Pregnancy in Chronic Myeloid Leukemia: Analysis of the 19 Cases

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Objectives

Treatment of chronic myeloid leukemia (CML) with tyrosine kinase inhibitors (TKI) and its impressive results led to much better survival and quality of life of these patients. Therefore planning of pregnancy, its management in this cohort and dealing with CML during its course are becoming an issue of increasing interest for many research groups. This report is an attempt to summarize our own data in this field with special focus on exposure to TKIs and their possible influence on the fetus.

Methods

Study comprises 19 cases of pregnancies in CML collected in several regions of Ukraine from 2009 until 2015: 13 pregnancies occurred in 8 women with chronic phase CML with different treatment and 6 pregnancies - in partners of male CML patients. Pregnancies were detected at different stages of leukemia course and treatment, summarized and analyzed with special focus on anti-leukemic therapy in this period. Standard hematological, cytogenetic tests were performed for monitoring. Molecular response was investigated only in some of the cases.

Results

Tab.1: Pregnancy outcomes for CML patients monitored at IBPTM, Lviv, Ukraine

	Total No. of pregnancies	Healthy infants	Ongoing	Premature	Fetal abnormalities	IM during pregnancy	No TKI treatment
Female pts	13	9	0	4	0	9	4
Partners of male pts	6	6	0	0	0	4	2
Total	19	15	0	4	0	13	6

Pregnancies in women with CML were divided into 2 subgroups: 1) 9 - with TKI uptake (imatinib) at any stage of pregnancy; 2) 4 - without anti-leukemic treatment during pregnancy. In the 1st subgroup 6 of 9 cases concluded with successful births of healthy newborns, in 3 cases early spontaneous abortions were reported. Interestingly, 2 of these spontaneous abortions occurred in 1 woman with CML who took imatinib (IM) at conception. This patient subsequently stopped the drug and became pregnant for the third time with successful outcome. In the 2nd subgroup of 4 cases without TKI during pregnancy 3 ended in successful childbirths, elective abortion occurred in 1 case. All pregnancies occurring in partners of men with CML resulted in birth of healthy newborns (Tab.1).

Analyzing the most interesting subgroup of pregnancies with TKI exposure it is important to note that no fetal abnormalities were found. This could be explained by the timing of imatinib exposure - either at very early stages (obstetrical week 4-5) or after week 22 omitting the period of active organogenesis. Due to limited availability and affordability of interferon in Ukraine most of the patients tended to interrupt and avoid anti-leukemic treatment during pregnancy (Fig.1) except for the 4 cases when imatinib was taken after week 22 due to the prominent disease progression. In all cases this treatment appeared to be safe both for mother and the fetus (Tab.2). Interestingly, in one of these patients who lost her complete hematological response (CHR) during pregnancy with quite rapid disease progression interferon (IFN) was initiated at 28 weeks of pregnancy (leukocytapheresis - not available). Due to unacceptable intolerance and low efficiency IFN was stopped and IM initiated in standard dose at obstetrical week 30 resulting in renewal of CHR and successful birth of healthy newborn (Fig. 3). In another case the patient was in major molecular response (MMR) at conception and for the first 24-25 weeks of pregnancy with subsequent *BCR/ABL* level rising to 5.187%. Due to patient decision and unavailability of leukocytapheresis and IFN (not reimbursed by the state) she initiated IM standard dose at obstetrical week 25 and subsequently delivered a healthy infant. Unavailability of IFN or leukocytapheresis was apparently the reason for use of IM in remaining two cases at the late stages of pregnancy with successful outcomes (Fig.2 and Fig.4).

Tab.2: Pregnancy outcomes and CML management in pregnant CML patients with IM exposure during pregnancy.

Pts	CML before Pregnancy	Treatment at conception	CML during pregnancy	Treatment during pregnancy	Outcome of pregnancy	CML After pregnancy	Treatment after pregnancy
OG	CCyR	IM 400	CHR	None	Miscarriage	Loss of CCyR	IM 600
OG	CCyR	IM 600	CHR	None	Healthy	Loss of CHR	IM 600
OM	MMR	IM 400	MMR	None	Healthy	MMR	None
ID	MinorCyR	IM 600	Loss of CHR	IM 400	Healthy	CHR	IM 400
VH	NA	NA	First Dx	IM 400	Healthy	CHR	IM 400
HT	CHR	IM 400	CHR	None	Miscarriage	CHR	IM 400
HT	CHR	IM 400	CHR	None	Miscarriage	CHR	IM 400
OO	Minor CyR	NA	Loss of CHR	IFN, IM 400	Healthy	CHR	IM 400
NP	MMR	IM 400	Loss of MMR	IM 400	Healthy	CHR	IM 400

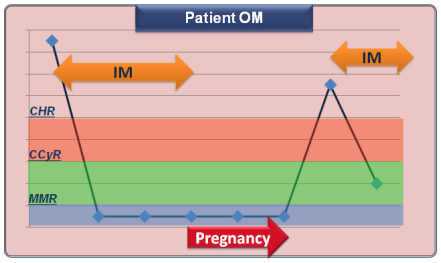

Fig.1: CML course of patient OM remaining in MMR during whole pregnancy

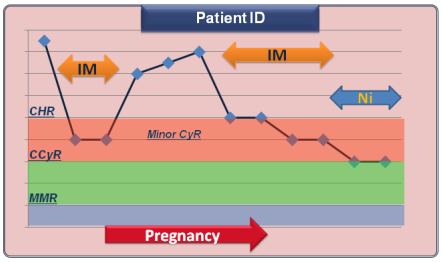

Fig.2: CML course of patient ID who lost her CHR and was treated with IM at late stages of pregnancy

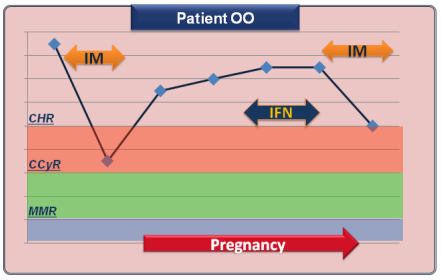

Fig.3: CML course of patient OO treated with IFN and IM during pregnancy due to loss of CHR

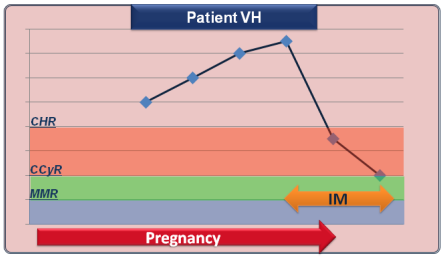

Fig.4: CML course of patient VH diagnosed during pregnancy and treated with IM during pregnancy

Conclusions

Management of CML in pregnancy should depend on the depth and duration of CML response and term of pregnancy. The issue of anti-CML treatment during pregnancy is controversial with current recommendations excluding all agents except for interferon. However, according to certain reports and also results of this small study collecting the bigger number of cases with exposure of imatinib in late stages of pregnancies possibly within related international registries could be expedient for further study.

References

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