R. Utili, A. Rambaldi, M. F. Tripodi, A. Andreana

Visceral Leishmaniasis during Pregnancy Treated with Meglumine Antimoniate

Summary: Data on the efficacy and safety of pentavalent antimony in the treatment of visceral leishmaniasis during pregnancy are scanty. A case of visceral leishmaniasis in a 39-year-old woman in the second trimester of pregnancy is reported here. The patient was hospitalized in poor condition with high fever and pancytopenia which had lasted for 6 weeks. A bone marrow aspirate revealed numerous amastigotes and serodiagnosis for *Leishmania* was positive at a high titer. The patient was successfully treated with meglumine antimoniate at a daily dose of 850 mg of antimony for 20 days. She delivered at term a healthy female baby who remains in good condition at 18 months of age. Thus a dose of 850 mg of antimony, which is lower than that presently recommended, seems to be effective and non toxic to the fetus when administered at the second trimester of pregnancy.

Introduction

Pentavalent antimony is still the first choice drug in the treatment of visceral leishmaniasis, although new drugs, such as liposomal amphotericin B, diamidines, purine analogues, aminosidine and ketoconazole are presently under investigation [1,2].

Visceral leishmaniasis is endemic in Mediterranean countries. However, according to a Medline search, in the last 10 years very few cases of this disease in pregnancy have been described and little is known about the efficacy and potential teratogenicity of standard Leishmania drugs in this situation. We report a case of visceral leishmaniasis successfully treated with meglumine antimoniate in a pregnant woman who lived in the Vesuvian area near Naples where the disease is endemic.

Case Report

This 39-year-old patient began to suffer from remittent fever (peaking to 38–39°C) at the 18th week of pregnancy. The patient was initially hospitalized in a general hospital, but later referred to us because of persistently high fever, which had been non-responsive to antibiotic treatment, and because of symptoms of pancytopenia. On admission she was pale, weighed 78 kg, and had a blood pressure of 140-50 mmHg, a pulse rate of 100/min, and a temperature of 40°C. Clinical examination revealed an abdomen as in the 24th week of pregnancy, hepatomegaly and a marked splenomegaly, a papular rash at the thorax, a systolic murmur 2/6, and no enlarged lymph nodes. Laboratory studies were as follows: hemoglobin 5.9 g/dl, hematocrit 18%, leukocytes $1.6\times10^3/mm^3$, platelets $72\times10^3/mm^3$, erythrocyte sedimentation rate 115 mm, blood glucose 145 mg/dl, albumin 2.7 g/dl, gamma globulin 2.38 g/dl, choline esterase 3,338 U/l, alkaline phosphatase 802 U/l, gamma glutamyl-transpeptidase 145 U/l. Kidney function tests were normal. Ultrasound examination showed an enlarged liver with regular margins, no focal lesions, and with ectasia of the portal (19 mm) and splenic (13 mm) veins. The spleen was clearly enlarged (maximum span 23 cm). The uterus was as in a normal pregnancy at 24 weeks, with physiological fetal movements, and amniotic fluid at lower normal limits. The patient received one unit of packed red blood cells, albumin, furosemide and potassium. Serodiagnosis for *Leishmania* (IHA) was positive at a titer of 1:8,192. A bone marrow aspirate revealed numerous amastigotes. Accordingly, on the second day treatment with meglumine antimoniate was initiated at a dose of 12 mg of pentavalent antimony per kg of body weight per day, corresponding to a dose of 850 mg of antimony per day. The treatment was carried out for 20 days. After a few days of therapy the physical condition of the patient improved, and the laboratory tests gradually normalized. The treatment was well tolerated. Close clinical and ultrasonography monitoring of the pregnancy showed a normal development of the fetus. The patient delivered a female baby weighing 4.2 kg at 41 weeks of pregnancy; on inspection, the placenta appeared to be normal. At birth the neonate was alert with an Apgar score >12 and no signs of disease were present. A close follow-up of the neonate revealed no signs of visceral leishmaniasis. Leishmania antibodies were found in the serum of the neonate at a titre of 1:1,024 (IHA). The antibody titre declined and became negative at the sixth month, indicating passive transplacental transmission. Both the mother and the child have been observed for 18 months after delivery. Up to now, the development of the baby has been normal and no symptoms or signs of visceral leishmaniasis have recurred in the mother.

Discussion

We were faced with a severely ill pregnant patient with visceral leishmaniasis who needed prompt treatment. Considering that no data were available on the toxicity of pentavalent antimony during pregnancy and that our patient was in the second trimester of pregnancy, it appeared clear that the risks of visceral leishmaniasis to the mother out-

Received: 27 October 1994/Revision accepted: 8 March 1995

R. Utili, M. D., *A. Rambaldi*, M. D., *Marie Françoise Tripodi*. M. D., *A. Andreana*, M. D., Institute of Medical Therapy, Chair of Tropical Medicine, Faculty of Medicine, 2nd University of Naples, Italy.

