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CASE REPORT

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Chronic Myeloid Leukemia During Pregnancy with Placental Involvement: Case Report and Literature Review

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ABSTRACT

Introduction: Chronic myeloid leukemia (CML) occurrence during pregnancy is unusual due to the low prevalence of the disease in women of childbearing age, with only three reported cases. **Case report:** The mother was diagnosed with CML with positive BCR-ABL gene fusion in her 32nd week of gestation. The placenta showed an increased population of myelocytes and segmented neutrophils in the intervillous space and features of maternal villous malperfusion (increased perivillous fibrinoid material and distal villous hypoplasia). The mother underwent leukapheresis and delivered the neonate at 33 wk gestation. The neonate demonstrated neither leukemia nor other pathology. The mother is in remission after four years of follow-up. **Conclusion:** Leukapheresis was performed safely during pregnancy and provided a safe management strategy until the delivery one week later.

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Chronic myeloid leukemia; metastasis; placenta; pregnancy

Introduction

Placenta is the flight recorder of pregnancy; it can give extraordinary information about the mother and baby. Placental and fetal metastases of maternal malignancies has a frequency of 1 per 1000 live births, and very few of them have presented as hematological neoplasia [1].

Seventy-four appropriate instances were found in the literature until May 2022, with placental and fetal metastases occurring in 63 (72.5%) and 24 (27.5%) of cases, respectively. A systematic search was performed to retrieve all studies on placental pathology in hematological neoplasia during pregnancy published in PubMed/Medline up to May 2022 (1956–2022).

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In the literature, there are thirty-two publications, twenty of which are leukemia cases. Of the thirty-two instances, eleven patients (34.4%) had placental metastases; there were no fetal metastases.

The most common malignancies associated with pregnancy include cervical cancer, breast cancer, melanoma, lymphomas, and leukemias [2]. The true frequency of leukemia during pregnancy is unknown. It is estimated that 1 in 75,000 to 100,000 pregnancies are affected [3]. Acute leukemias are more frequent. Chronic myeloid leukemia (CML) accounts for less than 10% of all chronic leukemia cases [2,3]. CML is a common hematologic cancer; however, its occurrence during pregnancy is unusual due to the low prevalence of the disease in women of childbearing age.

While a significant body of studies investigating and reporting maternal outcomes in solid tumors cases, studies on the placental and fetal effects of maternal hematologic malignancy and vertical transmission are scarce, with current literature primarily consisting of case reports. In this study, we examine one patient with a hematologic neoplasm during pregnancy, documenting placental pathology and neonatal follow-up.

Case report

A 31-year-old pregnant woman presented at 32 wk of gestation with leukocytosis. She had seven previous gestations with three spontaneous abortions due to unknown reasons. Peripheral white blood count was $281.75 \times 10^3/mm^3$ with 25% blasts, consistent with leukemia, suggesting CML. Cytogenetics demonstrated a reciprocal translocation of t (9:22). The mother underwent leukapheresis, improving the leukocyte count from $305.41 \times 10^3/mm^3$ to $179 \times 10^3/mm^3$. C-section at 33 wk delivered a 2825-gram appropriate for gestational age male infant. The infant was healthy, with no leukemia, and neonatal outcome was favorable- there was no vertical transmission. After treatment, the mother is in remission after a four-year follow-up. The latest leukocyte count was $4.34 \times 10^3/mm^3$.

The placental weight was above the >90th percentile (LGA: large for gestational age) at 606 grams. By light microscopy, the intervillous area was hypercellular due to white blood cells with an increased population of myelocytes, segmented neutrophils, and 20-25% blast cells by H and E (Figure 1A and B). In contrast, 1–2% of cells were

