A Case of Coloboma in a Newborn to a Woman Taking Mycophenolate Mofetil in Pregnancy After Kidney Transplantation

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ABSTRACT
Recently, mycophenolate mofetil (MMF) has been introduced in the immunosuppressive strategy after kidney transplantation. Recently, the existence of a MMF associated embriopathy has been hypothesized, namely, multiple craniofacial malformations. Only 1 report has described chorioretinal coloboma.

We report a case of woman who used MMF throughout pregnancy after kidney transplantation. Her newborn developed coloboma of the right eye associated with an ocular cyst without any other malformation. The other drugs used by our patient are not considered teratogenic. Therefore, it seems reasonable to conclude a causal relationship between MMF and the malformation observed in this newborn.

THE SIDE EFFECTS on the fetus in pregnant women using immunosuppressive drugs after solid organs transplantation have been studied. No teratogenic effects has been reported for steroids, calcineurin inhibitors, or azathioprine. Recently mycophenolate mofetil (MMF) has been introduced into the immunosuppressive strategy after kidney transplantation. It has had substantial success, partially because of its lack of adverse renal effects. MMF is an ester prodrug of mycophenolic acid, a reversible inhibitor of inosine monophosphate dehydrogenase, thereby blocking de novo purine synthesis in T and B lymphocytes. In vitro and in vivo studies have shown teratogenic effects of MMF. Recently, the existence of an MMF-associated embriopathy has been hypothesized, consisting of multiple craniofacial malformations. For these reasons MMF is considered potentially teratogenic. Its use is not recommended in pregnancy. Herein we have reported a case of a woman who used MMF throughout pregnancy after kidney transplantation. Her newborn developed coloboma of right eye associated with an ocular cyst without any other malformation.

CASE REPORT
In 2001, a 35-year-old woman received a cadaveric kidney transplant because of renal insufficiency after a streptococcus infection. Immunosuppressive therapy consisted of tacrolimus (4 mg/od), prednisone (5 mg every other day), and azathioprine (50 mg/od). MMF was added to the immunosuppressive regimen at the same time. She is now 2 years post-transplantation. The child was born by cesarean section at 36 weeks of gestation, with a birth weight of 3200 g. At birth, the baby had a coloboma of the right eye associated with an ocular cyst. The other drugs used by our patient are not considered teratogenic. Therefore, it seems reasonable to conclude a causal relationship between MMF and the malformation observed in this newborn.

Fig 1. Choroidal coloboma involving the optic disc.

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mg/od). Due to the development of rejection symptoms, MMF (500 mg/od) replaced azathioprine. When she became pregnant (6 months after MMF addition), she continued MMF owing to the short interval from the presence of rejection. Fetal ultrasound at 15 weeks of gestation did not show any malformation. Amniocentesis performed at 17 weeks revealed a 46 XY normal karyotype. This woman was referred to our center at 28 weeks of pregnancy. Although the evolution of pregnancy had been normal to 37 weeks, a Caesarian section was performed to deliver a male newborn, whose weight was 2850 g and length 48 cm, due to persistent mild proteinuria (300 mg/day). Physical examination by the pediatricians and laboratory tests did not show any abnormality. A few days after birth, the woman noticed that the right eye was smaller than the other and that the shape of the iris was abnormal as well. Ocular funduscopy showed a choroidal coloboma involving the optic disc (type 1 according to the Ida Mann classification; Fig 1). At present, the baby undergoes periodic funduscopy and MR to check the evolution of this abnormality (Fig 2). Coloboma is associated with impaired visual capacity.

DISCUSSION

The use of MMF in pregnancy has been associated with malformations that include cleft lip and palate, microtia plus external auditory canal atresia, micrognathia, hypertelorism, and agenesis of the corpus callosum. Sifontis et al reported cleft lip and palate and microtia to be associated with congenital diaphragmatic hernia and heart defects. Only in 1 report was a chorioretinal coloboma seen upon funduscopic examination. Teratologic studies of MMF in rats and rabbits showed fetal malformations, including anopthal mia. Recently, a cumulative dose-dependent effect of MMF has been reported to affect the severity of embryopathy, however, our patient was receiving the same amount of MMF as in previous reports.

It is often difficult to interpret single case reports of malformations, as they do not prove causation. But when a drug that is not commonly used in pregnancy causes rare malformations, a causal relationship is likely. Neither tacrolimus nor prednisone have shown specific teratogenic effects. It seems reasonable to conclude that there is causal relationship between MMF and the malformation observed in this newborn. Women should be advised about contraception during the course of MMF treatment and the European recommendations should be applied to pregnant women after kidney transplantation.

REFERENCES


