Digestive disease in chronic inflammatory diseases in children (about 10 cases)

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Abstracts :

Introduction:

Digestive involvement is not uncommon during chronic inflammatory diseases in children, it may be just digestive manifestations other than other systemic signs or association of two different pathologies with a common immunological terrain .

Objective:

To recognize the different types of digestive involvement encountered during chronic inflammatory diseases in children and to discuss the frequency of association of digestive involvement with chronic inflammatory diseases in children .

Material and methods:

Retrospective study involving 10 children with chronic inflammatory diseases with digestive involvement collected at the department of pediatrics IV and the consultation of pediatric rheumatology of the children's hospital of Rabat over a period of 17 years (2001-2018) .

Results :

Our series includes 7 female and 3 male children.

The average age of our patients at the time of diagnosis of JIA or SLE is 10 years and the average age of the digestive involvement is 07 years.

The types of digestive involvement found were diverse: Crohn's disease, ulcerative colitis and celiac disease.

The frequency of digestive involvement in chronic inflammatory diseases in our series is 1.58%. The incidence of association of juvenile idiopathic arthritis with IBD is 1.08% and with celiac disease is 0.4%, while the frequency of association of systemic lupus with celiac disease is 2.8%.

Conclusion:

There is a very strong link between digestive involvement and chronic inflammatory diseases, The common etiopathogenic mechanisms that explain this link are not yet well defined, but genetic predisposition seems to play an important role in these associations, as well as environmental factors such as long exposure to gluten, for celiac disease.

Introduction:

Chronic inflammatory diseases are a group of diseases related to an inflammatory and immunological attack on several organs, due to the similarity of the tissues that compose them.In children, there are many chronic inflammatory diseases, such as :

- Juvenile Idiopathic Arthritis (JIA)

- Disseminated Lupus Erythematosus, scleroderma, juvenile dermatomyositis

- Mixed connectivites (SHARP syndrome), Behçet's disease.

Digestive involvement is not uncommon during chronic inflammatory diseases in children, it may be just digestive manifestations other than other systemic signs or association of two different pathologies with a common immunological terrain common.

Objective:

To describe the epidemiological and etiopathogenic aspects of digestive involvement in chronic inflammatory diseases of children .

Material and methods:

This is a retrospective analysis of 10 children with chronic inflammatory diseases with digestive involvement collected at the pediatric department IV and at the pediatric rheumatology consultation of the children's hospital of Rabat over a period of 17 years (2001-2018). digestive disorders.

- Average age of association of chronic inflammatory disease and digestive involvement: 10 years.

- Average age at diagnosis of chronic inflammatory disease in our series: 10 years.

- Average age of digestive involvement: 07 years.

- Female predominance (70%).

Results :

Our study focuses on 10 cases of digestive involvement in chronic inflammatory diseasesdiseases in children:

- 5 cases of juvenile spondyloarthropathy associated withInflammatory bowel diseases(IBD)
- 1 case of systemic arthritis associated with IBD

- 1 case of Oligoarthritis associated with celiac disease (CD)
- 1 case of Psoriatic arthritis associated with celiac disease
- 2 cases of Systemic Lupus erythematosus associated with celiac disease

-The average age of the association of chronic inflammatory disease and digestive is around 10 years.

-The average age at diagnosis of chronic inflammatory disease in our series is around 10 years, while the average age of the digestive involvement is around 07 years .

-Overall, there was a 70% female predominance.

At the clinical level =

- ✓ Digestive involvement had occurred in cases of ***SPJ + Inflammatory bowel diseases (IBD)*** in our series by: Abdominal pain (100%) ,Rectorrhagia (80%) ,Diarrhea (60%), Vomiting (20%), Alternating constipation and diarrhea (20%) ,Rectal fistula (20%).
- ✓ The digestive involvement in ***The association of systemic arthritis and IBD(1 case)*** was manifested by:Abdominal pain ,Chronic diarrhea ,Vomiting ,Perineal fistula .
- ✓ Digestive involvement in ***Oligoarthritis associated with celiac disease (1 case)*** was manifested by : Chronic diarrhea ,Vomiting , Abdominal bloating .
- ✓ ***Psoriatic arthritis associated with celiac disease*** occurred in only 1 case ; The digestive involvement was manifested in this case by : Chronic diarrhea and Vomiting .
- ✓ ***SLE associated with celiac disease*** concerned 2 cases: brother and sister ; The digestive involvement in the 2 cases had manifested as: Chronic diarrhea , Vomiting , Bloating , abdominal bloating , Abdominal pain , Staturoponderal delay .