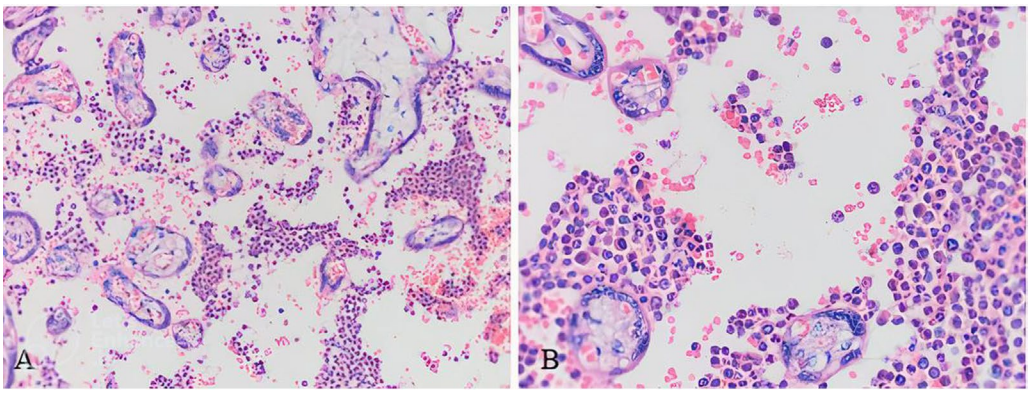


Figure 1. White blood cells, some with blastic configuration, in the intervillous space of the placenta. (H&E; ×20) (A) and (H&E; ×40) (B).

positive with CD34, and 3-4% cells were positive with CD117 (Figure 2A and B). There was no invasion into chorionic villi. Immunohistochemically, the blast cells were positive for CD10 (Figure 3A and B), MPO (Figure 3C and D), and CD15 (Figure 3E and F). CD3, CD4, CD5, PAX, and TdT were all negative. The placenta was considered involved with CML Maternal vascular malperfusion features included increased syncytial knots, distal villous hypoplasia, and increased perivillous fibrin deposition (Figure 4A and B). Chorioamnionitis (maternal stage 1, grade 2) was present.

Discussion

Placental metastases of maternal neoplasms is well documented in solid tumors, unlike hematologic neoplasms. We presented a case of a leukemic woman who had a placental spread of CML and successfully delivered a male infant.

Among all malignancies affecting the placenta and fetus, leukemia represents less than 10% of cases [2, 4–14]. Among these, CML, which is not expected to occur during pregnancy, has been reported in only three patients in the literature [2, 15] (Table 1).

In the study of Ashlie E. et al., in 11 cases with hematological neoplasia in pregnancy, eight leukemia cases, two of which were CML, were reported. In two of these cases (CML cases), involvement was observed only in the intervillous area.

Maternal vascular malperfusion was documented in 7/8 (88%) leukemia cases. Neonatal follow-up was available in eight patients; all children were alive and well [2].

In the review published by Wolters VERA et al. [20, 21], who investigated placental pathology in cancer during pregnancy and after exposure to cancer treatment, 111 cases of neoplasia were reported during pregnancy. As in solid tumor metastases, the most common involvement in leukemia cases was reported as intervillous space involvement, and the most common accompanying microscopic finding was MVM lesions [14]. In the same review, it was reported that the outcome of women with placental involvement was worse. It has been reported that the median survival of women without intravillous (intervillous, umbilical cord, or fetal vessels) involvement is longer

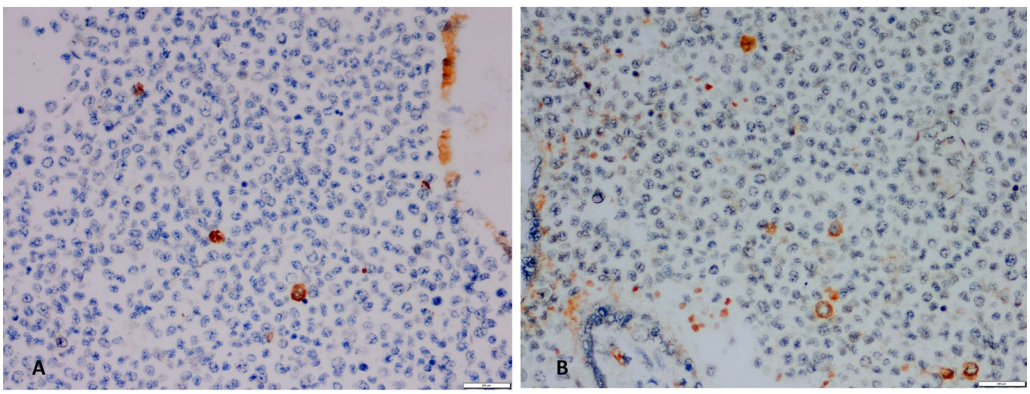


Figure 2. Few blast cells expressing CD34 (×40) and CD117 (×40).

