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Autoimmune Hepatitis: Best Treatment Practices

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UND FNP program

PERMISSION

Title

Department Nursing

Degree Master of Science

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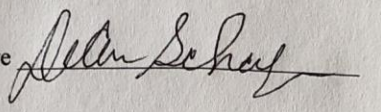
Signature 

Date 4.28.20

Abstract

This literature review was completed after the Objective Structured Clinical Exam (OSCE) exam was passed. The assigned case study was analyzed and the topic of Autoimmune Hepatitis was selected. A literature search was completed using the databases of PubMed and CINAHL. Keywords used included "autoimmune hepatitis treatment", publication dates were between 2015-2020 and no limits were added. Recommendations from Mayo Clinic, National Institute of Health (NIH), and Medscape were assessed.

The information in these articles were all similar for treatment recommendations for first- and second-line treatment, however there are new and advancing treatments being studied as autoimmune hepatitis is not fully understood.

Autoimmune Hepatitis: Best Treatment Practices

Background

Autoimmune hepatitis (AIH) is a chronic inflammatory disease of the liver of unknown cause that can affect children and adults (Lowe & John, 2018). The disease is not fully understood. It is a chronic illness in which a person's immune system attacks hepatocytes, causing inflammation and hepatocellular necrosis (Pullen, 2019).

Autoimmune hepatitis peaks in adolescence and at 30-45 years of age, but it can affect children and adults of all ages(Liberal et al., 2016). It is also more commonly diagnosed in women than in men. In the United States, women are affected 3.5 times more than men, and 76% of patients in a Swedish study were women (Lowe & John, 2018). Approximately 25%-50% of patients with AIH have overlapping autoimmune diseases, such as Hashimoto's thyroiditis, Graves' disease, systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, Sjögren syndrome, and diabetes mellitus (Pullen, 2019).

Research suggests certain viral infections, including viral hepatitis, cytomegalovirus, Epstein-Barr virus, measles virus, and herpes simplex virus, may interfere with immune system tolerance against hepatic autoantigens and trigger AIH (Pullen, 2019). Diagnosis is one of exclusion for any other causes of hepatitis and certain immune markers. Drug-induced liver injury is also an important consideration in the differential diagnosis (Sahebjam & Vierling, 2015).

In this literature review, a case report of a 47-year-old female who came to the clinic with complains of abdominal pain will be reviewed. She had no previous surgical history and she still had her gallbladder and appendix. In reviewing the lab work and ultrasound, it was revealed that

she had cholecystitis, however differentials included hepatitis and more specifically autoimmune hepatitis. The focus of this literature review is to look at recommendations that are evidence based regarding best treatment for autoimmune hepatitis.

Case Report

Chief Complaint: 47-year-old female, comes to the clinic today with complaints of abdominal pain.

HPI: The patient developed abdominal pain after having supper last evening. She had two glasses of wine and ate a meal of spaghetti with meat sauce. Within an hour after eating supper she developed periumbilical pain and right lower quadrant pain. Pain was worsened when lying flat and pain was colicky, described as coming and going. She has never had this pain in the past. She tried to take some pepto bismol when she developed the pain but it has not helped. She has vomited twice since developing the abdominal pain. Denies having diarrhea. Last menstrual period was one week ago. She is sexually active and uses condoms as birth control. Denies and dysuria.

Past Medical History:

Medical: two pregnancies with vaginal deliveries

Surgical: no surgeries

Medications: does not take medications

Allergies: NKDA

Social History: She is married and lives with her husband. She has two grown children. She has never smoked cigarettes or used recreational drugs. She has two glasses of wine per night with supper. She does not exercise. She works full time as a secretary.

ROS

General: alert female guarding her abdomen, denies nausea, fever or chills

HEENT: negative

Cardiovascular: denies chest pain or palpitations

Respiratory: denies shortness of breath

Abdominal: reports periumbilical and right lower quadrant pain

Musculoskeletal: full range of motion to all extremities, denies pain or discomfort

Neurologic: denies headaches, syncope or seizures.

Physical Examination

General: alert, well developed female. Appears in mild distress. Answers questions appropriately

Vitals: T99.5F, BP 116/70, HR 102, Resp. 20, BMI 30 kg/m2

HEENT: PERRLA, Full ROM to neck, trachea midline, Thyroid within normal limits, no lymphadenopathy

Respiratory: lung sounds are clear bilaterally

Cardiovascular: S1S2 regular without murmurs, no peripheral edema noted.

