Congenital Acute Lymphoblastic Leukemia with Placental Involvement: Case Report x

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Abstract

The authors describe a case of congenital acute lymphoblastic leukaemia (ALL), with extensive placental involvement, causing intrauterine fetal growth restriction and unexpected fetal demise at 33 weeks. Although rare, other congenital tumours, including neuroblastoma and hepatoblastoma, can metastasize to the placenta. Congenital malignancy must be considered in the differential diagnosis of an abnormally large placenta. This case emphasizes the important role of careful histopathologic examination of the placenta which, combined with immunohistochemistry and clinicopathologic correlation, may establish the accurate diagnosis.

Keywords: Congenital leukemia; Fetal malignancies; Intrauterine growth restriction; Unexpected fetal death; Placenta pathology

Background

Fetal and placental malignancies are rare complications during pregnancy [1]. Malignant congenital tumours of fetal origin, with placental involvement, are less commonly described. Congenital leukemia during the perinatal period occurs uncommonly and prenatal diagnosis of this entity is rare [2,3]. The authors describe a clinical case of congenital acute lymphoblastic leukaemia (ALL), with extensive placental involvement, causing intrauterine fetal growth restriction and unexpected fetal demise at 33 weeks. The rarity of this placental involvement may be artefactual and may result from failure to examine grossly enlarged placenta in cases of stillbirth.

Case Presentation

A 36-year-old woman, gravida 2 para 1, was referred to our hospital at 33 weeks with abdominal pain and premature rupture of membranes. Intrauterine fetal demise was diagnosed by ultrasound. Induction was performed and a vaginal birth occurred with a stillbirth of 1605g (25th percentile). Patient was discharged 48 hours after delivery. Few months later after delivery, the patient was diagnosed with a Large B-cell lymphoma.

The patient's previous pregnancy had been uneventful resulting in a spontaneous vaginal delivery at 36 weeks. There was no history of abortions, radiation or chemical exposure in the past. During this pregnancy, she had an uneventful first and second trimester. The three routine scans performed during pregnancy were normal. The patient's family history showed that her mother had chronic lymphocytic leukaemia (CLL).

Blood group incompatibility, fetomaternal haemorrhage, chromosomal abnormalities and infections were also considered as a possible cause of this intrauterine fetal growth restriction and fetal demise. The placenta and stillborn were sent for pathological evaluation.

Indirect coombs and Kleihauer Betke tests were negative. Infectious agents studies on maternal serum excluded recent infection with a variety of viruses, including cytomegalovirus, rubella, parvovirus B19, varicella zoster and Epstein-Barr Virus (EBV) and toxoplasmosis and syphilis. Blood group incompatibility was also excluded. Fetal karyotyping revealed a normal female karyotype, 46, XX.

Postmortem placental examination showed that the placenta was bulky, pale and heavy for the gestational age (>90%). Histological examination of the placenta revealed chorionic villi greatly expanded with a highly cellular stroma due to diffuse infiltration by hyperchromatic, poorly differentiated cells. The fetal villous vessels also contained clumps of blast cells and malignant cells were widely disseminated throughout the fetal vasculature. Abnormal cells were not found in the intervillous space nor in the adjacent decidua. Using light microscopy alone it was not possible to determine whether these blast cells were myeloblasts or lymphoblasts. Cytochemical staining of lymphoblast was negative for myeloperoxidase. Immunohistochemically, the blasts expressed B-cell markers: CD20+, CD45, CD3-, CD34-, TdT- (B-ALL).

The fetal necropsy showed mild hepatomegaly without other congenital structural defects. Microscopic examination of the liver showed marked congestion and an atypical lymphoid infiltrates mainly in the portal area or forming nests in the parenchyma.

Discussion

The frequency of leukemia in fetuses is less than in older children. Acute leukemia is classified as congenital when diagnosed at birth and it is usually acute myeloid leukaemia [4]. Congenital acute lymphoblastic leukaemia (ALL) is rare, most often of B cell lineage,
and with a worse prognosis than childhood ALL [4]. Prenatal features are non-specific, with hydrops and hepatosplenomegaly present in two-thirds of cases and intrauterine death complicating about half [2]. None of these signs were identified on the three ultrasounds performed during pregnancy. However, at fetal autopsy, a mild hepatomegaly was recorded.

Likewise intrauterine infections, genetic disorders (e.g.: Beckwith-Wiedemann syndrome) or maternal disease (e.g.: anaemia, diabetes), the congenital malignancies may cause placental enlargement [4,5]. Most frequent chromosomal abnormalities, including Down syndrome, more often associated with this diagnose, were excluded.

The diagnostic criteria for congenital leukaemia include proliferation of immature leucocytes, infiltration into the extra haematopoietic tissue and absence of diseases that can cause leukaemia or leucoerythroblastic reactions [4,5]. Moreover, genetic or chromosomal disorders that may be associated with unstable haematopoiesis, such as trisomy 21, leukemoid reactions and blood group incompatibility must be distinguished from acute leukemia [6].

Some authors have suggested a link between prenatal viral exposure and leukaemia risk but the only link found was the association between the Epstein-Barr virus (EBV) and ALL [7,8] and it was excluded in our case.

Few months later after fetal demise, the patient was diagnosed with a Large B-cell lymphoma. Metastases of maternal cancer to the placenta and fetus are rare in cases of maternal primary malignancy. Since malignant cells were never identified in placental intervilous space, placental and fetal metastasis from this maternal haematological cancer would be unlikely. An increased risk of non-Hodgkin lymphoma among individuals with a family history of hematopoietic malignancy (e.g.: chronic lymphocytic leukemia) was also reported [9].

Extensive stromal and vascular involvement of the placenta by leukemic cells was considered to be the probable cause of this IUGR and unexpected fetal death.

Conclusion

Congenital malignancy must be considered in the differential diagnosis of an abnormally large placenta.

The dissemination of fetal malignant disease involving the placenta, such as congenital acute lymphoblastic leukemia, and the fact that most congenital neoplasm are not apparent at birth still presents a considerable diagnostic challenge to healthcare professionals.

This case emphasizes the important role of careful histopathologic examination of the placenta which, combined with immunohistochemistry and clinicopathologic correlation, may establish the accurate diagnosis.

References