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Course of inflammatory bowel disease in concomitant paediatric primary sclerosing cholangitis

Przebieg nieswoistego zapalenia jelit u dzieci ze współistniejącym pierwotnym stwardniającym zapaleniem dróg żółciowych

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Słowa kluczowe

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S u m m a r y

Introduction. Primary sclerosing cholangitis is a progressive inflammatory disease of biliary tract that may be concurrent with inflammatory bowel disease. The predominant phenotype of IBD is ulcerative colitis. The paediatric data concerning the course of inflammatory bowel disease in those patients is scarce.

Aim. To assess the course of inflammatory bowel disease in paediatric primary sclerosing cholangitis.

Material and methods. We retrospectively reviewed medical charts of 10 children with primary sclerosing cholangitis and inflammatory bowel disease. Inflammatory bowel disease diagnosis was based on clinical, endoscopical and histological data.

Results. Ten children (7M/3F) mean age 10.7 and 10.5 at PSC and UC onset respectively were enrolled. Nine children had ulcerative colitis diagnosed while Crohn disease was diagnosed in one case. Five patients had no macroscopic lesions and UC diagnosis was based on signs of mucosal inflammation in histology. Three patients had pancolitis and one left-side colitis. Severity of inflammation in UC was moderate in 3 cases. The treatment regimen at the onset consisted of aminosalicylates and ursodeoxycholic acid. At the end of follow up 9 patients remaind in clinical remission. The patient with CD progressed to splenic flexure stenosis.

Conclusions. The course of IBD associated with PSC is benign. None of the children experienced severe colitis nor underwent colectomy.

S t r e s z c z e n i e

Wstęp. Pierwotne stwardniające zapalenie dróg żółciowych (PSC) jest postępującą zapalną chorobą dróg żółciowych, która może współwystępować z nieswoistym zapaleniem jelit (IBD). Głównym fenotypem IBD jest wrzodziejące zapalenie jelita grubego. Nieliczne prace oceniają przebieg nieswoistego zapalenia jelit w tej grupie pacjentów.

Cel pracy. Ocena przebiegu nieswoistego zapalenia jelit u dzieci z pierwotnym stwardniającym zapaleniem dróg żółciowych.

Materiał i metody. Retrospektywnie oceniono historię chorób 10 dzieci z pierwotnym stwardniającym zapaleniem dróg żółciowych oraz nieswoistym zapaleniem jelit. Diagnoza IBD została postawiona na podstawie objawów klinicznych, wyników badań endoskopowych i histologicznych.

Wyniki. Dziesięcioro dzieci (7 chłopców i 3 dziewczynki) włączono do badania, średnia wieku rozpoznania PSC i IBD wynosiła odpowiednio 10,7 oraz 10,5 roku. U 9 dzieci rozpoznano wrzodziejące zapalenie jelita grubego, a u jednego chorobę Crohna. Pięciu pacjentów nie miało zmian makroskopowych w endoskopii, a rozpoznanie postawiono w oparciu o badanie histologiczne. Zmiany zapalne u 3 dzieci występowały proksymalnie do zagięcia wątrobowego, u jednego pacjenta były zlokalizowane lewostronnie. W 3 przypadkach zmiany zapalne miały umiarkowane nasilenie. Leczenie składało się z preparatu kwasu 5-aminosalicylowego oraz kwasu ursodeoksycholowego. Na zakończenie obserwacji 9 pacjentów było w remisji klinicznej. Pacjent z chorobą Crohna rozwinął zwężenie w zagięciu śledzionowym.

Wnioski. Przebieg IBD związanego z PSC jest łagodny. Żadne z dzieci nie doświadczyło ciężkiego zaostrzenia choroby podstawowej ani nie wymagało kolektomii.

