OLGU SUNUMU CASE REPORT

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Succesfull Management of Pregnancy Complicated with Congenital AT-3 Deficiency

Konjenital Antitrombin-3 Eksikliği Olan bir Gebe Olgunun Başarılı Yönetimi: Vaka Sunumu

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ABSTRACT

Antithrombin-3 (AT-3) is a natural anticoagulant that inhibits thrombin, activated factor X and other serine proteases in the coagulation cascade, and its activity accelerated more than 1000-fold by heparin binding. Congenital AT-3 deficiency is inherited as an autosomal dominant trait and affects less than 0.2% of the general population.[1] This deficiency is considered to be a high-risk thromboembolic condition, with an odds ratio venous thromboembolism (VTE) of 16.3 compared with individuals with a nonthrombophilic status.[1] In this case report, succesfull management and delivery of a congenital AT-3 deficient pregnant woman was extensively discussed along with the lşterature findinds.

Keywords: Congenital antithrombin deficiency; venous thromboembolism; major thrombophilias; low molecular weight heparin; pregnancy

ÖZET

Antitrombin-3 (AT-3), koagülasyon kaskadındaki Faktör V ve serin proteaz tarafından aktive edilen doğal bir antikoagülan olup, etkisini heparine bağlanarak göstermekte ve heparinin aktivitesini 100 kat artırmaktadır. Otozomal dominant olarak kalıtılan ve tromboza yatkınlık şeklinde karşımıza çıkan konjenital AT-3 eksikliği, toplumun %0,2 'den azını etkiler olmayan hastalar ile karşılaştırıldığında venöz tromboemboli (VTE) için risk olasılığınını 16,3 kat fazla olduğu ortaya konulmuştur.[1] Özellikle gebelik döneminde, koagülasyon faktörlerindeki değişimler nedeni ile tromboza yatkınlık meydana gelebilmektedir. Bu vaka sunumunda, konjenital AT-3 eksikliği olan bir multipar gebe olgunun başarılı doğum yönetimi, literatür bilgileri doğrultusunda özetlenmiştir.

Anahtar Kelimeler: Konjenital AT-3 eksikliği; venöz tromboemboli; major trombofililer; düşük molekül ağırlıklı heparin; gebelik

Pregnancy carries a high risk of thromboembolic complications, especially in the postpartum period. This risk is particularly high in women with inherited thrombophilias; among this antithrombin deficiency seems to carry the highest risk because of its mechanism of action. Antithrombin-3 (AT-3) is a natural anticoagulant that inhibits thrombin, activated factor X and other serine proteases in the coagulation cascade, and its activity accelerated more than 1000-fold by heparin binding. Congenital AT-3 deficiency is inherited as an autosomal dominant trait and affects less than 0.2% of the general population.[1,2] Among all, autosomal inherited disorder; AT-3 deficiency carries the highest risk of VTE, with an estimated 20-fold increased risk of first VTE; in the affected families the lifetime risk of VTE is almost 50%.[3] Women with a congenital AT-3 deficiency present a high risk of developing VTE during pregnancy and the postpartum period.[4] The use of low molecular weight heparin (LMWH) is recommended in these patients, while the use of antithrombin concentrate is controversial.[5] In this report, we discussed the succesfull management

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of a pregnancy complicated with congenital AT-3 deficiency.

CASE REPORT

43 year old G2 P1 A0 D/C0 woman with a history of congenital AT-3 deficiency was admitted to our outpatient surveillance unit. Her medical history was unremarkable except mild hypothyroidis and she has been using oral levothyroxine 25mcg starting from her pregnancy. Her first pregnancy was uneventful with term C-section delivery without complications on 2004. Her family history revealed that her father was also diagnosed with the same congenital disease.. Initial diagnosis of AT-3 deficiency was documented in 2004 in this case and she has been receiving daily LMWH 4000 IU sc since that date. Other medical records were uneventful. Starting from 12th week of gestation, antenatal surveillance was documented and all relevant examinations including 1st trimester aneuploidy screening, 2nd trimester obstetric sonography and 75 gr glucose tolerance test results were unremarkable. Additionally, cell free fetal DNA testing was carried out to exclude fetal aneuploidy, revealing low risk. All laboratory examinations were within normal ranges except for low AT-3 activity; 39%(Ref. Val. 70-125).