Abdominal: periumbilical pain and right lower quadrant pain. Pain is worsened when pt is lying flat. Worse with percussion and light palpation. The pain radiates up to the right upper quadrant with palpation. Murphy's sign is positive.

Musculoskeletal: Full ROM noted to all extremities.

Neurological: alert, oriented, normal cognition

Differential diagnosis

Cholecystitis, biliary pancreatitis, choledocholithiasis, acute cholangitis, hepatitis, GERD, gastritis, gastrointestinal ulcers, nephrolithiasis, posterior wall MI, cystitis, appendicitis

Labs/Imaging:

1. CBC is unremarkable
2. CMP AST 76, ALT 103
3. Amylase, lipase unremarkable
4. Alk phos, GGT, Bili all unremarkable.
5. Ultrasound of the abdomen showed an enlarged liver.
6. ANA and SMA pending

Conclusion:

Lab results and ultrasound consistent with hepatitis. Awaiting send out labs ANA, SMA. If these results are positive, will order a liver biopsy to confirm diagnosis. Pt is not a heavy drinker and does not take medications that would cause elevated liver enzymes.

Recommendations:

Stop any and all alcohol intake. Do not take acetaminophen or NSAIDs.

Plan: 1. Will call the patient with lab results.

2. Return to clinic in one month with labs prior to appointment.

Literature Review

There is a fairly common consensus regarding the diagnosis and treatment of autoimmune hepatitis, although there is just slight variation. Diagnosis requires a rule out of

other causes of hepatitis and then positive autoimmune tests. Recommended treatment is often prednisone and azathioprine, however there are certain situations to consider. Vitamin D supplementation is being investigated to assist in the treatment of the disease.

Diagnosis

There is no single diagnostic test for AIH; therefore, diagnosis is based upon several indicative clinical, serological, biochemical and histological findings and the presence of other causes of liver disease must also be excluded (Liberal et al., 2016). Some of the other causes include drug induced liver injury; these include the antibiotics nitrofurantoin and minocycline, as well as statins, and the anti-TNF agents adalimumab and infliximab (Liberal et al., 2016). There is a simplified scoring system available to test for AIH. The system, which only uses four parameters (hypergammaglobulinemia, autoantibodies, histology and exclusion of viral hepatitis), has since received external validation (Liberal et al., 2016). A liver biopsy should be performed in all patients to make a diagnosis of AIH and before starting treatment (Lowe & John, 2018)

Treatment

Absolute indications for treatment are a serum AST greater than 10 times the upper limit of normal or an AST greater than 5 times the upper limit of normal in conjunction with a serum globulin level greater than 2 times the upper limit of normal (Cropley & Weltman, 2017). Furthermore, incapavitating systemic symptoms such as fatigue and arthralgia are also considered absolute indications for treatment (Cropley & Weltman, 2017) The goal of AIH

treatment is to induce and maintain complete suppression of the inflammatory activity, thus preventing progression to cirrhosis and liver decompensation (Liberal et al., 2016)

The gold-standard treatment for autoimmune hepatitis (AIH) is a prednisone/azathioprine combination, however subgroups of patients may be unresponsive to this treatment (De Lemos-Bonotto, Valle-Tovo, Costabeber, Mattos, & Azeredo-da-Silva, 2018). The reason that the combination therapy is preferred is due to the fact that lower dosages of prednisone can be used when combined with Azathioprine as many patients are not good candidates for long term high dose prednisone(Liberal et al., 2016). Other options of treatment include prednisone therapy alone, budesonide alone, calcineurin inhibitors, cyclosporine, and tacrolimus. The last three are all used in difficult to treat cases. On the horizon is vitamin D therapy.

The goal of drug therapy is complete remission of autoimmune hepatitis. The average time this is taking to achieve a response is 2 years, however once the patient has gone into remission it does not mean that they are cured for life. AIH can reoccur, so it is common that patients be continued on Azathioprine for the rest of their lives.

Prednisone

Prednisone is a corticosteroid used to suppress humoral immune response and leukocyte infiltration at the sites of liver inflammation (Pullen, 2019) Major side effects of prednisone include mental status changes (nervousness, hyperactivity, irritation, agitation, distraction, insomnia, depression), increased appetite, sweating, flushing, headache, hypertension, fluid retention, weight gain, osteoporosis/increased fracture risks, cataracts, glaucoma, infection, and acceleration of atherosclerotic heart disease (Pullen, 2019). If doing combination therapy with prednisone and azathioprine, the treatment regimen includes an induction phase and a

maintenance phase. During the 4-week induction phase, prednisone or prednisolone, 30mg daily is administered for one week, then the dose is reduced to 20mg daily for 1 week and then 15mg daily for two weeks; after 4 weeks of induction, the dose of prednisone or prednisolone is adjusted to 10mg daily (Czaja, 2016). If doing monotherapy with prednisone or prednisolone, the dosage is 60mg daily for one week, then 40mg daily for one week, then 30mg daily for two weeks; after 4 weeks of induction, the dose of prednisone or prednisolone is reduced to 20mg daily and the regimen is maintained until resolution of clinical, laboratory and histological findings (Czaja, 2016).