Correspondence to: Prof. Dr. *R. Utili*, Istituto di Terapia Medica, Facoltà di Medicina e Chirurgia, Seconda Università di Napoli, Via Cotugno 1 (c/o Ospedale Gesù e Maria), I–80135 Naples, Italy.

Infection 23 (1995) No. 3

weighed those of the drug to the fetus. Accordingly, we decided to use pentavalent antimony and exclude other drugs, as they are either more toxic (i.e. pentamidine), or as yet of uncertain efficacy (i.e. allopurinole or imidazoles) or were not available (i.e. parenteral aminosidine, or liposomal amphotericin B) [3]. After having informed the patient and her husband of the potential toxicity of this drug we received their consent to treatment.

The standard regimen of pentavalent antimony for treating visceral leishmaniasis is 20 mg/kg/day for 20 to 28 days. The WHO recommended that the maximum daily dose of antimony be limited to 850 mg per day. Even though this restriction is no longer enforced [3], we preferred to restrict the dose and time period in view of the pregnancy. This was also possible as there is no evidence of decreased antimony sensitivity of *Leishmania donovani* strains in our area. Thus the dosage we used (12 mg pentavalent antimony/kg/day) proved to be an effective and safe treatment of visceral leishmaniasis for our patient at the 24th week of pregnancy.

To our knowledge there is only one report of treatment of visceral leishmaniasis in a pregnant woman in the last 10 years [4]. In this report the authors used the same daily dose of pentavalent antimony as in our case, for a period of 12 days. Also in this case the treatment was effective and non toxic. Unfortunately, there is no information on the trimester when the disease occurred. No data are available at present of antimony toxicity to the fetus when it is administered during the first trimester of pregnancy. The risk of transplacental transmission of leishmaniasis has not been estimated and there are fewer than a dozen cases of congenital disease reported in the literature [5–8]. Therefore, even if the risk of congenital kala-azar seems to be very slight, we recommend treating the pregnant patient with the lowest effective dose and monitoring the neonate during the first 12 months of life.

Zusammenfassung: Viszerale Leishmaniasis in der Schwangerschaft. Behandlung mit Meglumin Antimonat. Zur Behandlung der Leishmaniasis mit pentavalentem Antimon in der Schwangerschaft liegen nur spärliche Daten vor. Bei einer 39 Jahre alten Frau trat im zweiten Schwangerschaftstrimester eine viszerale Leishmaniasis auf. Die Patientin wurde in schlechtem Zustand mit hohem Fieber und Panzytopenie, die schon über 6 Wochen bestanden hatten, stationär aufgenommen. Im Knochenmarkpunktat fanden sich zahlreiche Amastigoten, die Serodiagnose war hochtitrig-positiv für *Leishmania*. Die Patientin wurde erfolgreich mit Meglumin Antimonat mit einer täglichen Dosis von 850 mg Antimon behandelt. Diese Dosis liegt unterhalb der derzeit empfohlenen Dosis, doch scheint sie wirksam und nicht fetotoxisch zu sein, wenn sie im zweiten Schwangerschaftstrimester verabreicht wird.

References

1. **Berman, J. D.:** Chemotherapy for leishmaniasis: biochemical mechanisms, clinical efficacy, and future strategies. Rev. Infect. Dis. 10 (1988) 560–586.
2. **Rosenblatt, J. E.:** Symposium on antimicrobial agents. Antiparasitic agents. Mayo Clin. Proc. 67 (1992) 276–287.
3. **Olliaro, P. L., Bryceson, A. D. M.:** Practical progress and new drugs for changing patterns of leishmaniasis. Parasitology Today 9 (1993) 323–328.
4. **Massip, P., Goutner, Ch., Dupic, Y., Navarrot, P.:** Kala-Azar chez la femme enceinte. Presse Méd. 20 (1986) 95.
5. **Nyakundi, P. M., Muigai, R., Were, J. B. O., Oster, C. N., Gachihi, G. S., Kirigi, G.:** Congenital visceral leishmaniasis: case report. Trans. R. Soc. Trop. Med. Hyg. 82 (1988) 564.
6. **Yadav, T. P., Gupta, H., Satteya, U., Kumar, R., Mittal, V.:** Congenital kala-azar. Ann. Trop. Med. Parasitol. 83 (1989) 535–537.
7. **Kaplanski, G., Farnarier, C., Durand, J., Soubeyrand, J., Bongrand, P., Kaplanski, S.:** Leishmaniasis acquired in Belgium. Lancet 338 (1991) 885.
8. **Eltoum, I. A., Zijlstra, E. E., Ali, M. S., Ghalib, H. W., Satti, M. M. H., Eltoum, B., El-Assan, A. M.:** Congenital kala-azar and leishmaniasis in the placenta. Am. J. Trop. Med. Hyg. 46 (1992) 57–62.