CASE REPORT

Hyposplenism as a cause of pneumococcal meningoencephalitis in an adult patient with coeliac disease

Iposplenismo come causa di meningoencefalite pneumococcica in un paziente adulto con malattia coeliaca

Paolo Caraceni a,b, Barbara Benazzi a,b, Giacono Caio b, Giacomo Zaccherini a,b, Marco Domenicali a,b, Umberto Volta b,*

a Department of Clinical Medicine, Alma Mater Studiorum University of Bologna, Italy
b Department of Digestive Diseases and Internal Medicine, Azienda Ospedaliera-Universitaria Policlinico Santa Orsola-Malpighi, Bologna, Italy

Received 29 November 2010; accepted 21 February 2011
available online 3 April 2011

KEYWORDS
Coeliac disease;
Hyposplenism;
Streptococcus pneumoniae meningoencephalitis.

Introduction: Coeliac disease can be associated with hyposplenism and splenic atrophy, which may increase the patient’s risk for fatal infections caused by Streptococcus pneumoniae or Pneumococcus. It is general opinion that many more patients with coeliac disease have died from hyposplenism-related infections than those reported in literature.

Case report: A 62-year-old woman with recently diagnosed coeliac disease was hospitalized with high fever, disorientation, and nuchal rigidity. Cerebral computed tomography was negative. Laboratory tests showed an elevated leukocyte count and very high levels of C reactive protein. The cerebrospinal fluid (CSF) contained an increased number of mononuclear cells associated with a low glucose level and high protein concentrations. The CSF culture was positive for Streptococcus pneumoniae. Neurological conditions rapidly deteriorated with the onset of coma, and magnetic resonance imaging of the brain revealed initial signs of encephalitis extending above and below the tentorium. Abdominal ultrasonography disclosed splenic hypotrophy that raised the suspicion of hyposplenism. The diagnosis of hyposplenism was confirmed by demonstration of Howell-Jolly bodies in a peripheral blood smear.

Discussion: This is the first reported case of pneumococcal meningoencephalitis caused by splenic hypofunction in a patient with coeliac disease. When coeliac disease is diagnosed with...
Introduction

Coeliac disease (CD) is an immune-mediated disorder of the small intestine triggered by the ingestion of gluten in genetically susceptible individuals. Although it was initially considered a disorder developing almost exclusively in children or young individuals, it now appears evident that CD can manifest even in adult or advanced ages or remain misdiagnosed for many years due to the lack of symptoms [1].

The clinical manifestations of untreated CD range from significant malabsorption of multiple nutrients, with diarrhea, steatorrhea, weight loss, and the consequences of nutrient depletion (i.e., hypoalbuminemia, anaemia and metabolic bone disease) to the evidence of the malabsorption of a single nutrient (i.e., iron, folate and/or vitamin D deficiency) in the absence of any gastrointestinal symptoms. Furthermore, CD patients carry an increased risk of bacterial infections and sepsis [2]. Because the spleen plays a crucial role in the generation and survival of immunoglobulin (IgM)-producing memory B cells that are responsible for protection against encapsulated bacteria, the hyposplenism and splenic atrophy that may occur in CD patients represent a predisposing factor to the development of fatal infections caused by Streptococcus pneumoniae or Pneumococcus [3]. Although the presence of splenic hypofunction in CD is generally associated with a poor prognosis, its clinical relevance continues to be overlooked. Thus, general opinion holds that many more CD patients may have died from hyposplenism–related infections than those reported in literature [4,5].

We here describe the first known case of an adult woman with a recent CD diagnosis who developed pneumococcal meningocoecephalitis leading to a severe impairment of neurological functions.

Case report

A 62-year-old woman with CD was referred to the Emergency Department of our Hospital for the abrupt onset of high fever and mental disorientation. One month before, she had been diagnosed as having CD due to a positive serology [IgA antiendomysial (EmA) and tissue transglutaminase antibodies (tTGA) at medium-high titre], a typical histological pattern [partial villous atrophy — lesion type 3b according to Marsh-Oberhuber classification [6]] and a clinical picture characterized by abdominal pain, constipation and vomiting. Laboratory tests did not show any abnormality except for a marked thrombocytosis (platelet count: 684.000 mm$^3$). She immediately started to follow a strict gluten-free diet (GFD).

