THE RISK OF IDIOPATHIC THROMBOCYTOPENIC PURPURA IN A PATIENT WITH COELIAC DISEASE: PURE COINCIDENCE?

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[Il rischio porpora idiopatica trombocitopenica in un paziente celiaco: pura coincidenza?]

SUMMARY

Coeliac disease (CD) is an autoimmune disease, gluten-dependant, which affects the gastrointestinal tract, characterized by intestinal mucosal inflammation, with following villous atrophy and malabsorption.

A positive association between CD and other immune diseases, such as Idiopathic Thrombocytopenic Purpura (ITP) has been put forward in some studies. ITP is a relatively frequent autoimmune disease as coeliac disease.

For some Authors both CD and ITP share common factors, but since both these diseases are common a coincidental relationship can not be excluded. We report the case of a 2 year old child with CD who presented ITP.

Key words: Coeliac disease, idiopathic thrombocytopenic purpura, case report

RIASSUNTO

La malattia celiaca è una malattia autoimmune, glutine-dipendente, che colpisce il tratto gastrointestinale, caratterizzata da una infiammazione della mucosa intestinale, con conseguente atrofia dei villi e malassorbimento.

Associazioni positive tra malattia celiaca e altre malattia auto-immuni, come la porpora idiopatica trombocitopenica, sono state riportate in diversi studi. La porpora idiopatica trombocitopenica è una malattia autoimmune relativamente frequente così come la malattia celiaca.

Secondo alcuni Autori sia la malattia celiaca che la porpora idiopatica trmobocitopenica condividono fattori comuni, ma poichè entrambe queste malattie sono frequenti una relazione casuale non può essere esclusa.

Riportiamo il caso di un bambino di 2 anni affetto da celiachia che ha presentato porpora idiopatica trombocitopenica.

Parole chiave*: Malattia celiaca, porpora idiopatica trombocitopenica, caso clinico*

Introduction

Coeliac disease (CD) is an autoimmune disease, gluten-dependant, that affects the gastrointestinal tract, characterized by intestinal mucosal inflammation, with following villous atrophy and malabsorption[1]. CD occurs in genetically susceptible individuals who ingest gluten, a protein present in wheat, rye and barley.

Gluten, in these patients, causes an abnormal T cell-mediated immune response.

Approximately 97% of individuals with CD have genetic markers on chromosome 6 called HLA (human leukocyte antigen) DQ2 and HLADQ8, compared with 40% of the general population[2].

The incidence is gradually increasing, and today affects 1:100 people per year in Europe and the United States[3,4].

The symptoms are various, ranging from malabsorption with diarrhea to a spectrum of symptoms and signs.

A positive association between CD and other immune diseases, such as Idiopathic Thrombocytopenic Purpura (ITP) has been reported in several studies[5-14]. In the present report, we describe the case of a 2 year old child affected by CD who presented typical symptoms of ITP.

Case report

We first saw M.M. when he was a 2 year old child. Both parents were healthy and non-consanguineous. The diagnosis of CD was performed based on clinical signs, positive markers and confirmed with biopsy. Ten days before admission to our clinic he had a sore throat and felt unwell.

Over the next 24 h he became febrile and was started an antibiotic therapy. After 3 days he developed purpura first on his lower extremities, and then disseminated all over the body. He was evaluated at another hospital where his platelet count was 48,000/mm^3.

He was then admitted to the Department of Paediatrics, University of Catania. His platelet count was 14,000/mm^3. Ecchymosis and small hemorrhages were found all over the body.

The neurologic exam was normal. TORCH screen, ESR, and CD markers were normal. Free anti-platelet auto-antibodies were found (1/380).

Red blood cells were 5,000,000/mm3, hemoglobin was 13 g/dL, white blood cells were 14,000/mm^3, and platelet count had decreased to 10,000/mm^3.

During hospitalization an infusional therapy with IVIG was started followed by a gradual remission of the symptomatology. After five days the platelet count was 315,000/mm^3.

A week after demission the platelet count was normal and there was no purpura.

Discussion

CD is an autoimmune disorder characterized by an immune response and lack of tolerance to ingested gluten. Atypical forms without gastrointestinal symptoms are likely to be predominant and underdiagnosed[15].

ITP is a relatively frequent autoimmune disease[16, 17], with an incidence of 5/100,000 cases/year[18, 19].

It is possible to distinguish an acute and a chronic form[20]. The acute form is self- limiting and more frequent in children while the chronic form is typical of adults[21]. Several reports are present in literature about the association between CD and ITP since they share a common autoimmune pathogenesis[5-14]. Our young patient showed a typical ITP.

The question is if the correlation between CD and ITP is significantly due to the high frequency of both the conditions.

We report two papers, the first of Olèn et al.[22], and the second of Rischewski et al.[23]. These papers argue the thesis in contrast about considering CD as a major risk factor for the development of ITP.

Olèn et al studied a cohort of almost 15,000 patients with CD and a cohort of 70,000 patients without CD. Individuals with a diagnosis of CD suffered a 2-fold increased risk of later ITP of any kind, and a 3-fold increased risk of chronic ITP.

Moreover, prior ITP was a positive risk factor for subsequent CD. It is noteworthy that the positive association between CD and ITP was seen prior to diagnosis of CD as well as afterwards. Hence Olèn does not believe that one disease causes the other, but that these diseases share common factors.

Both CD and ITP are most likely immune-mediated diseases with autoantigenes playing an important role in their pathogenesis[24, 25].

The vast majority of individuals with CD are HLADQ2 or HLADQ8-positive. Although little is known about HLA in ITP, the few reports on this topic[26] indicate that shared HLA is unlikely to explain the association between CD and ITP.

The increased risk of ITP in CD is due to other shared immunological traits. Recent studies indicate that the innate immune system may play an important role in the pathogenesis of CD[27].

Zanoni et al.[28] reported that many individuals with CD have a subset of transglutaminase antibodies that activate TLR4, which belongs to the family of Toll-like receptors, key players in the innate immune system. It is therefore interesting that TLR4 expression in platelets seems to be a prerequisite for certain forms of thrombocytopenia[29].

Rischewski et al. show different opinion. The Authors studied 21 patients clinically investigated for symptoms of classical CD or non-classical CD, signs or symptoms of associated autoimmune disease apart from ITP, and CD-associated neurological disturbances or other CD associated diseases.

No patients had one of the above-named conditions apart from anemia, present in 1 of the 2 ES patients, and in 2 of the ITP patients. Rischewski et al concluded that neither typical nor atypical CD is a major risk factor for the development of ITP.

Considerations

In our study, we report a single example that can not resolve the dilemma about this association.

The question is whether to consider the association between CD and ITP only a coincidence, in as much as both are frequent, or if the presence of one disease is a risk factor for the other.

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