

CROHN'S DISEASE OCULAR MANIFESTATIONS

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Summary. Crohn's disease is an inflammatory bowel disease which causes inflammation of the digestive tract. Crohn's disease most frequently affects the ileum and the colon. In the active stage of the disease signs and symptoms may include diarrhea, abdominal pain and cramping, blood in the stools, reduced appetite and weight loss. In patients with severe Crohn's disease the following signs and symptoms may be observed: fever, fatigue, arthritis, eye inflammation, oral ulcers, skin disorders, inflammation of the liver or bile ducts or delayed growth. Heredity and dysfunctions of the immune system are considered to cause the development of Crohn's disease. About 10% of people with inflammatory bowel disease have also ocular problems. The most common ocular manifestations of Crohn's disease are uveitis, iritis, episcleritis, keratopathy, keratoconjunctivitis and retinal vasculitis. Untreated uveitis may cause glaucoma and vision loss. Uveitis and iritis are four times more common in women than in men. In patients in the active stage of the disease, episcleritis also flares. Symptoms of episcleritis include inflammation, bright red spots on the sclera and localized pain. Keratoconjunctivitis in Crohn's disease is caused by decreased tear production or increased tear film evaporation. Dry eyes can cause itching, burning or infection. Keratopathy usually causes no pain or vision loss, therefore in most cases no treatment is needed. In retinal vasculitis tortuosity of retinal veins, retinal edema at the posterior pole and intraretinal blood near blood vessels are observed. Intravenous fluorescein angiography shows intraretinal neovascularisation and haemorrhage in the posterior pole.

Key words: *Crohn's disease, ocular manifestations*

Crohn's disease is an inflammatory bowel disease. It causes inflammation of the lining of the digestive tract, which can lead to abdominal pain, severe diarrhea, and malnutrition. Inflammation caused by Crohn's disease can affect various areas of the gastrointestinal tract [1].

Inflammation often spreads deeper into the layers of the affected tissue of the colon. Similar to ulcerative colitis, Crohn's disease can be both painful and debilitating, and sometimes can lead to life-threatening complications.

CROHN'S DISEASE SYMPTOMS

In some patients the disease affects the small intestine only, while in others it can affect the colon. The most commonly affected organs of Crohn's disease are the ileum and the colon. Inflammation can affect only the intestinal wall, which may lead to scarring and can spread through the wall of the intestine [2].

Signs and symptoms of the disease may be mild or severe, developing gradually or suddenly. Patients may have periods of remission with no signs or symptoms [3]. The most common signs and symptoms of the active stage of the disease are:

- Diarrhea. Due to inflammation of the cells in the affected areas of the intestine large quantities of water and salt are collected. Because the colon cannot completely absorb this excess fluid patients develop diarrhea. Intensified intestinal cramping can also cause diarrhea. Diarrhea is a common manifestation of Crohn's disease.

- Abdominal pain and cramping. Inflammation and ulceration can lead to swelling of the walls of parts of the intestines and thickening of scar tissue. This affects the smooth movement of the food through the digestive tract and may lead to pain and cramping. Mild stage of Crohn's disease usually causes mild intestinal discomfort while the severe stage causes severe pain accompanied by nausea and vomiting.

- Blood in the stool. The food which passes through the gastrointestinal tract may cause bleeding of the inflamed tissue. Faeces may be tinged with dark red blood. There may be also occult bleeding.

- Ulcers. Crohn's disease may cause small wounds on intestinal surface which can grow and penetrate deeply in the intestinal wall. Patients may have oral ulcers similar to canker sores [4].

- Reduced appetite and weight loss. Abdominal pain, cramping and the inflammatory reaction of the walls of the intestine can affect appetite, digestion and absorption of food.

Patients with severe Crohn's disease may experience the following signs and symptoms [5]:

- Fever;
- Fatigue;
- Arthritis;
- Eye inflammation;
- Oral ulcers;
- Skin problems;
- Inflammation of the liver or bile ducts;
- Delayed growth.

CAUSES OF CROHN'S DISEASE

The etiology of Crohn's disease remains unknown. It is considered that a number of factors, such as inheritance and dysfunction of the immune system are involved in the development of Crohn's disease.

- Immune system. It is possible that a virus or a bacterium can cause Crohn's disease. When the immune system attempts to fight the invasion of microorganisms, impaired immune response makes the immune system attack the cells of the digestive tract at the same time [6].

- Heredity. Crohn's disease is more common in patients who have a close relative with the same disease. It is believed that one or more genes may contribute to the susceptibility to Crohn's disease. Despite that fact, most people with Crohn's disease do not have a family history of the disease.

CROHN'S DISEASE OCULAR MANIFESTATIONS

Approximately 10% of people with inflammatory bowel disease experience ocular disorders as well. Most of them are treatable and do not cause a vision loss [7].

The tissues of the eye are very similar to those in the other parts of the body, therefore the inflammatory diseases which affect the other organs, such as intestines in Crohn's disease, affect the eye also.

