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Unexplained infertility as primary presentation of celiac disease, a case report

P. Sirohi, Akhil Gupta*, P. Sameja, M. Meena, Alok Gehlot

Department of Medicine, S. P. Medical College, Bikaner, Rajasthan, India.

Correspondence Address: *Dr. Akhil Gupta, Department of Medicine, S. P. Medical College, Bikaner, Rajasthan, India.

Abstract

Introduction: Celiac sprue (gluten sensitive enteropathy) is an autoimmune disease which is hereditary and its pathology mainly bases on immunologic intolerance to gluten. It has a vast variety of signs and symptoms and its clinical features range from a silent disease to a typical gastrointestinal disorder. In this study we reviewed and summarized some other related issues about this disease and its relation with infertility

Case report: Gastrointestinal features are common features of coeliac disease but here we report a 21 year old Indian female presented with primary infertility with endoscopic feature suggestive of celiac disease, ruling out other causes of infertility, the cause of her infertility was related to celiac disease

Conclusion: Celiac disease should be considered as a cause of infertility in patients with no established etiology for infertility.

Keywords: Anemia, primary infertility, celiac disease

Introduction

Celiac disease (CD) is an autoimmune disorder characterized by inflammation of the small intestine's absorption surface, induced in genetically predisposed individuals by ingestion of wheat, rye or barley(5). Specific peptides of these grains, collectively called gluten, elicit an inappropriate immune response that damages the surface of the small intestine, causing malabsorption of nutrients. . In some patients, extra-intestinal or autoimmune changes may occur, e.g. hepatobiliary[4], neurological[3], or endocrine disorders, such as hypothyroidism and insulin-dependent diabetes in children. Of particular interest has been the effect of celiac disease and its treatment on fertility and pregnancy[6]. In recent years, there has been an increased recognition of possible changes in male and female fertility in celiac disease as well as the potential for adverse outcomes in pregnancy and the post-partum period that may lead to miscarriages and premature low birth weight fetal delivery, following table (table I) shows the reproductive changes in coeliac disease in female and male.

Case report

A 21 year old Indian woman presented with primary amenorrhoea, diminished secondary sexual character, asthenia, histoty of weight loss and chronic diarrhea, she had no past

history of any neurologic diseases such as anxiety or depression.

Table I.

Altered female fertility	Delayed onset of menarche, amenorrhea, early menopause, recurrent abortions, reduced rates of pregnancy
Altered male fertility	Gonadal dysfunction, altered sperm morphology and motility, reduced sexual activity

Any clinical disease, pelvic or abdominal surgery, and extensive weight loss and drug or alcohol abuse, there was no significant family history. On admission her Hgb was 4.2g/dl (normal range:11-15gm/dl), RDW was 39% (normal range :11.3-15.5%)and MCV was 63.6fl (normal range :79-97fl), reticulocyte count was low at 9000/mm3 (normal range:25000-100000), TIBC of 486 micro gram/dl(normal range: 250-450 micro gram/dl), percentage saturation of transferring been 5% with ferritin level of<3ng/ml (normal range:10-100ng/dl) ,serum iron level was reduced to 21micro gram/dl (normal range:37-173 micro gram/dl). Erythropoietin level was elevated at 8956mu/ml (normal range:0-27 mu/ml), her platelet count and WBC count was normal, on bone marrow core section ring sideroblast was not found and bone marrow iron store showed decreased amount of storage iron, upper GI endoscopy was performed showing loss of folds in the second part of duodenum and a biopsy from second part of duodenum showed intraepithelial lymphocytes, flatttenimg of duodenal mucosa with lymphoplasmacytic infiltrationin lamina propria and crypt hyperplasia(Marsh class3),Immunoglobulin A(IgA) anti tissue transglutaminase antibodies (IgA-tTG) was markedly elevated to more than 300microns /ml, BMD study shows osteopenia. Laboratory findings included: serum FSH, serum LH, serum prolactin, TSH, testosterone, progesterone and estradiol which all of them were at the normal range. Diagnostic laparoscopy showed no signs of tubal adhesion or endometriosis. Considering iron deficiency anemia, intestinal signs. Serological and tissue biopsy evidence coeliac disease with primary infertility was diagnosed. She received a complete gluten free diet and after 5 months all her clinical features including; diarrhea, flatulence and anemia were eradicated and mensturation occurred.

Discussion

Gluten sensitive enteropathy known as celiac disease (CD) or celiac sprue is an autoimmune disease with a prevalence varying worldwide (of 1/270 in Finland to 1/5000 in North America (7). Manifestations of CD range from no symptoms to overt malabsorption with involvement of multiple organ systems and an increased risk of some malignancies (11). Some common and rare signs and symptoms of CD are shown in table II.

