TRANSIENT GLUTENOPATHY AND ABDOMINAL TUBERCULOSIS, A CAUSE OR EFFECT?

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Abstract

Abdominal tuberculosis is one of the most common causes of prolonged hospital admission in pediatric gastroenterology unit.

While we are investigating children with abdominal tuberculosis, we noticed that they have positive serology for celiac disease, so we tried to find a correlation between abdominal TB and glutenopathy.

Ten children with abdominal TB were enrolled in a pilot study dividing them in two groups, one group was tried with gluten free diet, and the other group on normal diet. Both groups started on antituberculous for one year.

All children had small intestinal biopsy at the beginning, six months later and at one year, (they enrolled on gluten free diet according to their histopathological finding on the small intestinal biopsy) and they have their celiac serology at the same time in a form of IgA & IgG antigliadin antibodies and anti TTG.

The group on gluten free diet challenged with gluten after six months .They had remarkable quick recovery with no relapse after challenging them with gluten. While the group on normal diet took longer to recover and some of them continue to have abnormal serology and minor mucosal changes.

We tried to investigate this phenomenon and implicate the effect in our clinical practice?

1. Introduction:

Abdominal tuberculosis in Sudan is still a major health problem especially among young children and the common cause of prolonged hospitalization in children wards.

In our unit in Gaafar Ibn Auf specialized children hospital from Jan2005 – Jan 2006 we looked after 150 children aged 2 – 10 yrs with chronic diarrhea and malnutrition 15 of whom were confirmed abdominal TB making the incidence in our admission of 1:10.

We noticed, while we are investigating children for chronic diarrhea and malnutrition that almost all children who turned eventually to have abdominal TB have positive serology for celiac disease. When they started gluten free diet plus their anti tuberculous medications they made a remarkable and quick recovery and they didn't relapse clinically when they were challenged with gluten.

In order to test the hypothesis that abdominal TB can cause transient glutinopathy we set up a pilot study in our unit for the last eighteen months, we looked at ten children between the age of 2-10yrs diagnosed as abdominal TB.

2. Methodology:

All the 10 children enrolled in the study were diagnosed as abdominal TB on the clinical ground bases(fever , malaise, ill

health, chronic diarrhea, failure to thrive, and malabsorption) and laboratory data of high ESR, low albumin, anaemia , positive diagnostic BCG and positive finding on abdominal ultrasound (enlarged lymph nodes, thickened bowel and ascites ± hepatomegally).

They all underwent proximal small intestinal biopsy using paediatric video upper GI endoscope external diameter of 9.7mm. The biopsy was examined by light microscopy.

Three series of biopsies were taken, at the time of diagnosis, six months later and six months after challenging with gluten (for those on gluten free diet).

IgA and IgG antigliadin antibodies and anti tissue transglutaminase (anti tTG) were tested at the beginning, six months after treatment and six months later.

All children were positive for IgG & IgA antigliadin antibodies and TTG.

Four children have total villous atrophy, three had subtotal villous atrophy and three have abnormal mucosa (minimal changes).

All the four children with total villous atrophy and one with subtotal villous atrophy were started on gluten free diet, the rest were kept on normal diet. And all patients started antitubrculous medications (Streptomycin injections + Rifampicin +INH+ Pyrazinamide for two months and Rifampicin + INH for another 10months.

3. Result:

3.1. Serology:

At the beginning of diagnosis all patients had positive serology

for IgA & IgG antigliadin antibodies and anti tissue transglutaminase (anti tTG) (table 1)

After six months of treatment one patient of group A (on gluten free diet) was dropped from the study because she was discovered to be HIV positive , the remaining four patients were negative for tTG, three of them negative for IgA and all of them were positive for IgG antigliadin antibodies. While only two of group B were negative for tTG, three of them negative for IgA and all of them positive for IgG antigliadin antibodies (table 2),

The four patents in group A then challenged by gluten. Six months later the result is as follows; the four patients in group A were remained negative for anti tTG and IgA and became also negative for IgG antigliadin antibodies, while three patients in group B remained positive for IgG but all of them became negative for TTG and IgA antigliadin antibodies (table 3).

3.2. Mucosal biopsy:

At the start of treatment four patients were found to have total villous atrophy (TVA), three had subtotal villous atrophy (STVA) and three had minimal mucosal changes (MMC).

All of the four patients with TVA plus one with STVA were put in gluten free diet (group A) while the rest of the patients were put on normal diet.

After six months of treatment three children in group A their mucosa became normal, one continue to have MMC and one was dropped from the study because of her HIV status, while three out the five children in group B their mucosa became normal and two continued to have MMC.(table4)

At one year biopsy was done for only two children (group A) and it was normal. The rest of children were not done because they were clinically well.

