Title: Commentary on “Alkaline Phosphatase Activity Inconsistent with Patient’s Clinical Presentation: A Cautionary Tale”.

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Asfotase alfa (AA) is a human recombinant tissue-nonspecific alkaline phosphatase (TNSALP) used to~~in~~ treat~~ing~~ perinatal/infantile and juvenile-onset hypophosphatasia. This fusion protein comprises the TNSALP ectodomain, the constant region of the human IgG1 Fc domain, and a terminal deca-aspartate motif, effectively replacing the activity of the deficient endogenous ALP. However, the IgG Fc domain can interfere with assays, complicating the measurement of analytes during treatment (1).

This report highlights the challenges in quantifying ALP in the presence of AA. The authors conducted a~~A~~ series of ~~cases~~ experiments ~~were evaluated~~ to ~~explain~~ investigate the abnormal ~~value of~~ ALP result after AA treatment. Neutralizing antibodies to AA (~~,~~ which can reduce ALP activity)~~,~~ were considered; however, this possibility was ~~but~~ excluded as a significant factor, since treatment commenced ~~shortly before~~prior to blood collection. Additionally, the Fc domain of AA is unlikely to interfere with the enzymatic assay and has not been observed before.

To determine ALP activity accurately, a serial dilution of the patient’s sample was performed, yielding readings within the assay’s analytical range. Guidelines recommend clinicians request ALP activity analyses in a serial dilution when monitoring patients on AA therapy (2). This case underscores the importance of following these guidelines and informing laboratories about AA

treatment in analysis requests. Developing standard operating procedures and training laboratory staff are crucial to optimize resources, avoid unnecessary tests, and reduce healthcare costs.

Evaluating results outside the analytical range within the context of the patient's profile and medication history can enhance the accuracy of biochemical analyses. This report illustrates the risks of AA overdose based on undetectable ALP readings, which significantly increase the risks of ectopic calcification, such as conjunctival and corneal calcification, and nephrocalcinosis.

This case emphasizes the benefits of continuous dialogue between clinicians and laboratory personnel to foster mutual learning and improve practices and protocols. Such collaboration ensures high-quality patient care and efficient use of laboratory resources.

1. Piec ID, Tompkins B, Fraser WD. Interference of Asfotase Alfa in Immunoassays Employing Alkaline Phosphatase Technology. J Appl Lab Med. 2020;5(2):290–9.

2. Kishnani PS, Rush ET, Arundel P, Bishop N, Dahir K, Fraser W, et al. Monitoring guidance for patients with hypophosphatasia treated with asfotase alfa. Mol Genet Metab 2017;122(1):4–17.