#### Research and Reviews: Journal of Clinical and Medical Case Studies

# Diane-35 Induced Deep Venous Thrombosis: A Case Report

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## **Case Report**

Received date: 21/11/2016 Accepted date: 03/01/2017 Published date: 10/01/2017

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**Keywords:** Diane-35, Oral contraceptive, Venous thromboembolism

#### **ABSTRACT**

A case report of Diane-35 caused lower extremity deep venous thrombosis in China was reported in order to provide reference for safety use of oral contraceptives.

#### INTRODUCTION

Oral contraceptives (OCs) are compound oral short acting or long-acting contraceptives that composed of estrogen and progestin. For the majority of women, oral contraceptives are very safe if use in accordance with the provisions of usage and dosage. However, the serious side effects induced by OCs were concerned world widely. Especially the risk of venous thromboembolism (VTE) caused widespread controversy. We report and analyze a new case of lower extremity deep venous thrombosis that caused by Diane-35 because of the treatment of uterine hemorrhage, in order to provide reference for serious side effects diagnostic and preventive of oral contraceptives.

#### CASE DESCRIPTION

A 44-year-old woman was send to the emergency department with pain in the right lower extremity. 6 days ago, she had a diagnostic curettage because of uterine fibroids presenting as hypermenorrhea. After the operation, she started to take Diane-35 (cyproterone acetate and ethinyloestradiol OC) once daily and one tablet each time. On the next day, the usage and dose of Diane-35 was increased to twice a day because of an increased amount of bleeding. At the fifth day of taking Diane-35, the patient felt muscle pain of right leg and intensified when walking.

Many laboratory examinations were taken immediately for this woman in hospital. The uterine size enlarged as large as two months pregnancy by vaginal examination and gynecological ultrasound image showed multiple uterine fibroids. The circumference of right lower shin was 38 cm, which of left shin was 37 cm. Finally, color Doppler ultrasound showed: Right calf intra muscle venous thromboembolism was diagnosed. The blood flows of femoral, superficial femoral and popliteal vein are normal. Electrocardiogram (ECG) and blood tests including blood routine, blood type and coagulation function were all normal. The past history of the patient excluded thrombotic disease, alcohol and tobacco habits and abnormal weight.

When her illness was diagnosed as VTE, the woman was informed to stop Diane-35 treatment, have absolute bed rest and to

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raise the affected limb immediately. Treatment measures such as supplementary blood volume, anticoagulation and antiplatelet were taken meanwhile.

On the next day in hospital, a right internal jugular vein inferior vena cava angiography and temporary vena cava filter placement were taken <sup>[1]</sup>. On the third day, this woman stopped Warfarin treatment due to increased vaginal bleeding and transferred for gynecological treatment. The fraxiparine and warfarin were used for anticoagulation, and urokinase was used for thrombolysis, and other drugs such as panax notoginseng saponins and Aescuven Forte were used for adjuvant therapy during hospitalization period except for hysterectomy. Half a month later, examination of vascular ultrasound: double lower extremities venous thrombosis. One week later, she had changed a permanent filter implantation in inferior vena cava and maintained long-term oral warfarin.

#### DISCUSSION

The main components of Diane-35 are cyproterone acetate 2 mg/tablet and ethinylestradio 0.035 mg/tablet. It has reported that taking Diane-35 will induce upper extremity deep venous thrombosis <sup>[2]</sup>. The combined hormonal contraceptives with cyproterone confer a six fold increased risk of VTE as compared with nonusers <sup>[3]</sup>. The cyproterone acetate has more risk of thrombosis than others in the all third-generation oral contraceptives <sup>[4]</sup>. Recent meta-analyses and systematic reviews have consistently shown a small but significant increased risk of VTE among users of third-generation progestins compared with second-generation progestin's <sup>[5]</sup>. The most risk of thrombosis is in the first year of taking oral contraceptives <sup>[6]</sup>. It is important to raise awareness of the signs and symptoms of VTE when prescribing an OC on healthcare professionals.

### **CONCLUSION**

Although the incidence of VTE is rare in Chinese women, but Diane-35 could increase the risk of VTE. This report will promote to the safety use of oral contraceptives, beneficial to women's health.

#### REFERENCES

- 1. Department of vascular surgery of Chinese Academy of Medical Sciences. China Guidelines on the diagnosis and treatment of deep venous thromboembolism. Chin J Vasc Surg. 2013;3:23-26.
- 2. Kant A, et al. Reflections after the diane affair. J Thromb Haemost. 2014;12:1385-1387.
- 3. Lidegaard. Hormonal contraception, thrombosis and age. Expert Opin Drug Saf. 2014;13:1353-1360.
- 4. van Hylckama Vlieg A, et al. The venous thrombotic risk of oral contraceptives, effects of estrogen dose and progestogen type: Results of the MEGA case-control study. BMJ. 2009;339:561.
- 5. Practice Committee of the American Society for Reproductive Medicine. Combined hormonal contraception and the risk of venous thromboembolism: A guideline. Fertil Steril. 2016;107:43-51.
- 6. Van Hunsel FP, et al. Thrombosis and embolism during Diane-35 use: Analysis of reports made to the Netherlands Pharmacovigilance Centre Lareb. Ned Tijdschr Geneeskd. 2014;158:A6651.