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CASE REPORT ON WARFARIN INDUCED ABORTION

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Abstract

Cerebral venous sinus thrombosis (CVST) is the presence of acute thrombosis in the dural venous sinuses which is an uncommon cause of cerebral infarction relative to arterial disease, but it is an important consideration because of its potential morbidity. Pregnancy is one of the risk factor to develop CVST, because we know pregnancy induces several changes in coagulation system, Hypercoaguble state is seen which increases the risk of thrombosis. The use of Vitamin -K antagonist such as WARFARIN during pregnancy carries the potential for serious risks to the fetus especially when the drug is administered in the first 6-12weeks, generally it is contraindicated in pregnancy due to its teratogenecity, it is categorized as category X drug by FDA**.** Case Report: 24yrs Female, Primi with 20weeks of Gestational age had come with complaints of severe pain in abdomen since morning, she had a History of trauma on neck 3months back and had convulsions and diagnosed with Cerebral Venous Sinus Thrombosis(CVST) for which she was prescribed with Tab.warfarin-2mg once daily since 3months, Tab Levitiracetam 500mg twice daily which led to fetal death at 20weeks Gestational age and Emergency abortion was done and diagnosed as Warfarin induced abortion and rapid supportive care was initiated and patient was stabilized. Warfarin had become choice of drug in this case due to Risk-Benefit ratio, to prevent CVST complications. Due to lack of patient education and follow up of the patient to hospital led to this fatal event "Warfarin-associated fetal hemorrhage".

Keywords: Warfarin, cerebral sinus venous thrombosis, Gestational age, Abortion, Convulsions, Teratogenecity, Category X.

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INTRODUCTION

WARFARIN

Warfarin, a vitamin K antagonist, is an oral anticoagulant indicated for the prevention and treatment of venous thrombosis and its extension and the prevention and treatment of the thromboembolic complications associated with vascular disorders [1].

Mechanism of action

Warfarin inhibits the synthesis of clotting factors II, VII, IX, and X, as well as the naturally occurring endogenous anticoagulant proteins C and S. The anticoagulant and antithrombotic activity of warfarin depends on the clearance of functional clotting factors from the systemic circulation once the drug is administered. The earliest changes in INR are typically seen in 24 to 36 hours after administration of the dose. The antithrombotic effect of warfarin is not present until approximately the fifth day of therapy, which is dependent on the clearance of prothrombin [1]. The use of Vitamin -K antagonist such as WARFARIN during pregnancy carries the potential for serious risks to the fetus especially when the drug is administered in the first 6-12weeks of gestation, generally Warfarin is contraindicated in pregnancy, due to its teratogenecity [2] as it passes through the placental barrier and may cause bleeding in the fetus; warfarin use during pregnancy is commonly associated with featalanomalies [3], spontaneous abortion, cerebral haemorrhage, embroyopathies, stillbirth, neonatal deathand preterm birth so it is categorized as category X drug by FDA [3].

The safety and efficacy of warfarin therapy are dependent on maintaining the INR within the target range For Obstetric CSVT vitamin K antagonist can be used with a target international normalized ratio of 2.0-3 [4].

Cerebral venous sinus thrombosis (**CVST**) is the presence of acute thrombosis (a blood clot) in the dural venous sinuses, which drain blood from the brain is an uncommon cause of cerebral infarction relative to arterial disease, but it is an important consideration because of its potential morbidity [4].

Symptoms may include headache, abnormal vision, any of the symptoms of stroke such as weakness of the face and limbs on one side of the body, and seizures. The diagnosis is usually by computed tomography (CT/CAT scan) or magnetic resonance imaging (MRI) employing radio contrast to demonstrate obstruction of the venous sinuses by thrombus [4].

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Treatment is with anticoagulants (medication that suppresses blood clotting), and rarely thrombolysis (enzymatic destruction of the blood clot). The disease may be complicated by raised intracranial pressure, which may warrant surgical intervention such as the placement of a shunt [4].

Pregnancy is one of the risk factor to develop CVST, because we know pregnancy induces several changes in coagulation system, Hypercoaguble state is seen which increases the risk of thrombosis. CVST can present with tonic-clonic convulsions during pregnancy hence anti-epileptic medications need to be considered as prophylaxis or treatment [5-7].

