CASE REPORT

Sydenham Chorea On Indonesian 10 Years Old Boy Caused By Rheumatic Heart Disease : Case Report And Literature Review

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ABSTRACT

Sydenham's chorea (SC) is one of the manifestations of rheumatic fever, and is the most common cause of chorea in childrens. SC is characterized by involuntary movements such as jerking of the arms, legs, and face. The following case is a 10-year-old boy with complaints of moving his right arm and leg on its own. On physical examination, there was a grade 4/5 systolic murmur at ICS 5 2 cm lateral to the left MCL blowing radiating to the left arm. In ASTO examination there is an increase. CT scan of the head without contrast showed no abnormalities. The results of echocardiography showed severe mitral regurgitation. The patient was diagnosed with Sydenham cholera and rheumatic heart disease. The patient refused hospitalization and was treated as an outpatient with therapy erythromycin 250 mg four times a day for 10 days followed by a twice daily dose for the next two months, symptomatic haloperidol 1 mg and trihexyphenidyl 0.5 mg twice a day, aspirin 300 mg four times a day for one month. From this treatment, the complaints improved slowly, and the chorea disappeared within 10 days of the start of treatment.

Introduction

Sydenham's chorea (SC) is one of the manifestations of acute rheumatic fever. It is characterized by chorea involving the face and extremities and can include psychiatric symptoms, hypotonia and muscle weakness. Although the incidence is decreasing in high-income countries, SC remains the most common cause of childhood chorea, occurring in approximately one-third of patients with acute rheumatic fever. [1] But there are no exact number or prevalence about the Sydenham Chorea incident in Indonesia. Some evidence shows that in developing countries, the incidence of rheumatic fever is higher, presumably due to poor sanitation compared to developed countries.[2]

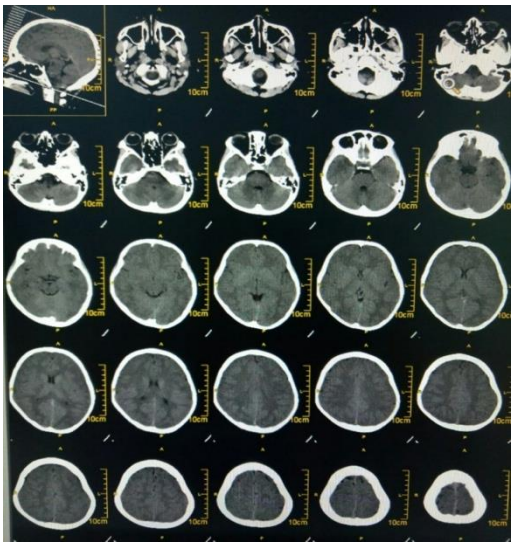
The severity of SC was assessed from mild involuntary movement to severe functional impairment. The involuntary movements that occur during an attack can be repeated from a few minutes to hours, either with breaks between movements or continuously.[3] The patient will experience pain or fatigue due to uncontrolled repetitive movements. Syndenham chorea is a self-limiting disease. However, symptoms can persist for months or years. Syndenham chorea rarely occurs repeatedly.[1]

Various drugs have been used to treat chorea, such as dopamine receptor antagonists (eg, haloperidol), antiepileptic drugs (eg, valproic acid or carbamazepine). [4–8] Studies that examine these drugs in SC patients are very limited and the studies are often observational, objective outcome measures are limited, and the study population is heterogeneous, so the best treatment options are uncertain. We present an Indonesian 10-year-old boy with SC that completely recovered with outpatient management.

Case(s)

A 10-year-old boy came to the neurology clinic with complaints of moving his right arm and leg on its own. Complaints occurred since one week before being taken to the hospital. The patient has difficulty performing activities due to the movement. There were no complaints of fever, cold cough, shortness of breath, painful swallowing, or joint pain. Normal urination and defecation. There is no history of taking certain drugs.

History of the patient's birth at term. The patient was born by spontaneous vaginal delivery. Birth weight 2900grams, birth length 50cm. Patients completed the mandatory immunizations. Growth and development according to milestones. Currently, the patient's education is grade fourth in elementary school. Before getting sick, patient has normal daily activities like any childrens in his age. None of the families experienced complaints as experienced by the patient.



