Open Access Library Journal
2024, Volume 11, e11061
ISSN Online: 2333-9721
ISSN Print: 2333-9705

The Association of Vogt-Koyanagi-Harada Disease and Pregnancy: Role of the Obstetrician (A Case Report and Literature Review)

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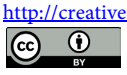
How to cite this paper: Fakhir, B., Abdelkhalki, M.H., Makrane, D., Benkaddour, Y.A., Harou, K., Bassir, A., Aboulfalah, A., Asmouki, H. and Soummani, A. (2024) The Association of Vogt-Koyanagi-Harada Disease and Pregnancy: Role of the Obstetrician (A Case Report and Literature Review). *Open Access Library Journal*, **11**: e11061.
https://doi.org/10.4236/oalib.1111061

Received: November 29, 2023
Accepted: January 19, 2024
Published: January 22, 2024



Abstract

Introduction: Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disease that can affect a multitude of organs affecting melanocytes. It is a provider of many complications, mainly ocular and cutaneous. **The goal**: Through a case study to discuss the impact of VKH disease on pregnancy as well as the role of the obstetrician in the management of pregnancy and disease. **Observation:** A 30-year-old patient who was diagnosed before her actual pregnancy. The patient was on systemic corticosteroids for disease control. The evolution of her VKH disease and the pregnancy were good. **Conclusion:** VKH disease has no negative impact on pregnancy outcome. Complications are possible. The best therapeutic option remains systemic corticosteroid therapy.

Subject Areas

Gynecology & Obstetrics

Keywords

Vogt-Koyanagi-Harada, Pregnancy, Systemic Disease, Autoimmune Diseases, Corticosteroids, Immunosuppressors

1. Introduction

Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disease that can affect a multitude of organs affecting melanocytes [1]. The main possible complications of the disease are: ocular (anterior or posterior uveitis, chorioretinitis which can lead to blindness); Cutaneous such as vitiligo and photosensitivity; Auditory as

deafness and neurological up to psychic disorder and aseptic meningitis [2]. Through a case study, our goal is to discuss the impact of VKH disease on pregnancy as well as the role of the obstetrician in the management of their association.

2. Observation

This is a 30-year-old patient with 3G3P (two children delivered vaginally). Having been diagnosed with VKH disease just a few months before her actual pregnancy. The VKH disease was revealed by bilateral diffuse choroiditis associated with anterior uveitis with no history of penetrating ocular trauma or surgery preceding the initial onset of uveitis. And no clinical or laboratory evidence suggestive of other ocular disease entities associated with alopecia and vitiligo. According to 2001 criteria [3] the diagnosis of incomplete VKH was made. She received oral corticosteroid at a dose of 1mg/kg/day making possible a successful control of VKH disease. At her first consultation, the parturient was pregnant at 11 weeks + 6 days. The clinical examination and the ultrasound data revealed no abnormality (**Figure 1**). The patient continued her oral corticosteroid therapy at the same dose during her pregnancy. The ophthalmologists and internists consider her pathology stable and have sent her to us for follow-up of her pregnancy

The follow-up assessment of her pregnancy reveals no abnormality: the sexually transmitted infection serology was negative, the screening for gestational diabetes was negative, the blood pressure profile during pregnancy was correct and no proteinuria was detected.