Case Report

24yrs Female, Primi with 20weeks of Gestational age, had come with complaints of severe pain in abdomen since morning, she had a history of trauma on neck 3 months back and developed focal onset seizures, Immediately CT brain was done and it revealed haemorrhagic infarct in right temporal lobe immediately medical management was provided using Inj.Heparin 5000u IV/TID, T.Clopidrogrel + aspirin 150mg PO/OD, Inj.Phenytoin 100mgTID, T.valproic acid 500mg/day. MRI brain showed right transverse sigmoid Cerebral Sinus Venous Thrombosis (CSVT) for which she was prescribed with T.warfarin-2mg PO/OD, T.levipil(levetiracetam)500mg PO/BD, T.Folvite PO/OD since 3months. Prothrombin time, a PTT and INR is monitored frequently and INR ranged from 1.27-2.7 .Patient suddenly developed severe abdominal pain on examination they found Intra-uterine fetal death at 20weeks gestational age and Emergency abortion was done and diagnosed that it might be due to warfarin and rapid supportive care is initiated and patient was stabilized.

DISCUSSION

Cerebral venous sinus thrombosis (**CVST**)

It is the presence of Blood clot in brain vessels. It is an important consideration because of its potential morbidity. Pregnancy is one of the risk factor to develop CVST, because we know pregnancy induces several changes in coagulation system, Hypercoaguble state is seen which increases the risk of thrombosis more over patient had a trauma on neck which aggravated the condition and was diagnosed as right transverse sigmoid Cerebral Venous Sinus Thrombosis (CVST). For which treatment options are anticoagulants [2]. The use of anticoagulants [1] and thrombolytics in pregnancy is an important consideration; pregnancy is associated with a 5-fold increase in the risk of venous thromboembolism (VTE). We know pregnancy induces several

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changes in coagulation system i.e enhancement of procoagulants, during pregnancy are considered to be physiological adaptation of the bosy in order to face the haemostatic challenge of delivery. Platelets play a very important role in coagulation. Their concentration remains same during pregnancy, However their aggregating ability increases. In addition their responsiveness to prostacyclin and cAMP formation is reduced. Over all these changes favor coagulation. Anticoagulant therapy [1] (inhibit blood coagulation) and thrombolytics (enzymatic destruction of the blood clot) are mainstay of treatment CVST. Epilepsy is a major complication managed with anti-epileptic drugs [8]. The disease may be complicated by Intra cranial hypertension which may warrant surgical intervention such as the placement of a shunt sometimes

In this case patient was diagnosed with CVST and pregnant with 20 weeks gestational age also presented with a episode of focal onset seizures,which is a complication of cvst which may lead to intracranial hypertension and may result in maternal mortality also, so anti epileptic drugs like levetiracetam phenytoin were prescribed, anticoagulants like Warfarin is a standard drug in treating cerebral sinus venous thrombosis because of the location of thrombosis in superior saggitalsinus as it works effectively compared to other drugs although warfarin is contraindicated in pregnancy due its potential risks, based on risk benefit ratio in order save the mother warfarin became the choice of drug. But unfortunately here in this warfarin led to fetal death due to internal haemorrhage. fetal autopsy can be done to exactly rule out the cause of abortion. Therefore, many patients and physicians have been reluctant to use a Vitamin-k antagonists in pregnancy.

Patient education regarding the potential risks of warfarin and dietary changes limiting the vitamin-k rich foods [9-11] like leafy vegetables, cabbage, liver, fish etc.. Frequent monitoring of warfarin dosing based on INR, prothrombin levels, a PPT levels would have been recommended in order to avoid further complications. Patients must have advised not to plan pregnancy when patient is on anticoagulants due to its potential risk on fetus growth and development. Due to lack of patient education regarding the medications using and its side effect led to this fatal event.

CONCLUSION

In the recent years oral anti-coagulants like vitamin-k antagonists has became preferred drug due to its high efficacy rates and its compliance. Warfarin had become choice of drug in this case due to Risk-Benefit ratio, to prevent CVST complications. Due to lack of patient education and follow up of the patient to hospital led to this fatal event "Warfarin-associated fetal hemorrhage[3]".

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Regular monitoring of fetal ultrasound study and strict control of warfarin dose with regular measurement of prothrombin time and INR are the best way to prevent intrauterine fetal death although there is no direct way to prevent fetal intracranial hemorrhage so far. Best way is to advise not to plan pregnancy when the patient is on anticoagulants like warfarin, acenocoumarol.

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