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Bilateral Ileofemoral Thrombophlebitis after Ten Contraceptive Pills in a 25-Year-Old Woman with Antithrombin III Deficiency

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Antithrombin III (ATIII) deficiency is associated with a well-known thrombotic tendency. About 50% of patients heterozygous for the abnormality become symptomatic during their life time [3, 5, 6]. In old age, only 10–20% appear to remain asymptomatic [5, 10]. The homozygous state is probably incompatible with life.

Several triggering factors, such as pregnancy, puerperium, trauma and oral contraceptives have been postulated to play a role. However the exact impact of any of these factors remains to be defined [5, 11]. Recently a concomitant defect predisposing to bleeding, namely von Willebrand's disease, has been demonstrated to play a potential role in protecting patients with ATIII Trento from thrombosis [8]. Estroprogestinics have been often associated with thrombotic phenomena both in patients with ATIII deficiency and in normal subjects [4, 9]. However the exact relationship existing between oral contraceptives and the occurrence of thrombosis in patients with ATIII deficiency remains to be clarified [1, 11].

We report here the unusual case of a young lady who developed thrombophlebitis of the legs after a short course of oral contraception. The proposita is a 26-year-old female who first came to our attention in March 1987. On that occasion she was found to have ATIII activity (chromogenic method) and antigen (Laurell method) consistent with a heterozygous true deficiency. (The levels were 60 and 50% of normal, respectively.) The mother and some family members on the maternal side were also found to have ATIII deficiency. One year earlier, at the age of 25, the patient was given an estroprogestinic preparation (Trigynon®, Schering AG, Berlin) to regularize menstruation. On the 10th day of therapy the patient started complaining of pain in the left inguinal area and pain and swelling in the left calf. A few days later, pain and swelling of right leg also appeared. The patient was admitted to a local hospital and a diagnosis of bilateral deep venous thrombosis was made. The suspicion was immediately confirmed by a phlebogram which showed parietal thrombi in both iliac veins and in the left popliteal vein. The contraceptive was discontinued (after 17 pills) and full dose heparin was given intravenously for 7 days. The clinical picture improved promptly. Oral anticoagulation was then started and continued for about 6 months while the clinical condition slowly reverted to normal. At the time of study the patient was in good condition and free of symptoms. The patient had never had previous thrombotic phenomena. However, the family history was positive in the sense that the mother had had a deep vein thrombophlebitis after parturition at the age of 37 and the maternal grandmother had also been known to have had thrombophlebitis of the legs. This observation is astonishing, because for the first time it supplies a close, direct demonstration of the relationship between oral contraceptives and thrombosis. It seems that the administration of low-dose estroprogestinics for only 10 days was sufficient to trigger an important thrombotic event. A total amount of 0.35 mg of an estrogen derivative (ethinyl Estradiol) and about 0.60 mg of a progestative preparation (Levonorgestrel) were sufficient to alter the hemostatic balance in the patient. It is likely that the estroprogestinics further decreased an already low ATIII level.

Oral contraceptives have been shown to lower variably ATIII in normal women [1, 2]. No other event known to predispose to thrombosis such as stasis, trauma, vitamin K or corticosteroid intake was present. Therefore, it seems inevitable to conclude that the short-term therapy with estroprogestinics was the only triggering event. The lack of recurrence of thrombosis after the discontinuation of the oral con-

traceptive is also consistent with this interpretation. The observation is even more striking if one takes into account that low-dose estroprogestinics such as those taken by the proposita have been showen recently to cause only minor, if any, change in the prothrombin complex factors [7].

This short report emphasizes further the importance of adequate coagulation control before the onset of estroprogestinic therapy and also indicates that no estroprogestinic should ever be given to a patient with heterozygous ATIII deficiency.

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