The patient was seen every month on an outpatient basis with no significant

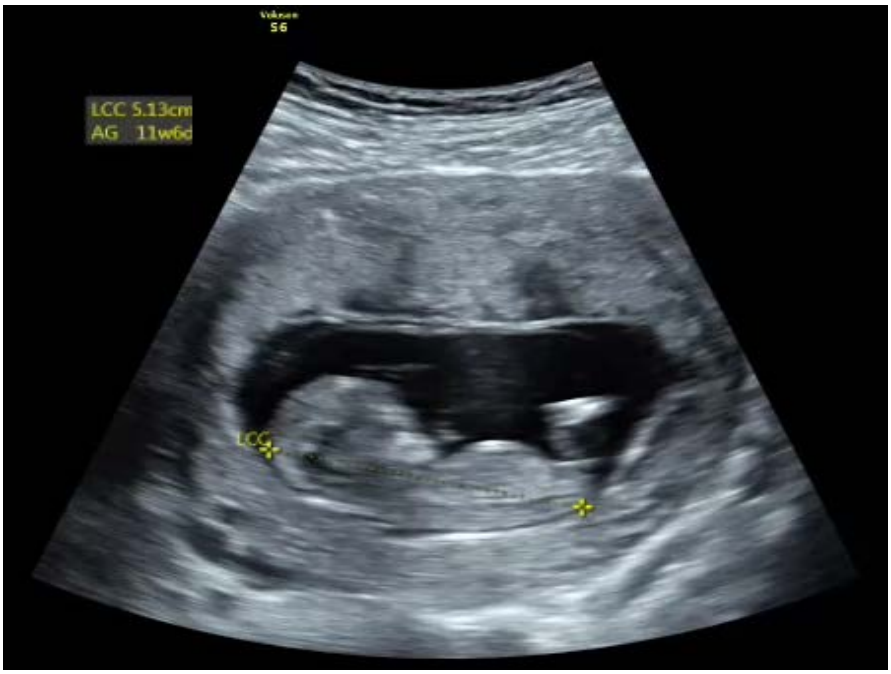


Figure 1. 1st trimester ultrasound without abnormality. (Between the calipers: Parasigital cut showing an embryo of 11 w + 6 d with positive heart activity).

abnormalities on clinical examination or ultrasound.

Morphological ultrasound has found no detectable malformation (Figure 2).

The weight gain remained regular and correct in relation to the gestational age. The uterine artery Doppler was normal. Doppler of the umbilical artery by calculation of the resistance index remained normal throughout the pregnancy. Cerebral Doppler did not find any risk of fetal anemia or any abnormality that could reflect fetal hypoxia.

At 35 weeks the patient presented with a premature rupture of the membranes. The infection test was negative. The patient was put on antibiotic therapy then followed by CRP every 48 hours. The triggering was decided at 36 weeks. A vaginal delivery was performed without incident with a newborn male at birth