Since eyes are very sensitive organs, ocular disorders in Crohn's disease may often manifest themselves before intestinal inflammatory symptoms.

Some therapeutic methods of Crohn's disease may worsen eye problems. For instance, oral steroids are often used for treatment of the disease, but they can cause cataracts or glaucoma.

The most common ocular problems associated with Crohn's disease include:

UVEITIS AND IRITIS

Uveitis is one of the most common ocular problems in Crohn's disease. It is an inflammation of the uvea, which causes swelling of the retina and the uvea leading to blurred vision.

Untreated uveitis may eventually lead to glaucoma and vision loss [8].

Iritis is a painful inflammation of the iris. Both of these conditions often occur in Crohn's disease, but they are less common than scleritis. Uveitis and iritis are four times more common in women than in men. Their treatment includes steroid eye drops or oral steroids that reduce the inflammation.

EPISCLERITIS

It is a common ocular complication of Crohn's disease. In active stage of Crohn's disease episcleritis also flares. Symptoms of episcleritis include inflammation, bright red spots on the sclera and localized pain [9].

KERATOCONJUNCTIVITIS

This ocular complication associated with Crohn's disease is caused by a decreased tear production and increased tear film evaporation. Dry eyes can cause itching, burning or infection.

Many people with Crohn's disease experience malabsorption of nutrients, including vitamin A. Vitamin A deficiency may contribute to the onset of dry eye syndrome or night blindness. The treatment of dry eye syndrome includes artificial tears and additives of vitamin A.

KERATOPATHY

Keratopathy is an abnormality of the cornea, which is also observed in Crohn's disease [10]. Keratopathy usually does not cause pain or vision loss and in most cases no treatment is needed.

RETINAL VASCULITIS IN CROHN'S DISEASE

Although systemic vasculitis can be a complication of inflammatory bowel disease, which affects different parts of the body (skin, eyes, brain, and lung), retinal vasculitis in Crohn's disease is not very common [11]. A 26-year-old woman examined with biopsy is diagnosed with Crohn's disease. She presented with severe bilateral retinal arteritis and phlebitis with vision loss.

Pathogenic mechanism of retina injury may be either vasculitis or thrombotic occlusion of vessels. The diagnosis of retinal vasculitis is performed with fluorescein angiography [12].

A 26-year-old woman, who has been suffering from Crohn's disease for seven years, was admitted to hospital after five months of abdominal pain associated with bloody diarrhea, vomiting, fever and weight loss. Her body temperature at the admission was 37.2°C.

The patient experienced severe vision loss. Visual acuity of her right eye was 0.1 and of the left eye – 0.6. Intraocular pressure of the right eye was 13 mmHg and 14 mmHg of the left eye. By fundoscopy scattered cotton-wool spots in both eyes are observed [13].

One cotton-wool spot is observed in the right eye macula. The retinal veins were tortuous. There was observed retina edema around the posterior pole and intraretinal blood near the some vessels. Later on uveitis and vitritis developed accompanied with preretinal hemorrhage. Intravenous fluorescein angiography showed intraretinal neovascularisation and haemorrhage in the posterior pole.

Cyclophosphamide (100 mg/day) and prednisone (50 mg/day) were applied, but only improvement of uveitis and vitritis was observed. There was no improvement in retinal vasculitis [14].

Six weeks later, the patient could only finger count at 3 m with the right eye. Visual acuity of the left eye remained unchanged.

In Crohn's disease and ulcerative colitis, vasculitis can affect many tissues (of the retina, skin, brain, bowel and lungs). One of the possible pathogenic mechanisms of Crohn's disease is an inflammatory microvascular occlusion associated with vasculitis [15]. The pathogenic sequence of events at Crohn's disease may include: vascular injury, focal arthritis, fibrin deposition and arterial occlusion or neo-vascularization [16]. Granulomatous vasculitis is suggested to result from tissue injury. Granulomatous inflammation is associated with focal destruction of the blood vessels walls, adhesion of the chronic inflammatory cells to the luminal surface of the lesion and fibrin deposition.

Retinal arterial occlusion is also observed in patients with Crohn's disease, but fluorescein angiography did not show evidence of inherent retinal vascular disease [17]. In a patient examined, the lack of prior systemic manifestation of thromboembolic phenomena, the normal coagulation studies and platelet count on the onset of acute vision loss did not suggest thromboembolic manifestations. Furthermore, by fluorescein angiography the patient was diagnosed with retinal vasculitis [18].

In this case, the inflammatory bowel disease complication manifests as severe vision loss caused by severe, bilateral, obliterative and proliferative retinal vasculitis, wherein the arteries were affected predominantly [19]. There were cotton-wool patches in the eye, which suggest for tissue ischemia, hemorrhage and neovascularization.

INNOVATIVE METHODS IN CROHN'S DISEASE TREATMENT

Stem cell transplantation

In children with immune deficiency the severe stage of Crohn's disease can begin before the age of 5 years.

In some cases stem cell transplantation may be used in the treatment. Transplantation can restore the missing elements of child's immune system or replace the dysfunctioning ones [20].

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