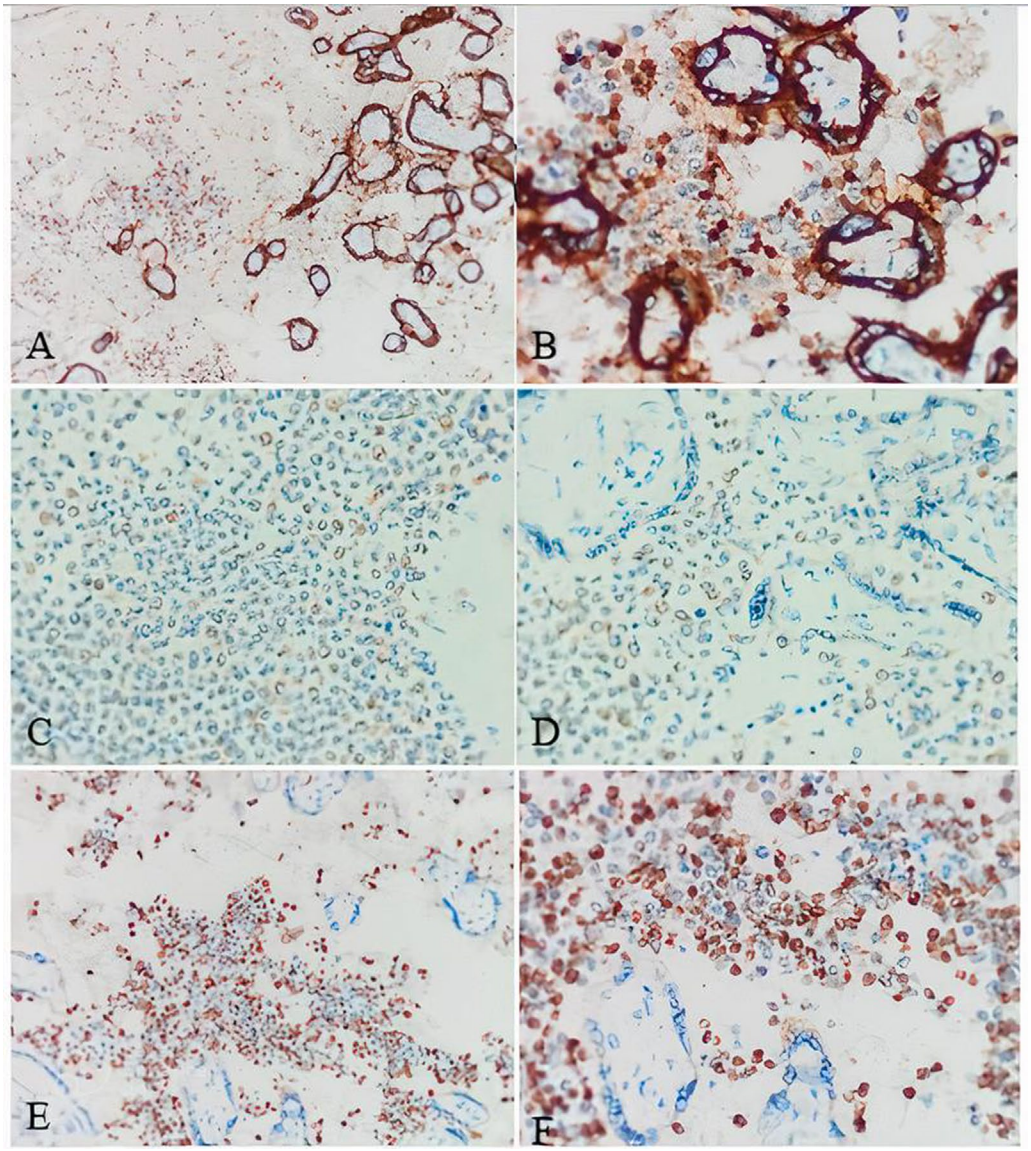


Figure 3. Blast cells were positive. (CD10; ×20) (A), (CD10; ×40) (B), (MPO; ×20) (C), (MPO; ×40) (D), (CD15; ×20) (E), (CD15; ×40) (F).

than that of women with intravillous involvement [14]. Although the presented case has placental involvement, the prognosis is good. The mother is in remission after four years of follow-up.

As in our case, in the literature, the intervillous space spread was the most common placental spread in pregnant women with hematological malignancies [2]. MVM lesions were the most common other accompanying pathological findings. Cases with MVM of the placenta are usually associated with placentas small for gestational age (SGA). In our case, LGA was seen. It is probably because of CML involvement in the placenta.