Picture 1. Head CT Scan Without Contras

From the physical examination, the general condition of the patients was adequate and has composmentis consciousness. Blood pressure 110/70mmHg, regular pulse 90x/minutes,

respiratory rate 24x/minutes, temperature 36.8 Celcius. Weigh 22 kg and height 124cm. The general head and neck status showed no abnormalities. Auscultation of the heart show that the patient S1S2 single, grade 4/5 systolic murmur at intercostal (ICS) 5 about 2cm from left midclavicular (MCL) blowing radiating to left arm. Pulmonary examination revealed vesicular sounds, no rhonchi or wheezing. Abdominal examination was normal, there was no hepatomegaly or splenomegaly. Extremity no deformity, edema, or cyanosis.

Neurological examination showed that GCS 456, normal cranial nerves, normal motor strength. Normal physiological reflexes, negative pathological reflexes. Involuntary movement was found in the form of hemichorea. Sensory, autonomic no abnormalities.

On echocardiographic examination, the results showed atrial sinus solitus, AV and VA concordance, normal venous drainage, normal heart chambers, no ASD/PDA/VSD, severe mitral regurgitation with a pressure gradient (PG) of 102 mmHg, no other valve abnormalities were found, normal left ventricular systolic function, normal left aortic arch.

Complete blood count: Hgb 13.6, Leukocytes 3.7, HCT 41.1, Plt 151. Serum electrolytes Na: 135, K: 3.9, Cl: 9.8. An increase in ASTO was found by a value of 442. The results of the head CT scan did not show any abnormalities (Figure 1).

Based on patient history, clinical manifestations, laboratory examination, echocardiography, and imaging, we diagnosed the patient with Sydenham Chorea caused by Rheumatic Carditis. Patients and their families refuse to do hospitization and was treated through outpatients with advice not to do much activity, not to be too tired, and to have regular check-ups at the cardiology and neurology departement.

In the management of this patient, for hemichorea, patient is given haloperidol 1 mg and trihexiphenidil 0.5 mg twice a day. Antibiotic erythromycin 250 mg four times a day for 10 days, then the dose is reduced to two times a day for two months. Aspirin is also given at a dose of 300 mg, taken four times a day for 1 month. The patient's complaints of involuntary movements improved slowly, and disappeared within two weeks of starting treatment.

Discussion

Rheumatic fever (RF) is considered a disease that often affects children (generally between 5-15 years).[9] This disease is rare in children under 5 years of age. Published data estimate that ARF occurs in 1-6.8% of children younger than 5 years. Arthritis and carditis are the most common clinical presentations in this age group. Sydenham's is most common in prepubertal children with a female predominance.[10] The ratio of the incidence of SC in girls to boys is 3:1. In our case it is a 10 year old boy from Indonesia. [2]

Streptococcus are a group of gram-positive bacteria that are morphologically characterized by cocci and chains. Streptococcus pyogenes, which belongs to the GABHS, has the ability to produce toxins that can lyse red blood cells. The cytoplasmic membrane is surrounded by a thick layer of peptidoglycan surrounded by an S layer consisting of carbohydrates, proteins, and glycoproteins. There is also a certain type of carbohydrate, a rhamnose-Nacetyl-glucosamine

dimer with the ability to cross-react with heart valve glycosides.[11]

In syndenham chorea (SC), stimulated antibodies targeted basal ganglia brain cells in the host and its cause a diffuse inflammatory process in the corpus striatum, especially the caudate nucleus. Symptoms of SC are caused by an imbalance between the dopaminergic system, the intrastriatal cholinergic system, and the inhibitory system of gamma-aminobutyric acid (GABA).[12]

SC pathogenesis explains that antibodies produced against GABHS under conditions of acute infection will cross-react with basal ganglia epitopes, disrupting the cortex-basal ganglia-thalamus-cortical (CBGTC) circuit, causing motor, behavioral and cognitive symptoms.[13,14]

