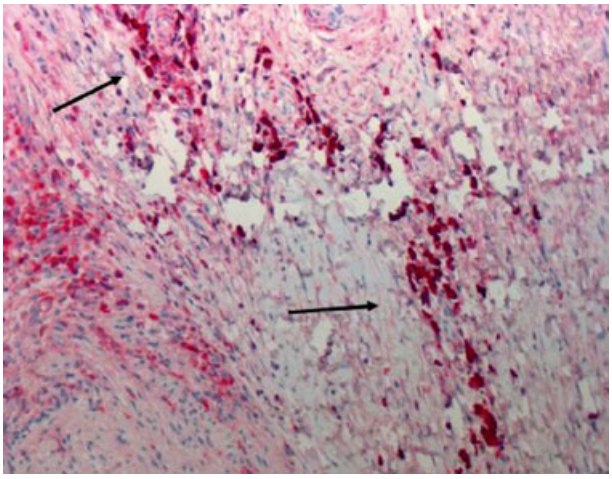

Figure 5 Histologic examination of the explanted multivisceral block from the patient. 100× magnification: numerous plasma cells show positive reaction against IgG4 antigen (→).

some eosinophilic aggregates, with venulitis and obliterative arteriitis. The majority of plasma cells expressed IgG4. There was no evidence for malignancy. Thus, histopathologic evaluation of the resected specimen demonstrated IgG4-related systemic disease of the mesenteric root. The pathological diagnosis was confirmed using ancillary immunohistochemical staining with IgG4, VEGF, VEGFR-2, and ASMA.

One year after the transplantation, the patient is in good clinical condition and back in his job.

Discussion

Semi-malignant tumors of the abdominal cavity with infiltration of the hepatoduodenal ligament, the pancreas, and the mesenteric root may be indications for multivisceral transplantation [1]. In the case described here, we performed a MVT for a symptomatic space-occupying lesion in the mesenteric root with consecutive portal vein thrombosis and encasement of the inferior vena cava. The differentiation of malignancies and IgG4 related diseases is not possible in imaging studies (CT, MRT, scintigraphy), but these are necessary to avoid unnecessary surgery [2,3]. Other authors, too, report about patients in whom the correct diagnosis of an IgG4-related disease was made only after surgery [4]. The differentiation from malignant lymphomas can also be difficult, as IgG4 producing lymphomas do exist [5]. Furthermore, some cases of autoimmune pancreatitis were reported to be associated with pancreatic cancer [6,7].

An IgG4 related disease is seen frequently in elderly male patients. Cheuk has reported that most patients are in good general condition without significant symptoms and fever [8].

In the definitive histology, we found an IgG4-associated autoimmunopathy, which never has been described as indication for MVT to our knowledge. IgG4 associated disease is characterized by high serum concentration of IgG4 and a high local concentration of IgG4 cells in the affected organs. The thyroid gland, pancreas, kidney, lung, prostate, and the retro-peritoneum may be affected, and the gallbladder and the biliary tree might also be affected [9]. These alterations may be evident in single or multiple locations and may become evident at different points in the course of the disease [10]. The diagnosis is made by proper serological and histopathologic proof of IgG4. The differentiation from malignant tumors may be difficult in individual cases [11]. Sarles *et al.* have first reported about a hypergammaglobulinemia associated pancreatitis [12]. Ever since, there have been reports about several patients with autoimmune pancreatitis [13]. IgG4-associated diseases belong to these. In 2006, Neild *et al.* have reported about IgG4-associated diseases, which may be evident at different locations [14]. In the histologic examination, there is a lymphoplasmatic inflammation with IgG4-positive cells as well as a pronounced fibrosis [13]. An idiopathic retro-peritoneal fibrosis is a typical example for an IgG4-associated disease. There are few cases of this disease. At the time of the diagnosis, patients have been occasionally treated successfully with steroids. There are, however, lethal outcomes under steroid treatment, particularly in cases with multi-location presentation. The etiology of IgG4-related diseases remains to be elucidated, and it is necessary to accumulate and analyze larger datasets from patients with IgG4-related disease worldwide. The precise pathogenesis and pathophysiology of IgG4-related disease remain unclear [6].The most common differential diagnosis is Morbus Ormond and Erdheim-Chester disease.

The results after MVT have steadily improved over the past years [15]. Indications for MVT have also been extended [9,15].

Our working diagnosis in that patient was Ormond syndrome at the time of transplantation, and the definitive diagnosis of an IgG4 autoimmunopathy was made after examination of the explanted multivisceral block.

As far as we are aware, this is the first case of IgG4 autoimmunopathy that has been treated by multi-visceral transplantation. In our case, having ruled out a malignancy by multiple biopsies during explorative laparotomy, the decision for transplantation was made after exclusion of malignancy on clinical symptoms.

Authorship

AB, FR, KJ, MG, LM, and US: wrote the paper. AB, FR, LM, and US: collected patient's data. MG: performed pathological analyses.

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