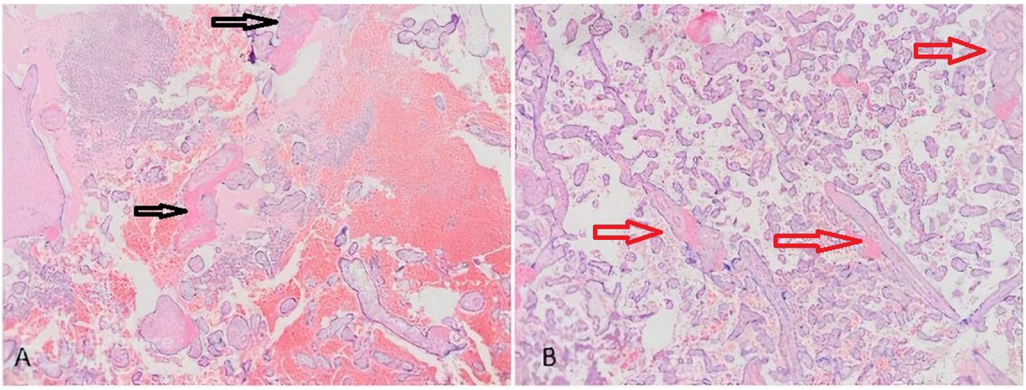


Figure 4. Black arrows show the bridging perivillous fibrinoid material, and red arrows show distal villous hypoplasia resembling maternal villous malperfusion. (H&E; ×4) A-B.

The proposed existence of a (partial) barrier between the maternal and fetal interface and the protective role of the fetal immune system explains why the intravillous area is less apt to be involved. If present, it should be construed as a sign of invasion into the fetal compartment of the placenta.

The mean gestational age at birth was 33 wk and five days in the literature [14]. Our case was consistent with the literature.

Although cases with placental weight above the >90 percentile were reported as in our case, the most common recorded weights were within the 10–90th percentiles in the literature [2].

Placental weight below the <10 percentile cases have been reported frequently in chemotherapy treatment cases [16,17]. Similarly, most of the infants in publications were born AGA.

The publications reporting placental involvement without intravillous space spread showed no evidence of disease in the infant [2, 14]. Fetal metastasis and poor outcome were observed in the fetuses of cases with intravillous involvement [16, 18]. In our case, intravillous space spread was not found, and the fetal outcome was favorable.

CML, unlike other hematological neoplasms, is usually treated conservatively. Aggressive treatments can be delayed to the postpartum period. Feto-maternal complications that may develop due to more aggressive treatments, such as

Table 1. A literature review of placental involvement by CML [2, 15].

Study	Cancer type	N	Cancer treatment(s)	GW	Placenta weight	MVM	FVM	II	VI	Other Involvement	Fetal/ infant metastasis	Other lesions	Infant outcome
Staley (2018)	CML	1	IFNa	38	n.r	–	–	–	–	–	–	ASC-CV	WED
Ashlie E. (2021)	CML	1	Yes*	35	%50-%75	+	–	+	–	–	–	–	WED-3 weeks
Ashlie E. (2021)	CML	1	Yes*	32	>%90	–	–	+	–	–	–	–	WED-5 weeks
The present study	CML	1	Leukapheresis	33	>%90	+	–	+	–	–	–	CA	WED-6 months

ASC-CV: Acutesubchorionitis and chorionic vasculitis, CA: Chorioamnionitis, CML: FVM: fetal vascular malperfusion, II: intervillousinvolvement, MVM: maternal vascular malperfusion, WED: without evidence of disease, VI: Villous involvement.
*The type of treatment was not specified.

chemotherapy during pregnancy, are not expected in cases of CML (such as SGA, stillbirth, preterm birth, and IUGR). In our case, leukapheresis was performed as a conservative therapy.

For differential diagnosis, chorioamnionitis should be considered. In chorioamnionitis, the infiltration pattern is denser in the sub-amniotic region than in the intervillous area, and infiltration components differ. For example, if it is chronic chorioamnionitis, we expect to see lymphohistiocytic infiltration of mature cells. Another entity for differential diagnosis is eosinophilic/T cell vasculitis; in this case, vasculitis should be seen in chorionic plate vessels, and the infiltration is composed of eosinophil leukocytes and T cells [19]. We can differentiate these two entities from CML involvement of the placenta by the absence of increased blastic cells in the intervillous compartment. Also, the mother's clinical findings should be considered.

Conclusion

Leukapheresis can be performed safely during pregnancy while the mother is in a blast crisis. This management allowed an additional week of gestation before delivery by cesarean section. The evaluation of the placenta demonstrated maternal but not fetal involvement, with further assurance that the child was not affected.

Disclosure statement

No potential conflict of interest was reported by the authors.

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