Celiac disease continues to be increasingly recognized as a clinically silent disorder with limited or few intestinal symptoms, such as mild diarrhea. Often, females with reproductive disorders or pregnancy complications have no overt symptoms, or at most, fatigue associated with iron-deficiency anemia. As a result, reduced fertility in females or changes that include delayed menarche, amenorrhea and early menopause may conceivably be the initial clinical feature that ultimately results in a diagnosis of celiac disease. As serological screening has resulted in an appreciation that celiac disease may occur in up to 1%-2% of the general population, it is not surprising that this disorder is more readily detected in young women of childbearing age. Indeed, young women are still the most common group diagnosed with celiac disease.

Table II.

- Abdominal pain and discomfort (diarrhea, IBS, flatulence, borborygmus and vomiting)
- Anemia (iron, vitamin B12 and folate deficiency)
- Arthralgia and arthritis
- Bone pain (osteoporosis and osteopenia, vitamin D and calcium deficiency)
- Dermatitis herpetiform
- Elevated liver enzymes, liver failure
- Fatigue and weakness
- Growth failure in children
- Gynecologic manifestations: delayed menarche, menstrual discomforts, premature menopause, recurrent abortion and infertility.
- Neurological dysfunction (such as depression, epilepsy, migraine and ataxia)
- Vitamin and nutrients deficiency related disorders (night blindness, edema, bleeding and hematoma, peripheral neuropathy, muscle cramps, etc)
- Weight loss

If changes in fertility can be documented in celiac disease, these may reflect underlying autoimmune complications of celiac disease or the negative nutritional effects of untreated disease.

In many studies including Westerberg *et al* it is shown that CD prevalence rate is somehow more than estimations because of its silent and subtle types (12). In a study by Collin *et al* it is suggested that in unexplained infertility, silent celiac disease should be screened (2). Collin *et al* showed that the prevalence of CD among unexplained infertile cases (4.1%) is significantly higher than control group (0.0%) (p=0.02). Also, in this study it is shown that iron deficiency anemia is an important associated condition in patient with CD and unexplained infertility. Additionally, osteopenia and osteoporosis as common complications of CD (9-1) put an especial importance on the time of diagnosis and treatment of suspicious cases.

The diagnosis of CD is based on clinical suspicion plus positive serological tests and positive histological findings (12). The standard serologic tests which include IgA endomysial and tTG antibodies, according to many studies have a sensitivity and specificity of more than 95% (8). An algorithm for step by step approach to a suspicious patient with possible CD is shown in figure 3. The important point is that serologic and biopsy samples should be taken before starting a gluten free diet.

Finally all the authors believe that complete and lifelong gluten free diet is the only treatment of CD. Most of the dietary gluten is presented in wheat, rye and barely (10). Like our case, in most of the studies, it is shown that all the complications of celiac patients can be completely cured by following a long life gluten-free diet

Conclusion

Screening for silent or subtle CD especially among suspicious cases such as unexplained infertility seems to be a cost effective action and in time administration of a gluten-free diet can lead to an almost complete cure.

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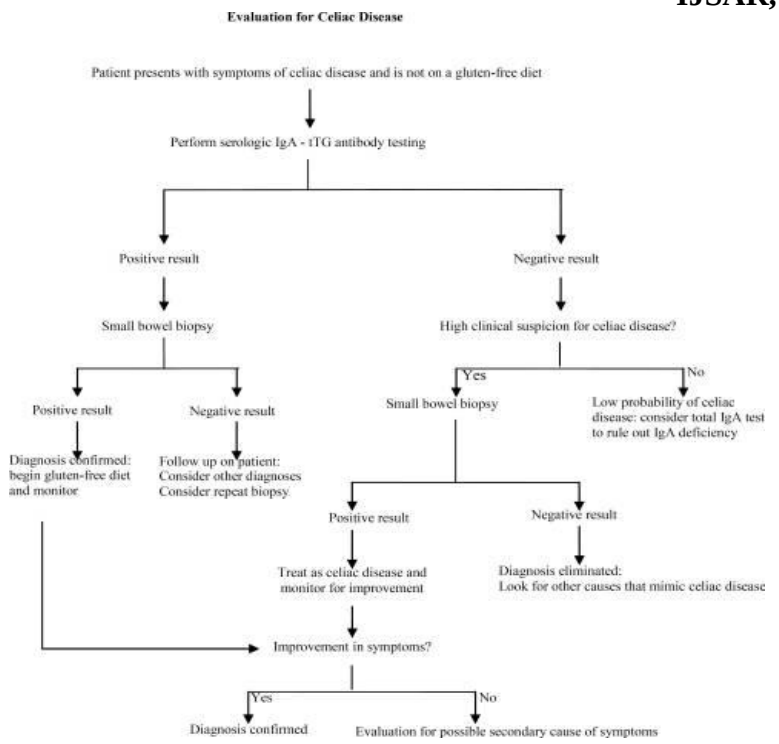

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