3.3. Clinical course:

In group A abdominal pain was the 1st to disappeared, diarrhea and malaise disappeared within one week and also they started to gain weight in the same week. Hospitalization took one to two weeks and there was no re admission. While patients in group B their diarrhea and malaise took up to two weeks to disappeared. They started to gain weight after 10 days, hospitalization for up to 3 weeks and few of them re admitted 2 – 3 times in the 1st six months (fig.1).

4. Discussion:

Abdominal tuberculosis seems to cause transient glutenopathy this could be due to either:

1) Mycobacterium bacilli itself , the same as infection with adenovirus type 12 &7, human herpes type 1 and rubella may predispose to celiac disease [1,2].

2) The severity of intestinal mucosal damage by gastrointestinal infection and it's extend on the small intestine barriers (Walker smith et al) [3]

3) Or due to host factors as (a) the child initial nutritional status in determining the ability of the small intestinal mucosa to recover after damage (b) immunological factors which determine the local and systemic response (c) genetic factors [3]

4) Environmental factors as the high incidence of celiac disease which was found in Sahara people [4]

5. Conclusions:

- Abdominal TB seems to cause some sort of transient glutenopathy.
- Gluten free diet seems to facilitate recovery and decrease hospital admissions and hiccup during treatment.

5.1 Limitation of the study:

- Small number of children
- Inability to perform serological test for celiac disease (anti endomyselial antibodies and anti reticulin antibodies)
- Inability to perform genetic studies.

5.2. Future aspect:

We are still looking into this phenomenon which relates to children with abdominal TB, randomizing our management and investigating further details into the mucosal changes, injuries, different serological results, nutritional and immunological status of the children as well as different genetic and environmental factors.

We are also looking into our adult celiac population with their background (regarding past history of abdominal TB, nutritional, immunological, genetic and environmental factors) for the possibility of latent celiac disease.

Table (1) serology of cases at diagnosis (N=10)

	Group A		Group B	
Test	positive	negative	positive	negative
Ani tTG	5	0	5	0
IgA	5	0	5	0
IgG	5	0	5	0

Table (2) serology at 6 months (n=9)

	Group A	Group B		
Test	positive	negative	positive	negative
Ani tTG	0	4	3	2
IgA	1	3	2	3
IgG	4	0	5	0

Table (3) serology at one year (N=9)

	Group A		Group B	
Test	positive	negative	positive	negative
Ani tTG IgA	0	4	0	5
IgG	0	4	3	2

Table (4) mucosal biopsy at diagnosis (N=10)

	Group A	Group B
TVA	4	0
STVA	1	2
MMC	0	3
Normal mucosa	0	0

STV =Total villous atrophy

STVA = Subtotal villous atrophy

MMC = Minimal mucosal changes

Group A on gluten-free diet

Group B on normal diet

Table (5) mucosal biopsy after 6 month of treatment (N=9)

	Group A	Group B
TVA	0	0
STVA	0	0
MMC	1	2
Normal mucosa	3	3

STV =Total villous atrophy

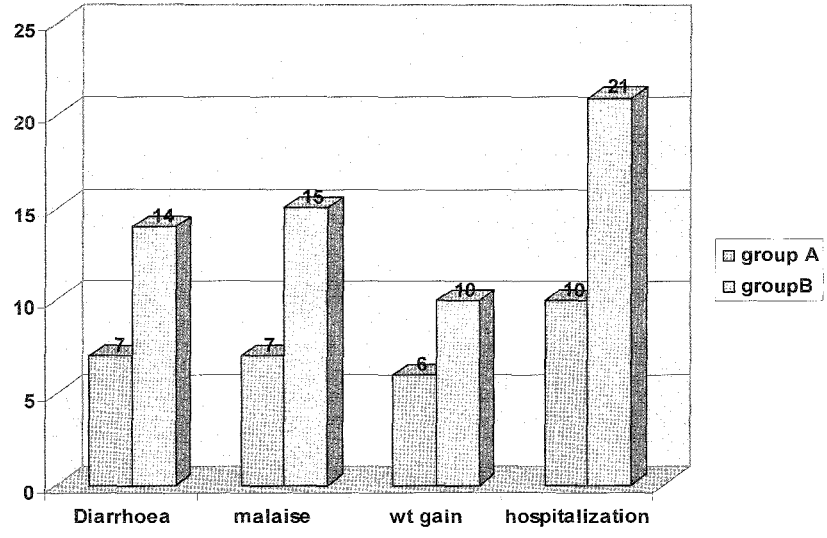
STVA = Subtotal villous atrophy

MMC = Minimal mucosal changes

Group A on gluten-free diet

Group B on normal diet

Fig 1 disappearance of symptoms, wt gain & hospitalization in days



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