American Journal of Medical Genetics 79:66–68 (1998)

Letter to the Editor

Vitamin K Deficiency Embryopathy

To the Editor:

Menger et al. [1997] presented the cases of three children with vitamin K deficiency embryopathy due to a disorder of embryonic vitamin K metabolism. We have had the opportunity to study a prenatal case, detected by ultrasound, with the same entity.

CLINICAL REPORT

Our case is a fetus of a young nonconsanguineous Portuguese couple. The mother, 25 years old and pregnant for the first time, was referred for a second opinion following the discovery of a thickness of the neck during an ultrasound study at 16 weeks of pregnancy. Ultrasound study at 17 weeks showed moderate lymphedema, mild dilatation of the cerebral ventricles, and hyperechogenicity of fetal bowel. The pregnancy ended spontaneously at 18 weeks and 3 days. The mother's tests carried out before the uterine evacuation showed a 36% prothrombin level (PTL) with factor II at 25%, factors VII and IX at 18%, and factor V at 91%. Considering that the patient had not taken any oral anticoagulants, these data indicated a vitamin K deficiency. After an injection of 10 mg of vitamin K, the evacuation took place.

The female fetus had pronounced frontonasal hypoplasia, a cystic hygroma, and metaphyseal spicules visible on the radiographs, and abdominal calcification (Fig. 1). Autopsy showed that frontonasal ossification was extremely deficient (Fig. 2), with long bones being abnormally short for gestational age. On the X-ray films, the metaphyses of the long bones (Fig. 3) are spiculated and when observed with a microscope the osseous trabeculae are abnormally wide.

The mother had undergone several abdominal operations for an idiopathic chronic intestinal obstruction which resulted in an ileocaecal resection, a duodenojejunostomy, and a cholescystectomy. After that the patient was followed by a nutritionist. The last tests 6 months before the beginning of the pregnancy were normal apart from a positive breath test, which led to the patient being treated with erythromycin and small quantities of copper, zinc, and selenium. The PTL was 78%. At the beginning of the pregnancy the patient was taking erythromycin, arginine, α-tocopherol, folic acid, and ferrous sulphate sesquihydrate.

The biological tests following the evacuation showed that there was a rapid improvement in the vitamin K–dependent factors 24 hr after the injection of vitamin K1 (PTL = 68%, factors VII + X at 52% and factor V at 100%). There were also deficiencies in vitamin E (3.65 mg/l; minimum, 4 mg/l), retinol (0.07 mg/l; minimum, 0.4 mg/l), vitamin C (0.4 mg/l; minimum, 0.8 mg/l), serum carotene levels (α-carotene, 12 μg/l; minimum, 130 μg/l and β-carotene, 20 μg/l; minimum, 205 μg/l), and copper and zinc. There was no infection, in particular no viral infection.

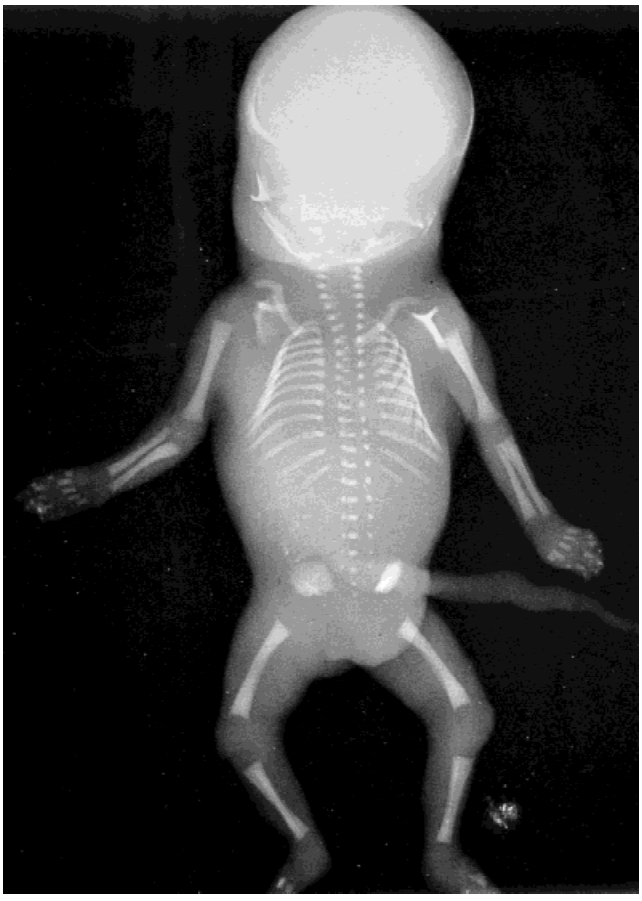

Fig. 1. Radiograph of the fetus.

