Rheumatol Int (1987) 7:47–48

Rheumatology INTERNATIONAL
Clinical and Experimental Investigations

Autometallographic demonstration of gold in human fetal liver and placenta

B. Møller-Madsen, G. Danscher, N. Uldbjerg, and J. G. Allen

Institute of Anatomy B and Department of Obstetrics and Gynecology, University of Aarhus, DK-8000 Aarhus C, Denmark

Received September 6, 1986/Accepted October 10, 1986

Key words: Gold toxicology – Human liver, hepatocytes – Human placenta, fibroblasts – Lysosomes

A 19-year-old woman suffering from rheumatoid arthritis for one and a half year had an abortion medio November 1984. Menstruation was regular and she had approximately 21 weeks' of amenorrhea. Pregnancy was estimated by scanning to be in its nineteenth week. She received 50 mg sodium-aurothiomalate (Myocrisine) per week intramuscularly for a period of 21 weeks prior to conception, for a total of 1050 mg sodium-aurothiomalate prior to the termination of pregnancy. The fetus and placenta were examined for external abnormalities immediately after a prolonged delivery (8 h). No macroscopic malformations were found.

Tissue sections were processed using a histochemical technique based on autometallography [1–3] in order to visualise trace amounts of gold at the light and electron microscopic levels. The prolonged delivery caused serious damage to the tissues. Gold was found in the lysosomes of fetal hepatocytes (Fig. 1) and in fibroblasts in the connective tissue of the villus core (Fig. 2). Gold was not detected in other cells or structures of the fetal liver or placenta.

Our results demonstrate that gold is transported across the human placenta barrier and accumulates in fetal hepatocytes and fibroblasts of placenta. These findings are in agreement with the observations made by Rocker and Henderson 1976 [4], who upon subjecting tissue samples from a human fetus of 20 weeks to an electron microscope microanalysis found gold deposits in placenta, liver, and kidney, without mentioning specific cell types. In addition, Cohen et al. 1981 [5] reported venous serum gold levels that demonstrated the transplacental passage of gold in a full-term neonate. The ultrastructural localization of gold in lysosomes of fetal hepatocytes has previously been visualized in rats [6] but not in human tissue.

Sodium-aurothiomalate has been shown to be teratogenic in rats [7] and rabbits [8]. Reports of malformations in humans are sparse and controversial. The fetal material used by Rocker and Henderson 1976 [4], Cohen et al. 1981 [5], and us did not have any obvious malformations. However, Rogers et al. 1980 [9] published data describing a possible teratogenic effect of gold in an infant of a mother who had been exposed to sodium aurothiomalate before and during pregnancy. The infant was born with a cleft lip and palate, and brain abnormalities.

Transplacental transport and ultrastructural localization of gold in human placenta and fetal liver has now been documented. Since malformations in the offspring of

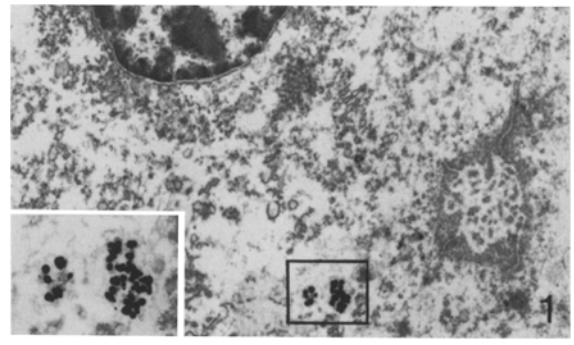

Fig. 1. Electron micrograph showing a fetal hepatocyte accumulating gold in the lysosomes. ×15 600. Inset: ×36 000

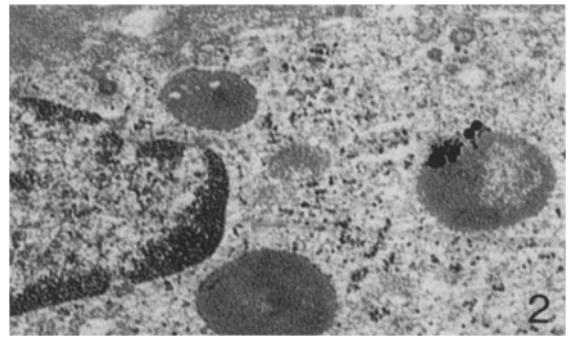

Fig. 2. Electron micrograph showing a fibroblast from the connective tissue of the villus core containing gold in the lysosome. ×25 200

mothers that have recived sodium-aurothiomalate have been described, avoidance of gold therapy during pregnancy must still be recommended.

Acknowledgement. The study was supported by the Danish Rheumatism Association Grant no. 233–458.

References

1. Danscher G (1982) Localization of gold in biological tissue. A photochemical method for light and electron microscopy. Histochemistry 71:81–88
2. Danscher G (1984) Autometallography. A new technique for light and electron microscopic visualization of metals in biological tissues (gold, silver, metal sulphides and metal selenides. Histochemistry 81:331–335
3. Danscher G, Hansen HJ, Møller-Madsen B (1984) Energy dispersive X-ray analysis of tissue gold after silver amplification by physical development. Histochemistry 81:283–285
4. Rocker I, Henderson WJ (1976) Transfer of gold from mother to fetus (letter). Lancet II:1246
5. Cohen DL, Orzel J, Taylor A (1981) Infants of mothers receiving gold therapy (letter). Arthritis Rheum 24:104–105
6. Møller-Madsen B, Danscher G (1983) Transplacental transport of gold in rats exposed to sodium aurothiomalate. Exp Mol Pathol 39:327–331
7. Szabo KT, Guerriero FJ, Kang YJ (1978) The effects of gold-containing compounds on pregnant rats and their fetuses. Vet Pathol [Suppl] 15:89–96
8. Szabo KT, DiFebbo ME, Phelan DG (1978) The effects of gold-containing compounds on pregnant rabbits and their fetuses. Vet Pathol [Suppl] 15:97–102
9. Rogers JG, Anderson RM, Chow CW, Gilliam GL, Markman L (1980) Possible teratogenic effects of gold. Aust Paediatr J 16: 194–195

Announcement

1st International Waaler Conference on Rheumatoid Factors. Bergen, Norway, December 10–13, 1987
Deadline for registration: June 1987
Information: Secretariat Waaler Conference, Dr. E. Munthe, Department of Rheumatology, The Deacon's Hospital, P.O. Box 23, Vinderen, N-0319 Oslo 3, Norway, Tel. +47-2-46 59 50