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Repository Citation

Stanley, Zachary; Vignes, Katherine; and Marcum, Miriam, "Extreme Elevations of Alkaline Phosphatase in Pregnancy: A Case Report" (2020). *Obstetrics and Gynecology Faculty Publications*. 27.

https://uknowledge.uky.edu/obgyn_facpub/27

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Digital Object Identifier (DOI)

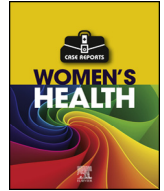
<https://doi.org/10.1016/j.crwh.2020.e00214>

Notes/Citation Information

Published in *Case Reports in Women's Health*, v. 27, e00214.

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Extreme elevations of alkaline phosphatase in pregnancy: A case report

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ARTICLE INFO

Article history:

Received 15 April 2020

Received in revised form 28 April 2020

Keywords:

Case report

Pregnancy

Alkaline phosphatase

Expectant management

ABSTRACT

Background: The normal serum concentration of alkaline phosphatase (ALP) in adults over the age of 18 ranges from 37 to 116 U/L, while in pregnant women levels of up to twice that upper limit can still be normal. There have been very few reports of extreme elevations in ALP, and here we present the case of a 29-year-old pregnant woman with an incidentally found 30-fold increase.

Case: The patient, G6P2-1-2-4, received routine prenatal care, though presented to obstetric triage at 36 weeks and 1 day of gestation for diagnosis and management of viral rhinosinusitis and was found to have an ALP level of 2817 U/L. She was expectantly managed and levels were monitored during the peripartum period.

Conclusion: The literature proposes that elevation of the placental isotype of ALP could be a marker for placental insufficiency, preterm delivery, or infants born large for gestational age. We report a case with delivery of a normal infant and no placental pathology at term.

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1. Introduction

Although obstetricians have observed elevations in serum alkaline phosphatase (ALP) during pregnancy, these typically are not much more than twice the pre-pregnancy upper limit of normal [1]. There is currently a paucity of cases in which exaggerated increases are observed. Seeing an atypically elevated value can be distressing to both the clinician and the patient, especially when it is unknown what the implications may be. Some retrospective and prospective cohort studies have shown that ALP could be a marker for preterm delivery, fetuses that are large for gestational age, or conversely placental insufficiency and intrauterine growth restriction [2,3,4]. This case serves to add to the literature as a demonstration that even abnormal elevations of ALP do not reliably predict fetomaternal pathology. This case is important because it highlights the association between a very abnormal biochemical value and good fetomaternal outcomes after expectant management.

2. Case

A 29-year-old woman, gravida 6 para 2-1-2-4, received routine prenatal care at an academic practice at a university medical center. Her obstetric history was significant for a preterm cesarean section of a monochorionic, diamniotic twin pregnancy at 33 weeks as well as a successful vaginal birth after cesarean. Her routine laboratory tests were unremarkable, including a normal glucose tolerance test at 26 weeks. An anatomy ultrasound at 21 weeks of gestation was within normal

limits. Her placental location was posterior with no correlation to her previous cesarean scar. She presented to the obstetric triage unit at 36 weeks and 1 day of gestation with complaints of shortness of breath and nasal congestion. Her workup was significant for positive human rhinovirus/enterovirus nasopharyngeal cultures. A comprehensive metabolic panel (CMP), which tests for serum electrolytes as well as hepatic and renal function, was obtained as a part of her initial workup and incidentally showed an elevated ALP level of 2817 U/L. She was sent home with recommendations for supportive care and was scheduled to follow-up for routine prenatal care the following day in clinic. At her office visit, a repeat CMP showed a continued ALP elevation, at 3143 U/L. Fundal heights were consistently appropriate for gestational age. At her next prenatal check the following week, the patient was still having persistent upper respiratory symptoms, for which a short course of azithromycin was prescribed and another CMP with ALP isoenzyme differentiation was obtained. This showed a markedly elevated placental isoenzyme, with low levels of both the liver and bone isoenzymes. Knowing this breakdown, along with the absence of right upper quadrant pain, jaundice, or other signs of hepatic dysfunction, allowed an investigation for any liver pathology to be safely forgone. In the absence of other indications for delivery, the shared decision was to plan for another trial of labor after cesarean section at 39 weeks. Her labor was induced with a Foley balloon and Pitocin. She had a successful vaginal delivery of a viable, male, 3160-g infant. She received routine postpartum care. ALP levels were checked immediately postpartum (2767 U/L), at two weeks postpartum (702 U/L), and at her six-week postpartum visit (191 U/L). Thus the placental isoenzyme of ALP was elevated up until the second week after delivery. Laboratory tests six weeks postpartum were unable to detect any placental isoenzyme.

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3. Discussion

Serum ALP has several different sources, but is found in all tissues of the body. Each isotype has a unique molecular fingerprint based on its origin. The main isotypes are found in the liver, bone, and placenta and they are key enzymes in many metabolic pathways. If we had not known that the increase was due to the placental isotype, there are other diagnoses that would rise to the top of the list. We classically see moderate increases in ALP associated with liver disease, which has a myriad of potential etiologies. When ALP is disproportionately elevated in comparison to hepatic transaminases and bilirubin, it is typically caused by an obstructive disease process such as with cholelithiasis. As alluded to above, previous case reports and small prospective and retrospective studies have attempted to understand the significance of abnormal elevations in serum ALP during pregnancy. In 1995, a retrospective review of blood samples of women who underwent preterm delivery had elevated ALP placental isoenzyme levels when compared to blood samples of women who delivered at term [2]. In 2018, a prospective cohort study found a correlation between early elevations of ALP (at 13–16 weeks of gestation) and babies born large for gestational age, even in the setting of normal glucose tolerance testing [3]. A case report from 2019 presents a patient with elevated ALP levels and signs of placental insufficiency with elevated umbilical artery dopplers and intrauterine growth restriction [4]. Our patient did not have any placental abnormalities, such as lacunae, and as its location was posterior, concern was low for abnormal placentation. This is a case of an extremely elevated placental isoenzyme of ALP in which the patient had low-risk outcomes for both the mother and the baby. This serves as a reminder that we cannot reliably use an isolated, marked increase in serum ALP to dictate management in the setting of an otherwise normal pregnancy.

Teaching Point

- Extreme elevations in alkaline phosphatase during pregnancy may be expectantly managed in the absence of other fetomaternal considerations.

Contributors

All authors contributed equally to the chart review and construction of this case report and meet criteria for authorship.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

No funding from an external source supported the publication of this case report.

Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

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