Till 38 weeks of gestation, she received 4000 IU of daily LMWH (enoxaparine) and on 38 weeks she was hospitalized due to finalizing consultations including anesthesia and hematology. There was no sign of fetal growth retardation. Careful antenatal fetal surveillance was scheduled. LMWH was ceased just 12 hrs before C-section and 3000 IU AT-3 derivate was infused intavenously (iv) during preoperative period on 3rd and 6th hours in an isotonic solution, each witihin 3 hours slow infusion. C-section was performed under regional anesthesia without any complication and a singleton 2770 gr fetus was delivered with APGAR scores 1-8 and 5-9. Hemovac drain was inserted into Douglas pouche and compression stockings were applied. Postoperatively, last dose of AT-3 derivate was infused on 24th hour of C-section and 4000 IU twice daily sc LMWH was started accordingly. On the 3rd of C-section, both mother and the fetus was discharged uneventfully. She was prescribed 4000 IU twice daily at least for 6 weeks postpartum. There were no thrombotic events detected till 10th week postpartum.

DISCUSSION

Hereditary clothing disorders during gestational period reveal potential thrombosis risks. As pregnancy provides a procoagulant state that increases the risk of suffering a venous thromboembolism, and imposes a risk 4-5 times higher than women who are not pregnant disorders as AT-3 deficiency is challenging.[6] Of the various inherited thrombophilias, with the possible exception of homozygous and compound heterozygous conditions, AT deficiency carries the highest risk of VTE, with an estimated 20-fold increased risk of a first VTE. A recent data including 18 pregnancies in AT-deficient women managed with LMWH and AT concentrates revealed 16.7% VTE and 55.6% adverse pregnancy outcome.[7]

Management of a pregnancy in hereditary AT-3 deficiency should include precise information of patients, close surveillance of gestation and relevant multidisciplinary approach with hematology. In order to prevent thrombotic events, thromboprophylaxis in AT- deficient women is required during pregnancy, even though there was a lack of consensus on appropriate dosage regimens.[8] It had been suggested, for pregnant women at higher thrombotic risk like AT-deficient ones, to use LMWH at therapeutic doses.[4,9] Even though the use of (LMWH) is recommended, the use of AT concentrate is controversial.[7] While it's us for secondary prophylaxis in the prepartum period requires individualized risk assessment for thrombosis. In the postpartum period antithrombin concentrate replacement therapy may be considered in the patient with the previous history of VTE.[1,3] If there is no VTE history priorly, a range of options can be considered from observation to prophylactic anticoagulation depending on the patient's other risk factors and her preferences. According to a recent expert consensus, AT concentrates would be prescribed if AT activity is very low (< 40%) even if there is no VTE history (Management of Hereditary Antithrombin Deficiency in Pregnancy). Basically, all of the information about management based on experts' opinion and case reports. We applied AT therapy before and after C-section mainly due to low AT lev-

els. Also, LMWH therapy was suggested at least 6 weeks post C-section with close follow-up.

Although many authors have observed a relation between different thrombophilias and pregnancy complications, systematic reviews have failed to find such relationship between AT deficiency and adverse pregnancy outcomes.[2,7,10,11] Adverse pregnancy outcomes may be due in part to vascular lesions in the placenta possibly due to thrombotic events. In our case, we have not documented any adverse events including IUGR or abnormal fetal well-being tests. This might be due to low BMI of the case, effective thrombophlaxis, regular physical exercise during gestation and appropirate diet.

As summary, such cases should be managed with precise caution considering the individual risk factors of the patient. Multidisciplinary approach should be the goal in the gestational period.

CONCLUSION

In conclusion, antithrombin deficiency is a rare and severe situation and necessitates a multi-disciplinary approach. The thromboembolism prophylaxis should be based on patients characteristics. Regardless of the delivery method antithrombin concentrate and LMWH using seems effective and safe.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu, Ahmet Çelik;* ***Design:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu, Ahmet Çelik;* ***Control/Supervision:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu, Ahmet Çelik;* ***Data Collection and/or Processing:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu;* ***Analysis and/or Interpretation:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu, Ahmet Çelik;* ***Literature Review:*** *Nede Destina Kavak, Tufan Arslanca;* ***Writing the Article:*** *Nede Destina Kavak, Tufan Arslanca;* ***Critical Review:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu, Ahmet Çelik;* ***References and Fundings:*** *Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu;* ***Materials:****Nede Destina Kavak, Tufan Arslanca, Emre Göksan Pabuçcu.*

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