*Correspondence to: Annie Nivelon-Chevallier, Centre de Génétique, CHU 10 bd M1 de Lattre de Tassigny, 21034 Dijon Cedex, France. E-mail: anivelon@planetb-fr

Received 4 December 1997; Accepted 16 May 1998

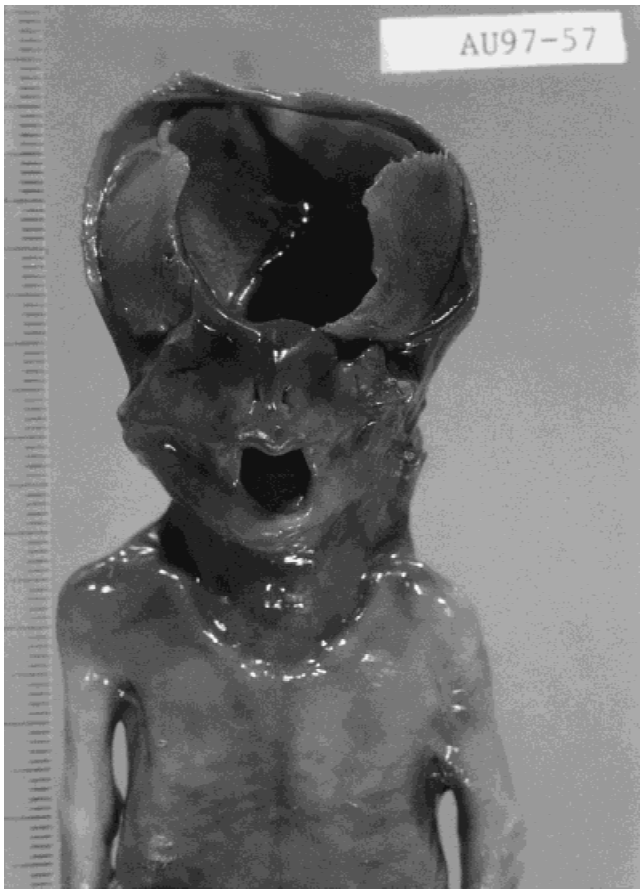

Fig. 2. Photograph of the fetus.

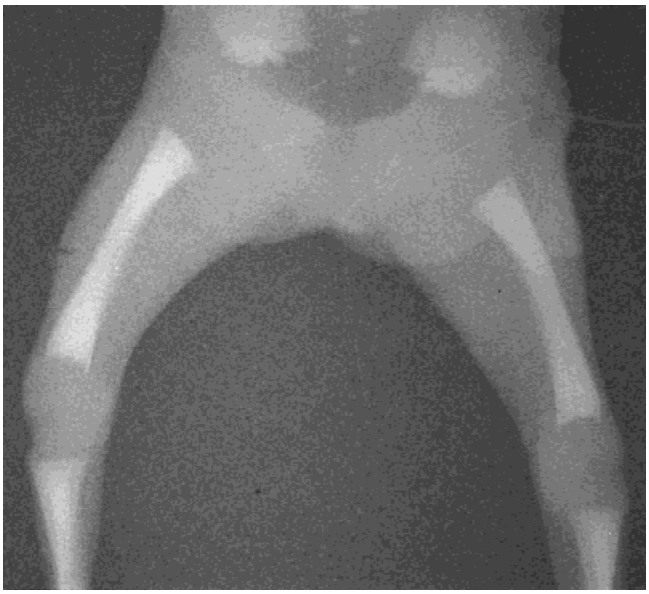

Fig. 3. Radiograph showing the long bones.

DISCUSSION

Our patient's deficiency in vitamin K has several causes: Her syndrome was linked to surgery and long-term antibacterial malabsorption treatment. During pregnancy daily needs of vitamin K increase by 20%, and a weak placental transfer may also occur [Suzuki et al., 1989; Israels and Israels, 1995].

This observation is the first to be made of a prenatal detection of this ailment. In our case the condition was particularly serious and the fetus did not survive. This case complements those described by Menger et al. [1997], supporting the hypotheses of Howe et al. [1995] drawn from their study of rats, among others [Howe and Webster, 1992].

The teratogenic period of the warfarin embryopathy is between the sixth and ninth weeks of amenorrhea [Howe et al., 1992]. Therefore we can postulate that besides the mechanism described by Franco et al. [1995] concerning arylsulfatase E, there is also an increased need of vitamin K, which is essential for frontonasal and metaphyseal ossification Thus, we confirm that it is necessary to watch closely and supplement every women of child-bearing age who might have a vitamin K deficiency in order to prevent such an embryopathy, a vitamin K deficiency being certainly teratogenic at an early stage of pregnancy.

The long-term intake of erythromycin can be considered an aggravating factor in malabsorption of vitamin K caused by surgery, probably because it alters the bacterial intestinal flora that produces menaquinones (vitamin K2). Lipsy [1994] describes this aggravating phenomenon in relation with other antibiotics (containing methyl tetrazole-thiol) that inhibit vitamin K metabolism, notably the gamma carboxylation of glutamic acid. Phenytoin [Howe et al., 1995] and alcohol [Howe et al., 1992] have also been postulated to disturb vitamin K metabolism and have also some similar effects in their phenotype translation in children who have been exposed to them during pregnancy.

CONCLUSION

Vitamin K deficiency is teratogenic at an early stage of human pregnancy. We think it is important to more accurately describe these situations in order to prevent the embryopathies they can cause in women whose pregnancies have not been diagnosed yet.

ACKNOWLEDGMENTS

We thank E. Justrabo for her anatomopathologic studies and C. Durand for her X-ray studies.

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Philippe Khau Van Kien
Annie Nivelon-Chevallier*
Centre de Génétique
Centre Hospitalo-Universitaire
Dijon, France

Gilles Spagnolo
Serge Douvier
Catherine Maingueneau
Département de Gynécologie-Obstétrique
Centre Hospitalo-Universitaire
Dijon, France