Another study found that in SC patients Antibodies also show cross-reactivity to mammalian GM1 lysogangliosides (neural gangliosides) and N-acetyl-β-D-glucosamine (GlcNAc), the carbohydrate dominant epitope of GABHS, and can react with other basal ganglia epitopes. , including the tubulin and dopamine receptors D1 and D2 (D1R, D2R).[15]

Studies linking autoantibodies to SC symptoms showed that serum antiD1R and anti-DR2R autoantibodies were higher in SC patients compared to controls. More importantly, the anti-D2R/anti-D1R ratio correlated with symptom severity in SC patients, as assessed by The Universidade Federal de Minas Gerais (UFMG) SC Rating Scale. [16]

The usage of dopamine antagonists in the treatment of SC indirectly supports the role that dopaminergic-directed autoantibodies play in the pathophysiology of SC.[17] Decreased serum autoantibody titres are associated with improvement in symptoms, while patients with persistent SC exhibit still high titers of anti-basal ganglia autoantibodies. [17]

The use of plasmapheresis and intravenous immunoglobulin is considered to be able to affect circulating antibody levels and is therefore considered effective in the treatment of SC. This is consistent with the theory that the motor and neuropsychiatric symptoms of SC patients are the result of autoantibodies acquired by GABHS targeting neurons, leading to alterations in the cortical-basal ganglia-thalamic circuitry of CBGT.[13,14]There have been case reports that have successfully treated SC patients using intravenous immunoglobulin.[1]

Intranasal GABHS infection in mice is also known to increase a strong specific Th17 response in cranial lymphoid tissue, and that these T cells can migrate to the brain. In the brain, GABHS-specific Th17 cells can induce an IL-17-mediated inflammatory response and/or activate microglia and macrophages leading to BBB damage. This process causes autoantibodies to leak into the olfactory bulb and spread to the basal ganglia and other brain areas.[18]

In addition to antibodies, direct action of cytokines and other immune mediators may contribute to neural dysfunction leading to motor, behavioral, and cognitive symptoms in SC. Studies on B1-cell lymphocytes involved in chronic antibody-mediated autoimmune disease, in SC patients with persistent chorea compared with patients with cured or control chorea. [19]

Genetic factors controlling the immune response to GABHS appear to play a relevant role in susceptibility to ARF and its complications, including SC. The major histocompatibility

complex human leukocyte antigen (HLA) polymorphisms, particularly HLA class II, a class of molecules involved in antigen processing and presentation, have been consistently associated with susceptibility to ARF. [20] Furthermore, each copy of the immunoglobulin heavy chain allele IGHV4-61*02, located in the gene segment IGHV4-61, was found to have an increased risk factor of 1,4 times the risk of rheumatic heart disease. [20]

The Jones criteria are commonly used to diagnose acute RF. The diagnosis of acute rheumatic heart disease (acute or recurrent) can be made if there are two major criteria or one major with two minor. Major criteria are carditis (clinical and/or subclinical), arthritis (polyarthritis only), chorea, erythema marginatum, subcutaneous nodules. Minor criteria are monoarthralgia, fever (≥ 38.5oC), increased ESR (60 mm in the first hour) and/or CRP (3 mg/dL or more than normal), prolonged PR interval (except carditis which is a major criteria), evidence of previous GABHS infection (positive throat culture, positive rapid antigen detection test (RADT), and elevated anti-streptococcal antibody titer). [21]

In SC patients, the characteristic 'dance like movement' is usually described as a randomly occurring sequence of one or more involuntary movements affecting other parts of the body. Movement can also occur in only half of the body called hemichorea, which affects a quarter of people with SC. The severity varies significantly, from mild SC, which has mild or no impact on daily life activities, to severe SC, which makes it difficult for patients to carry out daily life activities. In addition to chorea, patients with CS exhibit other motor symptoms, such as motor impairment, hypometric saccades, hypotonia, and dysarthria. Tic-like movements and vocalizations have been reported, but they usually don't have the typical signal impulses.[12,22]In rare cases, patients may develop hypotonia so severe that the patient is confined to bed, the most severe form of SC known as chorea paralytica. Hyperkinetics and decreased muscle tone are characteristic of acute CS, but patients in CS remission exhibit bradykinesia, suggesting that CS remission patients may develop parkinsonism which may be a marker of CS severity after remission.[12]

