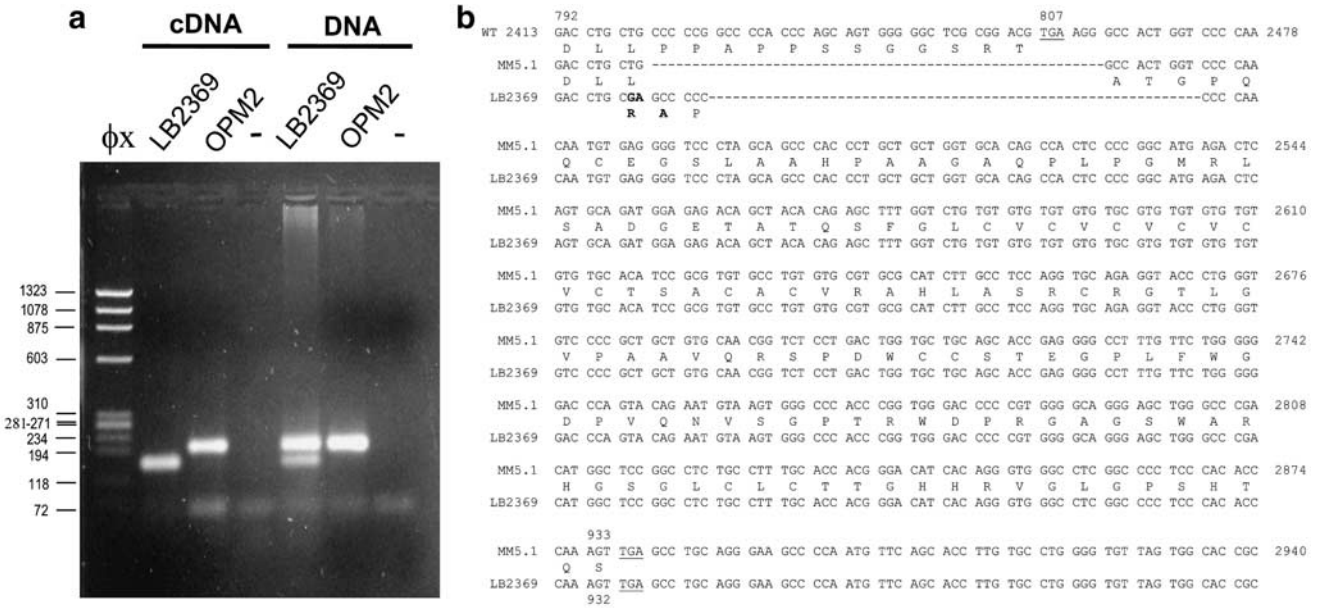

Figure 1 Mutation analyses of MM tumor LB2369. (a) RT-PCR and PCR analyses of case LB2369. mRNAs from the case and OPM-2 cell line (used as a wild-type control)[1] were reverse-transcribed and cDNA were amplified using primers across stop codon 807 (5′ primer nt 2325–2349; 3′ nt 2518–2494)[9] as previously described.[7,8] An expected 193 bp fragment is detected in the wild-type control but not in case LB2369 showing a single band smaller in size. PCR amplification of tumor LB2369 DNA demonstrates the presence of both the normal and abnormal fragments in tumor DNA. (–), water control. (b) Nucleotide sequence of the 3′ end of the *FGFR3* gene. Nucleotide and amino acids are numbered according to the sequences previously reported.[9,10] Nucleotide deletions (– – –) and changes (bold type) in LB2369 are shown and compared with the MM5.1 cell line.[11] Predicted amino acid sequences are indicated; substituted amino acids (position 794–795) in LB2369 are in bold.

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Successful treatment of chronic myeloid leukemia during pregnancy with hydroxyurea

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TO THE EDITOR

The incidence of chronic myeloid leukemia (CML) associated with pregnancy is estimated to be 1/75 000.[1] The management of CML during pregnancy poses a therapeutic dilemma because of the potential teratogenic effect of therapy. Several types of treatment have been used for CML during pregnancy included cytotoxic drugs, alpha interferon and leukapheresis. Hydroxyurea (HU) is thought to have the lowest mutagenic potential among the cytotoxic agents. In places like the rural parts of Malaysia where leukapheresis or interferon is not available and termination of pregnancy is unacceptable, the majority of CML patients are managed with HU. Literature review shows that only a few patients treated with HU during pregnancy have been reported. Neither teratogenic nor hematologic consequences to the fetus were detected in these cases.[2–6] We present a patient with CML in whom HU was used during pregnancy with a successful outcome for both mother and fetus.

A 28-year-old patient was referred at 27 weeks for hyperleukocytosis and thrombocytosis. She was asymptomatic and there was no hepatosplenomegaly. Her white blood cell count (WBC) was 248 × 10^9/l (65% neutrophils, 10% myelocytes, 4% metamyelocytes, 4% blast, 10% lymphocytes, 1% monocytes and 6% basophils), platelet count (PC) 1340 × 10^9/l and hemoglobin 10.4 g/dl. Bone marrow examination showed CML in chronic phase. Philadelphia chromosome test was positive. HU, 4 g daily was initiated after obtaining informed consent. Three weeks after receiving HU, the WBC was 8.7 × 10^9/l and PC, 541 × 10^9/l. The disease was kept under control with doses of hydroxyurea ranging from 3 to 1.5 g daily. Throughout her pregnancy, ultrasonography showed a normal appearing fetus. Labor was induced at 38 weeks of gestation. The patient's WBC at that time was 17.7 × 10^9/l. A healthy baby boy weighing 2.68 kg, with Apgar score of 8 at 1 min and 9 at 5 min was delivered vaginally. Clinical examination of the baby showed no abnormality and the blood count was normal. As HU passes into breast milk with the risk of inducing bone marrow suppression, breast-feeding was avoided. The patient and her child continue to do well following delivery. One month postpartum, the patient's blood counts remained stable and alpha interferon therapy was initiated.

The management of CML in pregnancy involves prevention of placental insufficiency and other complications of hyperleukocytosis by control of maternal WBC, while avoiding harmful fetal exposure to cytotoxic drugs. Busulphan and HU inhibit DNA synthesis, and may cause abortion, malformation or fetal growth retardation. Congenital malformations have been observed with busulphan therapy during

Correspondence: Fadilah S-Abdul-Wahid, Mater Medical Research Institute (MMRI), Aubigny Place, Raymond Tce, South Brisbane, Queensland 4101, Australia; Fax: 61 7 38402556
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pregnancy.[7] Pre-eclampsia, intrauterine growth retardation and stillbirths have been documented in patients on HU during pregnancy, although they could not be ascribed to the HU therapy with certainty.[2,5] In our patient, HU treatment initiated at 27 weeks of gestation had no adverse effect on the mother and her fetus. However, the baby's growth and development has to be monitored because of the unknown long-term potential risks of the drug. Although, it appears at this point that HU therapy given after the second trimester is safe and effective for the treatment of CML during pregnancy, more data are required before HU could be considered as the treatment of choice among this group of patients. HU may thus be a useful and cheaper alternative to interferon for pregnant patients with CML in situations where leukapheresis is not available.

SAW Fadilah[1]
H Ahmad-Zailani[2]
C Soon-Keng[1]
M Norlaila[1]

[1]*Clinical Haematology and Stem Cell Transplantation Services, MAKNA-HUKM Cancer Institute, Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM), Kuala Lumpur, Malaysia; and* [2]*Department of Obstetric and Gynaecology, Faculty of Medicine, Universiti Kebangsaan Malaysia (UKM), Kuala Lumpur, Malaysia*

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