Conflict of interest
Konflikt interesów

None
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INTRODUCTION

Primary sclerosing cholangitis (PSC) is a chronic cholestatic inflammatory disease of intra and extra hepatic biliary tract of unkown etiology. It leads to liver cirrhosis and end stage liver disease. The incidence of PSC is estimated at 0.2 cases per 100 000 children (1). The only treatment option is orthotopic liver transplantation with median time free of liver transplantation 12.7 years (2). In up to 80% of cases PSC may be concurrent with underlying inflammatory bowel disease (IBD) predominantly ulcerative colitis (UC) (1, 2). On the other hand 9.9% patients with UC will develope PSC (1, 3). The adult phenotype of IBD in PSC is distinctive. The main features are pancolitis, rectal sparing, backwash ileitis, frequently asymptomatic course, increased risk of colon cancer and cholangiocarcinoma (4). Paediatric data describing PSC/IBD phenotype are scarce. So far released paper showed consistent with adults results where pancolitis and rectal sparing were observed in 89.7 and 24.3% respectively. Both features were more frequently observed in PSC/IBD than in UC alone (5, 6).

AIM

We describe the course of inflammatory bowel disease in children with PSC.

MATERIAL AND METHODS

We retrospectively reviewed the medical charts of children with PSC and concurrent IBD. Clinical, radiographic, laboratory, histological, serological data was collected. IBD diagnosis was based on clinical, endoscopical, histological data according to Revised Porto Criteria (7). The extension of the disease was assessed with Paris classification. The severity of mucosal inflammation was assessed according to Mayo score (8). PSC diagnosis was based on clinical, biochemical, cholangiographic examination and/or liver biopsy results. The cholangiographic findings included multifocal strictures and segmental dilations. Histological records were reviewed to find characteristic for PSC onion skin fibrosis. In those patients who had elevated levels of IgG, gammaglobulins and interface hepatitis in liver biopsy autoimmune sclerosing cholangitis was diagnosed (9). The initial treatment consisted of aminosalicylate (ASA) and ursodeoxycholic acid (UDCA) in IBD and PSC respectively. Steroids (ENC) and azathioprine (AZA)were introduced if features of autoimmune hepatitis were present. The primary endpoint was to analyze the phenotype and course of IBD with incidence of IBD, rate of exacerbations and colectomies.

RESULTS

Ten children were enrolled. There is male predominance in the study (7M/3F). The average age at the diagnosis were 10.7 and 10.5 for PSC and IBD respectively. Timing of the diagnosis is described in table 1.

Tab. 1. Timing of IBD diagnosis

PSC first	4 cases
Simultaneously	3 cases
IBD first	3 cases

IBD course

According to endoscopic findings 9 patients were diagnosed with ulcerative colitis while one patient presented features of Crohn disease. Half of the patients had no macroscopic lesions, another 3 patients had pancolitis and 1 left sided colitis. Severity of inflammation was moderate in 3 cases and mild in one case. None of the children had severe macroscopic inflammation in endoscopy Rectal sparing was observed in one case while none of the patients had back wash ileitis. Patient with Crohn disease had duodenal ulcers and distal 1/3 ileum and limited cecal disease according to Paris classification. Patients with no macroscopic findings had microscopic lesions mainly cryptitis and crypt abscesses.

The initial treatment regimen consisted of 5-ASA in almost half of the patients. One patient had induction of remission with ENC and another received 5-ASA with AZA. One patient received no treatment at the onset of the disease. Relapse of the UC occurred in a single patient with moderate pancolitis in colonoscopy. The remission was induced with tapering dose of steroids. At the end of follow up 9 patients were in clinical remission. The treatment consisted of 5-ASA and AZA in 6 and 1 patient respectively. Three patients received no treatment due to deep remission. Five patients underwent surveillance endoscopy, mean time from diagnosis 4 years. In each patient no macroscopic lesions were observed. Patient with CD had aftous lesions confined to the ascending colon and splenic flexure stenosis. There was no need to use biological treatment and rescue therapies in course of steroid refractory/dependant UC. None of the patients underwent colectomy due to severe flare of UC.