There are several things that the patient needs to be educated on in regards to using high dose and/or long-term prednisone use. Patients need to know that they cannot abruptly stop taking prednisone(Pullen, 2019). They need to make sure that they have all their vaccinations up to date including pneumonia and influenza and to stay away from sick people as prednisone can affect a person's immune system(Pullen, 2019). Patients need to eat a healthy diet which is low salt because prednisone makes a person retain sodium(Pullen, 2019). Prednisone also makes people prone to bleeding, so patients need to report this to their providers. Take vitamin D supplementation and perform weight bearing activities as prednisone decreases bone formation(Pullen, 2019).

Azathioprine

Azathioprine is an immunosuppressant used to inhibit T-cell activation and suppress the immune system to decrease inflammation in the liver; also administered to prevent organ transplantation rejection (Pullen, 2019). Major side effects of azathioprine are dependent upon dosage and length of treatment time and these include infection, bone marrow suppression,

bleeding, malignancies, hepatotoxicity, skin rashes, nausea, photosensitivity and infertility (Pullen, 2019, p. 46). When using azathioprine in combination therapy with prednisone, the dosage is 50mg daily during both the induction and maintenance phases. If the serum aminotransferase level increase after discontinuing the maintenance dosages of prednisone and azathioprine, then azathioprine will need to be used long term. A long-term maintenance regimen can then be instituted after normalization of liver tests by increasing the dose of azathioprine to 2mg/kg/day and gradually withdrawing the corticosteroid (Czaja, 2016)

Patient education is of vital importance when they are being treated with azathioprine. They are at a much higher risk of community acquired illness as azathioprine is an immunosuppressant, so they need to make sure they have their vaccinations up to date including pneumonia and influenza and they need to avoid anyone who is sick. It can be very irritating to the stomach so it should be taken with food to prevent nausea. Report and skin lesions or lumps as this may be a sign of malignancy (Pullen, 2019). Patients should be educated prior to starting azathioprine therapy that it may have an effect on their fertility.

Budesonide

Budesonide is a steroid that is avidly extracted from portal venous blood by the liver, this first pass hepatic extraction significantly reduces entry of budesonide into the systemic circulation, minimizing the risk of steroid side effects (Sahebjam & Vierling, 2015). Budesonide is used in combination therapy with azathioprine when prednisone is not an option due to the side effects that prednisone has on patients. Budesonide can be given at doses of 3mg twice or three times daily in combination with azathioprine (Cropley & Weltman, 2017). Budesonide is much more expensive than prednisone.

Other Alternatives

Vitamin D therapy has shown some promise in regard to autoimmune diseases. In addition to the classical effects of vitamin D which include calcium homeostasis and bone metabolism, there are non-classical effects which include immunomodulatory, anti-inflammatory, anti-fibrotic, and anti-oxidative(Czaja & Montano-Loza, 2018). The combined inhibitory effects of vitamin D could reduce the T cell-mediated adaptive immune response, promote immunosuppression, and reduce the activity of immune-mediated liver disease (Czaja & Montano-Loza, 2018). There are, however, no recommendations as of yet as to what a safe dosage of vitamin D may be in managing AIH.

Calcineurin inhibitors, cyclosporine and tacrolimus, have been used as a rescue treatment for the difficult-to-treat cases of AIH (Liberal et al., 2016). Before alternative therapies are contemplated, however, patients who fail to respond to standard regimens should be tried on higher doses of steroids (up to 100mg/day) and/or azathioprine (up to 150 mg/day) (Liberal et al., 2016).

Summary Recommendations

- Autoimmune hepatitis is a disease that affects young and old alike
- All other forms and causes of hepatitis need to be ruled out prior to the diagnosis of autoimmune hepatitis.
- Liver biopsy is the final step in diagnosing autoimmune hepatitis.
- Gold standard of treatment is prednisone/azathioprine combination therapy.
- Length of treatment before remission is about 2 years.

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