On admission to the Emergency Department, her Glasgow Coma Scale (GCS) was 13/15, and the neurological examination revealed neck stiffness. Hemodynamic and respiratory parameters were stable and within the normal range. Laboratory tests revealed the persistence of raised platelets, an elevated leucocyte count (12.56 x 10$^3$/mmc with 89.1% neutrophils) and C reactive protein (35.26 mg/dl). Renal and hepatic function, serum electrolytes, metabolic parameters and coagulation tests were within normal limits. The analysis of the cerebrospinal fluid (CSF) revealed the prevalence of mononuclear cells associated with low glucose and high protein concentrations, while a computed tomography (CT) scan did not show brain alterations. She was admitted to the Department of Infectious Diseases and treated empirically with ceftriaxone (2 grams b.i.d.) and levofloxacin (500 mg b.i.d.) together with desametasone (4 mg q.i.d.). On the fourth day, the neurological conditions rapidly deteriorated with the onset of coma (GCS 5/15). The patient was transferred to the Intensive Care Unit and then intubated, mechanically ventilated and maintained on the same antibiotic regimen, as the CSF culture was positive for Streptococcus pneumoniae sensitive to levofloxacin and cefotaxime [Minimum Inhibitory Concentration (MIC) was 1 μgr/mL and 0.25 μgr/mL for levofloxacin and cefotaxime, respectively, according to the CLSI reference]. A second CT and a magnetic resonance (MR) of the brain showed initial encephalitis extending both above and below the tentorium (Figure 1). Intravenous immunoglobulins were added to the treatment.

The following day, neurological conditions remained stable, and the patient regained spontaneous breathing and was tracheotomised. A second lumbar puncture was performed on the 8th day of treatment, and the CSF culture was negative. An abdominal ultrasound showed a splenic hypotrophy (diameter, 5.2 cm; area, 10.67 cm$^2$) (Figure 2), raising the
suspicion of a condition of hyposplenism. The finding of
Howell-Jolly bodies in the erythrocytes on a peripheral blood
film confirmed the diagnosis of splenic hypofunction
(Figure 3).

When the patient was transferred to the Department of
Rehabilitation after 17 days of stay in the Intensive Care Unit,
the neurological conditions were not improved (GCS 5/15),
while the cardiovascular and respiratory functions were
normal. A third CT scan revealed the persistence of the
neurological lesions. The patient underwent vaccination with
a pneumococcal conjugate vaccine in order to prevent other
pneumococcal infections.

At present (after two months of physical rehabilitation),
her clinical conditions have significantly improved, and the
patient has partially regained her motor autonomy with
assisted walking, although her mental function is still signi-
ficantly compromised. The relatives of the patient gave
written informed consent to the publication of the present
case report.

Discussion

Although some cases of overwhelming pneumococcal infec-
tion and sepsis in patients with CD and hyposplenism have
already been reported [4,5], we describe, to the best of our
knowledge, the first case of pneumococcal meningoencepha-
litis in an adult patient with sprue and hyposplenism.

Splenic hypofunction has been classified as a complication
of CD predisposing the patient to autoimmunity, lymphoma
and pneumococcal septicaemia [1]. The occurrence of hypo-
splenism in CD, which can sometimes manifest with spleen
atrophy, is very high with a prevalence varying from 20% to
60% in the different series of patients studied and is much
more frequent in adults than in children [3,7–9]. In CD
patients, hyposplenism appears to be closely related to
the development of autoimmune disorders and it is found
in more than 50% of CD patients with insulin-dependent
diabetes mellitus, autoimmune thyroiditis and connective
tissue disorders. Moreover, splenic hypofunction has been
reported in 80% of CD patients with lymphoma, refractory
sprue or ulcerative jejuno-ileitis. In CD patients without
associated autoimmune disease and the above-mentioned
life-threatening complications, the prevalence of hyposple-
nism is far lower (19%) [3].

Splenic hypofunction and spleen atrophy predispose
the patient to severe infections because the spleen plays a
crucial role in the generation and survival of IgM-producing
memory B cells that are responsible for protection against
infection by encapsulated bacteria such as Pneumococcus
[3]. Although the epidemiological data on bacterial infec-
tions and sprue are still scarce, it is widely accepted that CD
patients present a greater risk of pneumococcal infection
than healthy individuals, although the risk is not as high as in
those with splenectomy [10]. Thus, patients who are sple-
nectomised or have impaired splenic function should be
immunised by the administration of a pneumococcal conju-
gate vaccine [1,3,10].