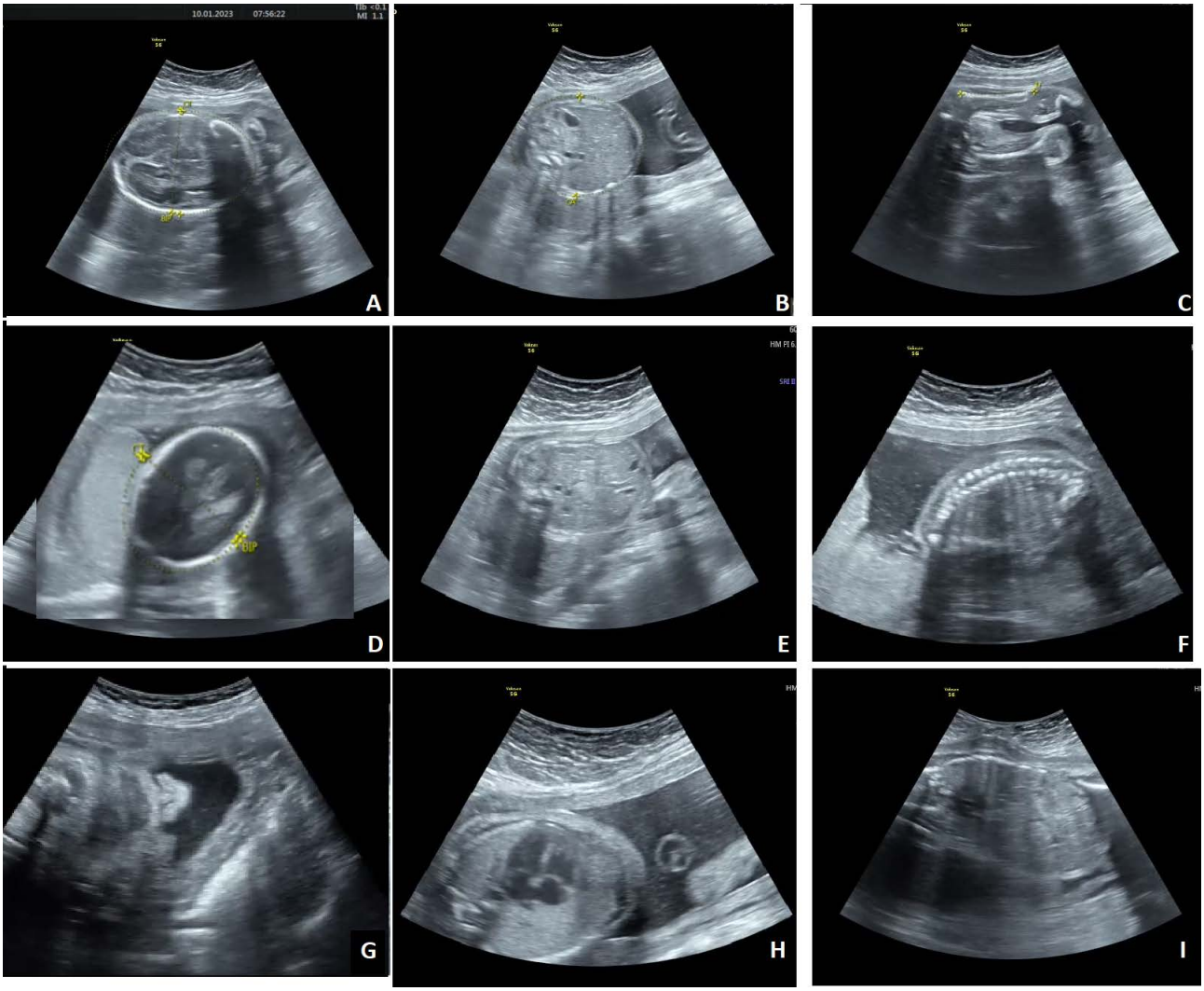


Figure 2. Ultrasound sections without anomalies in the context of a morphological ultrasound. (A) Axial section of the cephalic pole with measurement of the biparietal diameter and cranial circumference; (B) Axial section of the abdomen at the level of the portal sinus showing the abdominal contour; (C) Longitudinal section of the femoral diaphysis; (D) Oblique axial section of the cephalic pole passing through the cerebellum; (E) Axial section of the kidneys at the level of the renal pelvis; (F) Sagittal section showing the spine; (G) Frontal section of the face centered on the nose-mouth; (H) Thoracic axial slice at the level of the 4 cardiac chambers; (I) Para-sagittal thoraco-abdominal section.

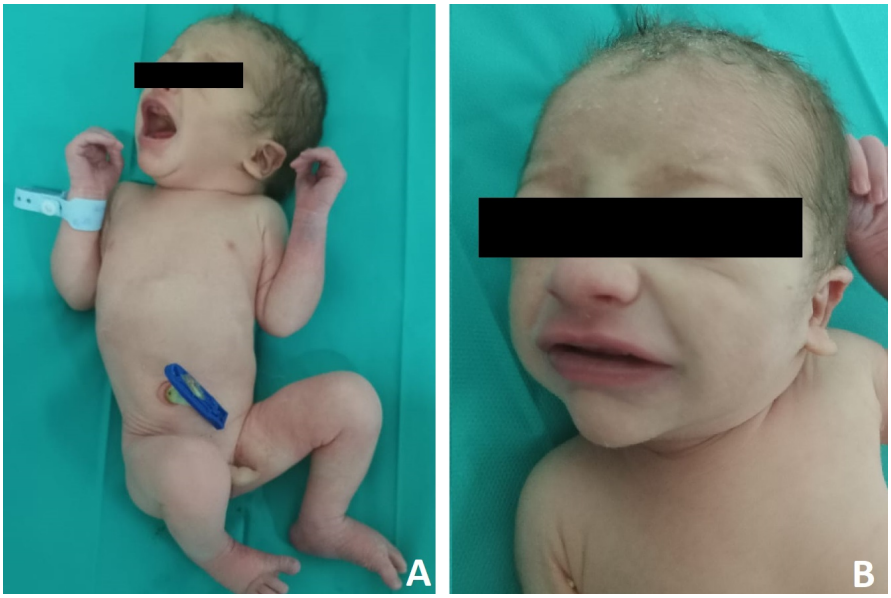


Figure 3. Preview of newborn (A) Overall view; (B) Close-up of the face. (Pink skin, gestures spontaneously; good axial and peripheral tone, normal archaic reflexes, with no clinical evidence of malformation.)

weighing: 2900 g APGAR: 10/10. The pediatric examination found no abnormality (**Figure 3**).

Throughout the pregnancy, the patient remained on oral corticosteroids at the same dose without relapse or exacerbation of her VKH disease.

3. Discussion

Vogt-Koyanagi-Harada disease is an autoimmune disease that can affect a multitude of organs affecting melanocytes [1]. Cellular immunity plays an important immunological role in this disease. Recent studies have provided important insights into the mechanisms of VKH disease. Cytokines, mainly interleukin (IL)-6 and IL-2, play an important role during inflammation, by regulating the various functions of lymphocytes and monocytes [4]. During pregnancy, there is generally a decrease in cellular immunity: for a pregnancy to continue, the mother must tolerate fetal tissue that is foreign to her immune system [5].

This data is important when we know that the treatment of VKH disease involves either corticosteroids (local or general route) or, in rare cases, immuno-suppressor [6]. Although it is accepted that a certain immunosuppression sets in during pregnancy, everything leads us to believe that pregnancy should be a protective factor against VKH flare-ups [7]. However, the immunological influence of pregnancy on VKH disease has not yet been fully elucidated [7]. Re-peated and/or high-dose use of corticosteroid therapy during pregnancy is well documented: it can lead to an increased risk of gestational diabetes, intrauterine growth retardation, low birth weight and, in rare cases, congenital malformations [8]. Data from the literature concerning the association of autoimmune disease in general and pregnancy is correlated with the increased risk of

occurrence of pre-eclampsia, hence the need for close monitoring [9].

