údaje, MELD skóre, Child-Pugh skóre, etiologie, CIT (čas studené ischemie), KS (krevní skupiny), tacrolimus (TAC) 5. den po LTx a při propuštění, délka hospitalizace, přežití. TCMR byla definována histologicky, biopsie jater byla provedena pouze u pacientů se zvýšenou hodnotou jaterních testů nebo neobjasněnou dysfunkcí jater.

Výsledky: Do studie bylo zařazeno 193 pacientů, jejich medián věku byl 53,6; 41,3 % byly ženy; medián MELD skóre byl 16,0; Child-Pugh skóre 10. TCMR byla diagnostikována u 21 pacientů (11,4 %). Srovnání mezi skupinami (s TCMR a bez TCMR) ukázalo následující rozdíly: věk: 54,3 vs. 42,3 let (p = 0,073); etiologie autoimunitní hepatitidy (AIH) 33,3 vs. 6,7 %, (p = 0,001), PSC (primární sklerozující cholangitida) 19,0 vs. 6,7 %, (p = 0,13). Co se týká jiných etiologií, CIT a KS, žádné významné rozdíly jsme nezaznamenali. Hladina TAC 5. den po LTx byla 5,90 [4,00–9,30] vs. 4,80 [2,60–7,00] ng/ml (p = 0,097); hladina TAC při propuštění byla 9,00 [6,80–11,3] vs. 8,9 [7,50–10,6] ng/ml (p = NS); délka hospitalizace byla 35,0 vs. 24,5 (p = 0,001). Mezi skupinami jsme nepozorovali žádný rozdíl v celkovém přežití. Multivariantní analýza odhalila faktory nezávisle asociované s TCMR: AIH (OR = 4,76; 95% CI 1,37-16,46; p = 0,014), nepřítomnost významného ascitu před LTx (OR = 3,15; 95% CI 1,11–8,95, p = 0,024) a hladina TAC 5. den (OR = 0,85; 95% CI 0,73–0,997; p = 0,045).

Závěr: Klinicky diagnostikovaná a histologicky potvrzená T buňkami zprostředkovaná rejekce nastala u 21 pacientů (11,4 %). Etiologie AIH, nepřítomnost ascitu a nízká hladina TAC byly nezávislými rizikovými faktory TCMR. TCMR neměla vliv na celkové přežití pacientů.

Klíčová slova: transplantace jater od zemřelého dárce, diagnóza, výsledek, rizikové faktory, T buňkami zprostředkovaná rejekce.

Introduction

Despite significant improvements in immunosuppressive therapy, rejection is still one of the most common non-surgical complications following liver transplantation (LTx) both in the early and later the post-transplant period. T-cell mediated rejection (TCMR) as a complication following LTx was defined in 1995 (1, 2). The prevalence of TCMR has varied between 20 %, and 40 %. More than 60 % of rejection episodes are manifested in the first 3 months after LTx, usually from the 5th to 30th post-transplant day (3, 4). Risk factors for TCMR include a low level of immunosuppression, infancy and younger age, female gender, positive lymphotoxic cross-matching, and autoimmune etiology of underlying liver disease (3–5). Rejection is mediated by antigen-presenting cells (APC), T-lymphocytes, and allogeneic MHC (Major Histocompatibility Complex) peptide complex. There are two well described pathophysiological pathways: the so-called direct activation pathway and indirect pathway (3, 6–9). In TCMR, the direct pathway prevails in the immediate post-transplant period, while the indirect one is more frequent at later stages (6–8). Clinical presentation is non-specific and often vague – patients may present with fever, fatigue, abdominal pain, icterus, progression of ascites and/or liver dysfunction. Often, the only manifestation is the increased activity of liver enzymes and serum bilirubin.

Liver biopsy (LB) remains the gold standard for diagnosing TCMR, where the diagnostic triad is:

A. inflammatory cellular infiltrate in portal fields,
B. inflammation beneath the endothelium of the portal and central veins (endothelitis), and
C. damage to the interlobular bile ducts.

Banff Classification stratifies TCMR histological findings according to Rejection Activity Index (RAI) into mild, moderate and severe (9, 10). There is still a controversy concerning indication strategy for LB, with some centers performing protocol biopsies and some performing LB only in patients with clinical evidence of graft dysfunction (4). Prevention of TCMR is based on the timely initiation of immunosuppressive treatment. Immunosuppressive agents used to treat TCMR are corticosteroid pulses (11, 12), the most common treatment of steroid-resistant TCMR is anti-lymphocyte thymoglobulin (ATG) – a polyclonal lymphocyte preparation (13–17), than antibody-based agents including anti-CD3 muromonab (OKT3), anti-CD20 antibody rituximab, basiliximab and daclizumab (18–21).

Aims

To determine the prevalence, risk factors and outcome of TCMR in patients undergoing liver transplantation from deceased donors (DDLT) in a small-volume transplant center (TC) over the last ten years.

Patient and methods

We conducted a retrospective study at the liver unit in teaching hospital in Central Slovakia. We extracted data from the hospital information center – Care Center® (NIS-CC). Study interval: May 2008 – December 2017. Inclusion criteria: DDLT at this TC; exclusion criteria – patients treated with CyA and basiliximab.

At the moment of listing, we recorded the following variables: age, sex, MELD score (Model for End-Stage Liver Disease), Child-Pugh score, etiology of liver disease, and its cirrhosis complications. Also, we recorded parameters immediately related to the liver transplantation: CIT – Cold Ischemia Time, recipient BT – blood type, tacrolimus (TAC) levels on day five following LTx and at the time of hospital discharge, length of hospital stay (LOS), and overall survival post liver transplantation.

We did not evaluate the donor-recipient matching (mismatches in HLA loci) and cross-matching.

Immunosuppression protocol in our TC includes a triple combination of intravenous methylprednisolone 500 mg in the anhepatic phase followed by a daily intravenous dose of 20 mg, tacrolimus 0.1 mg/kg/day and mycophenolate mofetil 2 000 mg/day. We excluded patients receiving immunosuppressive induction therapy with basiliximab.

We suspected TCMR in patients having an increase in serum levels of AST (aspartate aminotransferase), ALT (alanine aminotransferase), GGT (gammaglutamyltransferase), ALP (alkaline phosphatase) and or