On the biological level = :

- An **inflammatory syndrome** was objectified in all cases.
- **24-hour proteinuria** was positive in only 1 case who had a nephrotic syndrome and in whom a renal biopsy renal biopsy showed combined class IV+V lupus glomerulonephritis.
- All of our patients underwent a **global immunological workup** for the purpose of diagnosis including :ANA assay (positive in 2 cases of SLE+ crohn desease) , rheumatoid factor assay (positive in only 1 case of PJS+ICD) , Anti-DNA assay (positive in 2 SLE+ MC cases) , Anti-SSA/Ro assay (Positive in 2 SLE+ MC cases) ,Anti-Rnp assay (Performed in 2 patients :1 case of SLE+ CD and 1 case of AS+ IBD; was negative in both Cases), Anti-neutrophil cytoplasmic antibodies (ANCA) assay (Performed in 3 cases of SPJ+MICI; found positive in only 1 case) Anti-saccharomyces cerevisiae antibody (ASCA) assay (Performed in 3 cases of SPJ+MICI; found positive in only 1 case) , Anti-tissue transglutaminase and anti-endomysial antibodies(Performed in 4 patients :2 cases of SLE+MC, 1 case of AO+MC, and 1 case of AP+MC; found to be positive in all 4 cases) , Anti-gliadin Ac assay (Performed in 2 cases of SLE+MC; found to be positive in both cases).
- The 5 cases of SPJ+ IBD had undergone a **genetic study** including the search for of the HLA B27 antigen which was positive in 3 cases .

Data from radiological examinations =

- All patients had undergone an abdominal ultrasound which was normal in 7 cases normal in 7 cases and had shown in the others :
    - A homogeneous hepatomegaly in 2 cases with juvenile spondyloarthropathy + IBD.
    - Thickening of the digestive wall in 2 cases (1 case of juvenile spondyloarthropathy juvenile spondyloarthropathy + IBD and 1 case of systemic arthritis + IBD).
- Abdominal scanhad shown a Crohn's aspect with ileo-colic and ano-rectal localization in a patient with systemic arthritis + CD .

Endoscopic and histological examination data =

- Performed on all our patients ,The most common digestive disorder was Crohn's disease in 6 cases (50%) followed by celiac disease in 4 cases (40%). celiac disease in 4 cases (40%).

Therapeutic data =

- 2 patients had received **NSAIDs** (Diclofenac 25 to 75mg/d), i.e. 20%, including :One case with oligoarthritis + CD , One case with psoriatic arthritis + CD.
- **Oral corticosteroids** (Prednisone) were prescribed in 7 patients, i.e. 70%, of whom 5 had juvenile spondyloarthropathy of which 5 cases had juvenile spondyloarthropathy+ICD and 2 cases had SLE+MC.
- **Corticosteroid infiltration** with triamcinolone hexacetonide was performed in 1 patient with oligoarthritis+MC.
- In our series, 4 patients had received **Sulfasalazine** (Salazopyrine), i.e. 40%; 4 cases of juvenile spondyloarthropathy + IBD .
- **Methotrexate**-based background treatment was used in 3 patients, including 1 case of juvenile spondyloarthropathy patients, including 1 case of juvenile spondyloarthropathy + IBD, 1 case of SLE + CD and one case of systemic arthritis + IBD.
- **Cyclophosphamide** (Endoxan*) was prescribed in 1 patient with SLE + CD , who had lupus nephropathy.
- **Synthetic antimalarials** were prescribed in the 2 cases of SLE + CD .
- 2 patients had received **biotherapy**(Anti-TNF alpha) , including 1 case of juvenile spondyloarthropathy + IBD and 1 case of oligoarthritis + CM.
- A **gluten-free diet** was instituted in the 4 cases followed for celiac disease .

Discussion:

1. Association of juvenile idiopathic arthritis and inflammatory bowel disease diseases:

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood and represents a heterogeneous group of conditions.

common in childhood, it represents a heterogeneous group of conditions including enthesitis-related arthritis, also known as juvenile spondyloarthropathy, which represents the juvenile spondyloarthropathy which represents the pediatric form of spondyloarthropathies.

Classically, five entities define spondyloarthropathies: Ankylosing Spondylitis ankylosing spondylitis, psoriatic arthritis, reactive arthritis, arthritis associated with Inflammatory bowel diseases (IBD) and Undifferentiated spondyloarthritis.

In addition to skeletal disease, extra-articular disorders such as uveitis, and inflammatory bowel disease (IBD) often occur in the course of spondyloarthropathies , offering a significant aid in the diagnosis of these diseases .(1)

It should be noted that IBD contributes to the diagnosis of axial SpA in patients with chronic low back pain .(2)(3)

Chronic inflammatory bowel disease (IBD) occur much more frequently in spondyloarthropathy than in the general than in the general population and are associated with disease activity. (4)

Similarly, in a large population-based study, it was shown that the incidence rate of IBD was shown to be 5.3 times higher in patients with SpA compared to healthy controls.(4)

Axial and peripheral SpA is more common in Crohn's disease than in ulcerative colitis . This is consistent with the results of our study.(1)(5)

It is well known that there is a close association between IBD and SpA (6).Several etiopathogenic mechanisms have been suggested to link these two entities, including genetic predisposition.

