American Journal of Obstetrics and Gynecology (2004) **191**, 2016–20

ELSEVIER

AMERICAN JOURNAL of OBSTETRICS and GYNECOLOGY

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Interferon alfa treatment for pregnant women affected by essential thrombocythemia: Case reports and a review

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Received for publication January 22, 2004; revised March 24, 2004; accepted May 4, 2004

KEY WORDS
Essential thrombocythemia
Pregnancy
Fetal outcome
Interferon therapy

Objectives: In the past essential thrombocythemia was considered a disease of the elderly. At present, the number of young people suffering from this disease is growing, with a slightly higher frequency in females. We investigated the effects of interferon alfa therapy in these patients.
Study design: We describe 9 pregnancies in 4 women affected by essential thrombocythemia.
Results: Four pregnancies were carried out without interferon alfa therapy, and resulted in 2 intrauterine deaths, 1 spontaneous abortion, and 1 neonatal death. Interferon alfa was given during another 5 pregnancies; among them, 2 ended in preterm deliveries with normal infants, and 3 in full-term deliveries. The literature is reviewed.
Conclusion: Our cases and published series suggest that fetal outcome is improved by therapy, and that interferon alfa may be the best therapeutic option.

Essential thrombocythemia (ET) is a clonal hematopoietic disorder[1] that can be diagnosed in adherence to the Polycythemia Vera Study Group (PVSG) criteria.[2] Pregnancies in women affected by ET can be complicated by recurrent abortion, fetal growth restriction, stillbirth, and placental abruption.[2] The increasing number of young people affected, and the slight female preponderance suggest the elaboration of appropriate guidelines for pregnant women. Present therapeutic approaches in pregnant patients vary from no treatment to treatment with platelet reductive agents as monotherapy or in combination with antithrombotic medications (acetylsalicylic acid [ASA]).[2]

We describe 4 women affected by ET. From 1991 to 2001, they had 9 pregnancies; during 4 of them, they were left untreated or under ASA treatment as a result of patient decision or resistance to therapy, while in the course of the subsequent 5 pregnancies, they received interferon alfa (α-IFN) treatment, with or without ASA.

Case report

The clinical characteristics of our patients at diagnosis are described in Table I. Information about platelet count, type, dose, and length of therapy for all of our cases are summarized in Table II.

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doi:10.1016/j.ajog.2004.05.001

Table I Patient characteristics at diagnosis of ET

Patient	Age	Plt $\times 10^3/\mu L$	Spleen volume by US scan*	Cytogenetics	bcr/abl	BM fibrosis
1	25	812	NA	46,XX	Absent	Absent
2	22	732	115 mL	46,XX	Absent	Absent
3	28	720	150 mL	46,XX	Absent	Absent
4	25	1200	1270 mL	NA	Absent	NA

Plt, Platelet; *US*, ultrasound; *BM*, bone marrow; *NA*, not available.
* Normal spleen volume is considered 60 to 200 mL.[32]

Table II Patient obstetric history

			Platelet count*								
Patient	Pregnancy	Age at pregnancy	Start of pregnancy	Peak	Nadir	At delivery	α-IFN therapy schedule	Length of therapy	ASA	GA at delivery	Pregnancy outcome
1	I	24	814	NA	NA	NA	None		Yes	36 wks	IUD
	II	25	467†	560	362	280	3 MU, 3/W	From preconception to delivery	Yes	34 wks	A&H
	III	30	825	NA	NA	875	None		Yes		SA
	IV	31	650	NA	NA	635	None		Yes	30 wks	NND
2	I	23	440†	399	328	315	3 MU, 1/W	From preconception to delivery	No	FT	A&H
	II	27	458†	399	263	334	3 MU, 1/W	From preconception to delivery	Yes	FT	A&H
3	II‡	28	310†	317	265	380	3 MU, 1/W	From 14wks to delivery	Yes	36 wks	A&H
4	I	30	800	NA	NA	NA	None		Yes	27 wks	IUD
	II	35	1742	1503	641	400	3 MU, 3/W	From 8wks to delivery	Yes	FT	A&H

GA, Gestational age; *NA*, not available; *IUD*, intrauterine death; *A&H*, alive and healthy; *SA*, spontaneous abortion; *NND*, neonatal death; *FT*, term.
* $\times 10^3/\mu L$.
† The first pregnancy occurred before ET diagnosis.
‡ Pregnancy started during α–IFN treatment.

Patient 1

This patient had thrombocytosis (platelet count 814 $\times$ $10^3/\mu L$) since 1992. At her first pregnancy (October 1992 to May 1993), intrauterine death occurred while she was receiving only ASA. In August 1993, a diagnosis of ET was made at our institution, and α-IFN therapy at the dose of 3 international megaunits (MU), 5 days per week, was started. In November 1993, still under α-IFN therapy, she became pregnant again. After counselling, α-IFN was continued, and ASA (100 mg daily) was added, starting from 12 weeks of gestation. At 34 weeks of gestation we opted for cesarean section because of mild asymmetric intrauterine growth restriction (IUGR) with reduced amniotic fluid, and pathologic umbilical artery Doppler with absence of diastolic flow. A healthy female newborn of 2150 g weight (below the 25th percentile) with Apgar score 8 and 9 at 1 and 5 minutes, respectively, and normal number of platelets was delivered. Post partum, a modest rebound from 440 $\times$ $10^3/\mu L$ to 651 $\times$ $10^3/\mu L$ after operation was recorded. α-IFN therapy was discontinued to allow the patient to breast-feed. After 6 months, α-IFN therapy was resumed because of increasing platelet count. It was then definitively stopped because of insufficient response (the platelet count was constantly over 800 $\times$ $10^3/\mu L$). The patient had 2 more pregnancies under treatment with only ASA (100 mg daily). The first pregnancy, in October 1998, resulted in a spontaneous abortion after a few weeks of gestation; the other pregnancy, in July 2000, was complicated by symmetric IUGR, severe oligohydramnios, and absence of diastolic flow in the umbilical artery Doppler. A cesarean section was performed at 30 weeks of gestation. The Apgar score was 3 and 6 at 1 and 5 minutes, respectively, and the infant died after a few days from prematurity.

Patient 2

This woman was diagnosed with ET in March 1997, and soon started α-IFN therapy (3 MU 5 days per week) because of her history of bleeding episodes. In June 1997, she became pregnant. After counselling, she agreed to continue α-IFN therapy, and the dose was