PSC characteristic

Features of autoimmune sclerosing cholangitis were present in 9 of the patients. At the disease diagnosis mean laboratory values of ALT, AST, GGTP were 119.5, 99.2, 238.6 U/L respectively. Bilirubin level was within the range in 9 children, average 0.43 mg/dL. The most frequently detected antibodies were ASMA (9/10), pANCA (6/10) and ANA (4/10). One of the patients had elevated titers of HLA-B27, ds. DNA and ASCA. None of the patients presented features of hypersplenism at the onset. Each of patients had liver biopsy to confirm the diagnosis. None had features of liver cirrhosis at the onset. 8 patients had MRCP done but features of PSC were present in 4 cases, in each multilevel. None of the patients had ERCP with stenting due to intractable pruritus. The mean follow-up was 4.3 years. The average laboratory values were ALT – 38.6, AST – 39.6, GGTP – 146.9. None of the patients had esophageal varices banding nor experienced variceal bleeding at

the end of follow up. Treatment of ASC consisted of UDCA alone, ENC/AZA/UDCA and AZA in 2, 5 and 3 patients respectively.

DISCUSSION

In our study 90% of patients had UC diagnosed. 5/10 patients had no macroscopic lesions observed in colonoscopy and diagnosis was based on the histological findings. The others had mild to moderate mucosal inflammation. The distinctive features of IBD observed in adults were present in 1 patient (rectal sparing). The course was mild in the half of the cases. At the end of follow up only 1 patient experienced exacerbation, while the others were in clinical remission. Lascurain et al. compared the phenotype of IBD-PSC with non-PSC matched IBD controls. The study showed that pancolitis is more frequent in PSC-IBD subgroup. Rectal sparing exists at the same rate in both compared groups. The 5-year risk of colonic surgery is lower in PSC-IBD than IBD (16.4 vs 24.7%), however it is not statistically significant. The risk factors for colonic surgery based on the multivariate model were male sex and the presence of a non-PSC immune mediated disease (5). Two-thirds of the patients is diagnosed with PSC and UC simultaneously. Hospital admission are significantly less common in patients with PSC-UC than UC. The need for colectomy is also smaller in PSC-UC patients performed in up to 6 of patients while almost 25% of patients with UC require surgery. Median time from UC diagnosis to colectomy is longer in PSC-UC patients (6.37 vs 2.5 years) (5). Diagnosis in adults IBD precedes PSC (61%) and median interval is 9 years. 94% of patients is diagnosed with pancolitis. Backwash ileitis and rectal sparing occur in 6 and 10% of patients respectively (10). The independent risk factors to develope PSC in course of UC are male sex, pancolitis, non smoker at diagnosis, history of appendectomy. PSC is associated with CD in 0.6% (11). 95% of CD/PSC have colitis (10). Comparison between patients with CD/PSC vs CD alone revealed that isolated CD is less common in the former group. No difference in treatment requirements is observed. PSC/CD are more frequently female with small duct PSC than PSC/UC (12). Aminosalicylate monotherapy is more common in the PSC-IBD than IBD. Children with UC-PSC are less commonly treated with corticosteroids and fewer receive Infliximab (5). Anecdotal papers depict use of Infliximab in PSC/IBD patients. It does not provide IBD control and may be a cause of poor hepatobiliary disease control (13). No differences in use of corticosteroids, methotrexate, anti-tumor necrosis factor is observed in adults (8). PSC/IBD and small duct PSC seem to be associated with better prognosis (1). Ananthakrishnan et al. proved in multi-institutional study that PSC-IBD patients have significantly higher risk of cancers than PSC patients. It is valid for gastrointestinal tumors: pancreatic cancer, colorectal cancer and cholangiocarcinoma. Moreover there is no increased risk of other solid organ and hematologic tumors. Mortality rate is also higher in PSC-IBD than PSC alone. Associated comorbidities were the single strongest mortality risk factor. On the other hand therapy with immunomodulator had the lowest adjusted odds of death (14). Meta analysis of 16 studies proved that there is increased risk of colorectal neoplasia in PSC-UC than UC alone. Such an association exists also between PSC and CD, however it is not significant (15). The prevalence of cholangiocarcinoma in paediatric cohort from Utah was 1% (1).

CONCLUSIONS

The course of IBD in PSC is quiescent in a half of the patients. None of the children underwent colectomy.

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