The review of the literature concerning VKH and pregnancy remains rather poor. Table 1 illustrates the different results.

Literature data suggest that VKH disease has no negative impact on pregnancy outcome [20]. The control of the disease in those cases is generally done by systemic corticosteroids [10] [13] [14] [16] [18] [20] rarely by local corticosteroids [11] [17] [18]. Close monitoring without treatment is possible but does not prevent the risk of flare [15] [19]. An unfavorable evolution of VKH disease could be correlated with an unfavorable evolution of pregnancy [12] [14] [19]. Complications are dominated by miscarriage and premature delivery [12] [14]. A case of intra uterine growth restriction has been reported with low birth-weight infants associated with a malformation syndrome reported in another member of the family without it being able to have a proven relationship with VKH disease [19].

Table 1. Different studies on the VKH association and pregnancy classified by date of publication.

Author	Year	Number of cases	Term of pregnancy at time of treatment	Therapeutic	Pregnancy outcome	Evolution of VKH disease
Friedman *et al.* [10]	1980	2	5 months	Systemic corticosteroids	Good	Good
			7 months	Systemic corticosteroids	Good	Good
Sato *et al.* [11]	1986	1	10 weeks	Local corticosteroids	Good	Good
Lance [12]	1990	1	3 months	Systemic corticosteroids	Abortion	Recurrence
Yamagami *et al.* [13]	1990	1	7 months	Systemic corticosteroids	Good	Good
Steahly [14]	1990	2	Unspecified	Systemic corticosteroids	Premature delivery	Recurrence
			Unspecified	Systemic corticosteroids	Abortion	Recurrence
Nohara *et al.* [15]	1995	1	12 weeks	Close monitoring	Good	Good
Watase *et al.* [16]	1995	1	26 weeks	Systemic corticosteroids	Good	Good
Taguchi *et al.* [17]	1999	1	3 months	Local corticosteroids	Good	Good
Miyata *et al.* [18]	2000	3	19 weeks	Systemic corticosteroids	Good	Good
			31 weeks	Systemic corticosteroids	Good	Good
			17 weeks	Local corticosteroids	Good	Good
Doi *et al.* [19]	2000	1	16 weeks	Initially monitoring then systemic corticosteroids	Low birth-weight infants with presence of documented malformations in the family.	Good
Tien *et al.* [20]	2009	1	7 months	Systemic corticosteroids	Good	Good
Ingolotti *et al.* [21]	2018	1	13 weeks	High dose corticosteroids then azathioprine	Prematurity at 31 week for cholestasis of pregnancy	Good
Our case repport	2023	1	12 weeks	Systemic corticosteroids	Premature membrane rupture	Good

A case of prematurity on cholestasis of pregnancy was reported in a patient on immunosuppressant (azathioprine) without its being linked either to VKH disease or to the use of immunosuppressors. The use of immunosuppressors is strongly discouraged and is only possible after failure of high dose of corticosteroid therapy. Azathioprine is the molecule of choice in this case, the risk benefit must be discussed on a case-by-case basis in consultation with the mother, obstetricians, internists and ophthalmologists [21].

4. Conclusion

VKH disease does not have a negative impact on the outcome of pregnancy according to literature data. Complications are possible but are often associated with poor control of VKH disease, showing the importance of effective treatment. The best therapeutic option remains systemic corticosteroid therapy. It is advisable to follow up to watch for complications due to the autoimmune disease (pre-eclampsia) or the use of corticosteroids (low birth-weight, gestational diabetes and congenital malformations). Heavy therapeutic decisions (use of immunosuppressors for example) can have a significant impact on the outcome of pregnancy and should be discussed on a case-by-case basis by obstetricians, internists and ophthalmologists.

Declarations

Acknowledgements

The authors thank in general the management of the Department of Obstetrics and Gynecology, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco and the management of the Mohamed the VI university hospital of Marrakesh.

The authors dedicate also this work to all the victims of the deadly earthquake of Morocco on 8th September 2023.

Funding Source

None.

Ethical Approval

As this is a case report which do not contain any patient identification details, ethical approval is not required.

Informed Consent

Informed written consent was taken from the patient to publish this case report without her identification details.

Author Contribution

The author confirms sole responsibility for study conception and design, data

collection, analysis and interpretation of results, and manuscript preparation

Conflicts of Interest

The authors declare no conflicts of interest.

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