The pathogenesis of splenic hypofunction in CD remains
unknown. The duration of exposure to gluten due to a marked
delay in CD diagnosis is considered the main factor influen-
ting the occurrence of hyposplenism and its severity [3]. In
some patients, splenic hypofunction is related to generalized
lymph node atrophy, and it has been suggested that it is an
expression of a more widespread atrophy of the lympho-
reticular system [11]. This hypothesis is not supported by the
demonstration that Kupffer cell function in patients with
functional hyposplenism, assessed by the clearance of micro-
aggregated albumin, was similar to that of control splenecto-
tomised subjects [12]. Increased levels of circulating immune
complexes, frequently found in CD, have been considered a
possible cause of hyposplenism through a functional blockade
of the splenic reticulo-endothelial system, but the very low
prevalence of hyposplenism in childhood CD, which is cha-
racterized by the highest levels of immune complexes, does
not support this hypothesis [13].

Splenic function must be assessed with appropriate tests.
A commonly used method is to count “pitted” erythrocytes
(“red cells with membrane excavation”) by interference

---

**Figure 2** Abdominal ultrasound showing reduced spleen size
(diameter, 5.2 cm; area, 10.67 cm²).

**Figure 3** Peripheral blood smear showing the presence of
Howell-Jolly bodies (see arrows) in the erythrocytes (character-
istic features of functional hyposplenism).
contrast microscopy [14]. A pitted erythrocyte count of more than 2% to 4% is consistent with a diagnosis of hyposplenism. Unfortunately, this test is available only in a few laboratories. Alternatively, the finding of Howell-Jolly bodies in the erythrocytes on a peripheral blood smear is an important clue to the diagnosis of functional hyposplenism [15]. However, they may not be evident in patients with milder forms of hyposplenism. Splenic hypofunction can also be demonstrated by performing a 99 tc-labelled radiocolloid scan of the spleen [3]. Moreover, the finding of a marked reduction of the spleen size in a routine abdominal ultrasound is consistent with a suspicion of hyposplenism that should be confirmed by the above-mentioned procedures.

Regarding this patient, CD was diagnosed in the 7th decade of age suggesting a very prolonged exposure to gluten as a possible explanation of splenic hypofunction. The only abnormality of routine tests was thrombocytosis; in CD, this is more frequently secondary to inflammatory mediators (with an expected normalization after GFD) or, less frequently, secondary to iron deficiency or an expression of splenic hypofunction [9]. Splenic hypofunction was not ruled out in our patient at the time of CD diagnosis, even though it seemed highly improbable due to the good general condition of the patient, excluding major CD complications, and the absence of associated autoimmune disorders, which are possible clues of splenic hypofunction. The rapid occurrence of pneumococcal septicemia with meningoencephalitis did not allow us to monitor the behaviour of the thrombocytosis and to investigate for spleen dysfunction. The suspicion of a coexistent hyposplenism in our patient became evident when the CSF turned out to be positive for Streptococcus pneumoniae, and an abdominal ultrasound showed a reduced size of the spleen. The presence of functional hyposplenism was then confirmed by the finding of Howell-Jolly bodies in the blood smear.

This case report should teach us that all patients diagnosed as coeliacs in the adult age, and particularly in the elderly, should be evaluated for the possible presence of hyposplenism, even when in the clinical picture, the absence of associated autoimmune disorders and the normality of laboratory tests do not support this complication. To assess this CD complication, it is enough to verify the presence of Howell-Jolly bodies in a peripheral blood smear, keeping in mind that this procedure must be specifically requested to hematologists.

Because pneumococcal septicemia in its different clinical manifestations is life-threatening, in all cases with well-documented hyposplenism, it is mandatory to perform immediate vaccination with a pneumococcal conjugate in order to protect CD patients from pneumococcal sepsis.

**Conflict of interest statement**

The authors have no conflict of interest to declare.

**Acknowledgements**

The authors wish to thank Dr Nicola Vianelli from the Haematology Unit, Dr Mariangela Taricco and Dr Mario Gaiba from the Rehabilitation Unit and Prof. Pierluigi Viale from the Infectious Disease Unit of St. Orsola-Malpighi Hospital for their helpful assistance in the evaluation and treatment of the patient described in this paper.

**References**