1.1. Genetic susceptibility :

Genetic factors play an important role in the link between SpA and IBD, by modifying the adaptive and innate immune pathways .(7)(8)

1.1.1. HLA genes :

Certain human leukocyte antigen (HLA) alleles have been identified in IBD patients who are patients with IBD who are at greater risk of developing SpA, in fact HLA-B27 confers an additional risk of an additional risk of inflammatory low back pain in IBD patients. ThusHLA-27 typing may be a potential factor, as the frequency of HLA B27 in IBD patients is generally no higher than in the general population.

A prospective study regarding genetic variability found a significantly higher level of HLA B27 B27 in IBD and SpA patients, 25% to 78% of the cases with this combination 78% of cases with this combination of SpA and IBD are HLA-B27 positive .(8)(9)

Other alleles have been incriminated in the JIA-ICHD association; the MHC class II allele DRB1 0103 as well as HLA-B35 are frequently associated with peripheral SpA . MHC class II allele and HLA-B35 are frequently associated with peripheral SpA , while approximately 38% of patients with UC or active Crohn's disease have been identified as carriers of the identified as carriers of the DRB1 0103 allele . (9)(10)

1.1.2. Non-MHC (non-HLA) genes :

Genetic factors outside the HLA system have also been described. The variations in the CARD15 gene (which codes for the NOD2 protein product) increase the risk ofof Crohn's disease approximately 4 to 40 times and have been linked to the development of sacroiliitisin IBD patients . (11)(12)

NOD2 is an intracellular receptor for bacterial molecules that is expressed on the surface of macrophages, lymphocytes, and expressed on the surface of macrophages, lymphocytes, Paneth cells and intestinal epithelial and intestinal epithelial cells.

This receptor plays a role in the innate immune response by activating the nuclear factor κB (NFκB) which is a transcriptional regulator of a wide variety of genes encoding pro-inflammatory cytokines, adhesion molecules, cytokines, growth factors and growth factors and enzymes) .(7)(8)(10)(13)

Accordingly, NOD2 is responsible for the up-regulation of the immune immune defense in the gut and the induction of a pro-inflammatory state .(13)

In our series, the genetic study could not be performed due to lack of means. only the search for HLA B27 was carried out in the 5 cases presenting the association HLA B27 was positive in 3 cases.

1.2. The intestinal synovial axis :

Several other results also highlight the underlying etiopathogenic mechanisms underlying etiopathogenic mechanisms common to IBD and SpA.

Notably, the integrin aEβ7 that is expressed by intraepithelial T cells in the intestinal mucosa and which binds to the glycoprotein E-cadherin expressed by intestinal intestinal epithelial cells, and has been shown to be elevated in patients with SpA .(14)(15)

2. Association of celiac disease and autoimmune diseases :

The causal relationship between celiac disease and other autoimmune diseases such as juvenile idiopathic arthritis and systemic lupus erythematosus is still a controversial. The two most accredited theories propose: this association is secondary to a common genetic background predisposing to celiac disease and the associated autoimmune disease (16) or untreated celiac disease leads to the onset of other autoimmune diseases in genetically predisposed individuals .(17)

Genetic susceptibility :

The genetics of celiac disease are complex because multiple genes contribute. Some linkage and association studies have identified several genomic regions that likely contain susceptibility genes susceptibility genes for celiac disease. The most important genetic factor identified is the MHC region that contains the haplotypes coding for the celiac molecules HLADQ2 and HLA-DQ8. These two haplotypes are necessary but not sufficient for the development of the disease. This suggests that other non-HLA genes contribute to pathogenesis of the disease .(18)

In our study: the association of celiac disease and lupus erythematosus and systemic lupus erythematosus in brother and sister points to the almost certain existence of a genetic component.

Unfortunately the genetic study could not be done (lack of means).Similarly for the association of juvenile idiopathic arthritis and celiac disease disease, the genetic study could not be carried out .

In total:

The pathogenesis pathways involving the association of celiac disease and juvenile idiopathic arthritis juvenile idiopathic arthritis and systemic lupus erythematosus are not yet well elucidated.

The development of systemic lupus or juvenile idiopathic arthritis in a celiac patient is thought to be due to the celiac patient would be due to the presence of a common genetic background HLA B8 DR3 and to the duration exposure to gluten, and the contribution of IL-21 in the etiopathogenesis is considered to be today among the theories that can explain the association between celiac disease and autoimmune diseases.

Because of the existence of a common immunogenetic background, the association between celiac disease and autoimmune diseases or even JIA and SLE deserves the attention of attention of researchers.

Conclusion:

Digestive involvement in chronic inflammatory diseases of children can be asymptomatic as well as clinically asymptomatic as it can be manifested by a clinically severe form.

These gastrointestinal manifestations can be induced by drugs or the chronic inflammatory disease itself, but can also be chronic inflammatory disease itself, but can also be attributed to other primary diseases other primary diseases: IBD, celiac disease...

Juvenile idiopathic arthritis and systemic lupus erythematosus are the most common pediatric chronic inflammatory diseases with digestive involvement.

IBD and even Crohn's disease and ulcerative colitis, as well as celiac disease, are the most common digestive celiac disease are the digestive disorders most often associated with these chronic diseases of children.

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