Behavioral or psychiatric symptoms are also frequently found in SC patients. Obsessive compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD) were more common in SC patients than ARF patients without SC and healthy subjects. In 50 SC patients followed serially with comprehensive psychiatric interviews it was found that the most frequently observed psychiatric disorders included major depression (14%), generalized anxiety disorder (16%), social phobia (24%) and OCD (24%).[23]

As would be expected by immune-mediated CBGTC dysfunction, SC is associated with a range of cognitive deficits that require processing speed and attention. Even patients with SC who had recovered showed impairment in executive function tests, especially verbal fluency, decreased verbal comprehension, which affected their social and occupational functioning. SC patients recover within a few months, and are often considered a benign monophasic condition, with complete remission in more than 80% of patients within six months.[24]

Management goals in SC include: 1) treating and preventing additional GABHS

Infections; 2) control of chorea symptoms; and 3) decisions regarding the need for immune modulation.[12] The most commonly used regimens include a single dose of 1.2 million units of intramuscular (IM) benzathine penicillin G or administration of penicillin VK 500 mg orally for ten days twice daily.[25] The most commonly used for antibiotic prophylaxis regimen is benzathine penicillin G 1.2 million units in children weighing ≥20 kg and using a dose of 600,000 IU in children weighing < 20 kg given IM every three to four weeks.

Patients with mild SC and not affecting activities of daily life (ADL) do not require symptomatic treatment of SC. When SC affects speech, gait, hand skills, affects self-care, academic and social activities, the use of anti-chorea interventions should be considered.[12]

Administration of dopamine antagonists (antipsychotics) and anticonvulsants in the treatment of SC, leads to more rapid symptom resolution and functional improvement. It is based on an autoimmune-induced basal ganglia dysfunction characterized by excessive dopaminergic activation and decreased activation of the basal ganglia inhibitory pathway.[17] While dopamine antagonists may counteract dopaminergic over-activation, the anticonvulsant effect on this pathophysiological process is less clear, and may involve different mechanisms, such as regulating GABA neurotransmission and calcium flow to basal ganglia neurons preventing neuronal hypersynchronization.[12]

Valproic acid and carbamazepine are the most commonly prescribed anticonvulsants for SC. Valproic acid and carbamazepine have the same effectiveness in clinical improvement, remission and recurrence rate of SC patients without significant side effects.[26]

Haloperidol is a dopamine antagonist that is often used to treat SC patients. In the study SC patients treated with haloperidol improved more rapidly and had a lower rate of treatment refractoriness, but had more side effects. The administration of haloperidol should be used with caution because SC patients are at high risk for parkinsonism.[8]

Immunomodulatory drugs that are widely used in SC therapy and are effective include corticosteroids, including oral prednisone, oral deflazacort, and intravenous (IV) methylprednisolone. However, there are some side effects of using high doses of corticosteroids including weight gain and acne and in more severe cases progress to Cushing's disease.[4,6]

SC pathophysiology involves autoantibodies that bind to basal ganglia neurons and affect their function, IVIG can inactivate these autoantibodies, whereas plasmapheresis will extract them from plasma. Thus, all SC patients who received IVIG or plasmapheresis showed clinical improvement.[1,5]

Syndhenham chorea is expected to recover completely in one to six months. A retrospective study of 90 patients showed complete remission of motor symptoms in 85% within six months, and an additional 5% had complete remission within one year.[27]One prospective study of 32 patients with CS, followed for more than 2.5 years, found that symptoms persisted for 2 years or more in 50% of their cases.[28]

Conclusion

Sydenham chorea is a disease caused by group A beta hemolytic streptococcal infection which is characterized by involuntary movements that can be accompanied by behavioral disorders, cognitive impairment, and OCD. Sydenham chorea is a self-limited disease but may show recurrence and/or persistence of motor and neuropsychiatric symptoms in adulthood. Syndenham chorea treatment strategies are antibiotic and prophylactic therapy, symptomatic treatment of syndenham chorea, and immunomodulating interventions. In this case, rheumatic heart disease was also found, which was supported by echocardiography.

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Conflicts of Interest

There are no conflicts of interest declared by the author.

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