

## Case Report

# A likely pathogenic variant in the *Butyrylcholinesterase* gene was found in an agricultural engineer with a low pseudocholesterase level

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## ABSTRACT

Butyrylcholinesterase (BChE) can hydrolyze acetylcholine and partially replace it in case of acetylcholinesterase inhibition or deficiency. In this case report, we aimed to present a case who applied due to coincidental low pseudocholesterase levels and had a BChE novel variant genetic deficiency, which was expected to be low due to her occupation. The patient was a 29-year-old female. She was admitted to the occupational medicine outpatient clinic for further examination and evaluation after a low level of pseudocholesterase was detected in the pre-employment tests. The most common causes of low pseudocholesterase levels are postnatal diseases, medications, and occupational exposures. Even in cases where occupational exposure is considered in the foreground, it should not be forgotten that the occupational anamnesis should be deepened and genetic deficiency may be in the back of our minds.

**Keywords:** Butyrylcholinesterase, Genetic deficiency, Occupation, Pseudocholesterase

## INTRODUCTION

In humans, there are two types of cholinergic enzymes, acetylcholinesterase (AChE), and butyrylcholinesterase (BChE), which hydrolyze acetylcholine. BChE is the co-regulator of AChE in cholinergic transmission, but the physiological role of BChE is not yet clear.<sup>[1]</sup> BChE is found in smooth muscles, fat cells, plasma, and serum. Although the function of BChE is not known exactly, it is known that it detoxifies xenobiotics and bioactivates various drugs. Furthermore, BChE can hydrolyze acetylcholine and partially replace it in case of AChE inhibition or deficiency.<sup>[2]</sup>

The causes leading to a decrease in BChE activity are mostly postnatal factors. The most common causes include liver and kidney disease, dystrophy, burn, malignancy, hypothermia, uremia, and pregnancy.<sup>[3-5]</sup> The second most common cause is drugs, and the most responsible drugs include anticholinergic drugs, glucocorticoids, oral contraceptives, monoamine oxidase inhibitors, and pesticides, including organophosphates (OPs).<sup>[6,7]</sup> The other factor is genetic factors.<sup>[8]</sup>

In this case report, we aimed to present a case who applied due to coincidental low pseudocholesterase levels and had a BChE novel variant genetic deficiency, which was expected to be low due to her occupation but was not previously detected as a result of evaluations.

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## CASE REPORT

A 29-year-old female was admitted to the occupational medicine outpatient clinic for further examination and evaluation after a low level of pseudocholesterase was detected in the pre-employment examination. She worked for 7 years as an agricultural engineer in a company selling pesticides. She only sold packaged products as a salesperson, had no active contact with the products, and was not involved in production. During her employment, her pseudocholesterase level was not checked either at the start of the job or during her periodic examinations. The pseudocholesterase level of the patient is given in Table 1.

The patient had no active complaints and symptoms, no medication, and no comorbidities. In the physical examination of the patient, head-and-neck system, respiratory system, cardiovascular system, abdominal examination, and extremity examinations were evaluated as normal. She stated that her mother and father lived in her family and she had no additional disease. She did not experience any complications due to a curettage and a nose surgery for which she had anesthesia 2 times. No pathology was detected in the tests which performed, and no organ pathology was detected in abdominal ultrasonography. Hematological and biochemical data are given in Table 2.

The patient was referred to the medical genetics outpatient clinic for genetic evaluation among the reasons for low pseudocholesterase levels. BChE deficiency (OMIM# 617936) carriage was considered in the patient and for molecular diagnosis, sequence analysis was performed with the next generation sequencing (Miseq-Illumina) method for all coding regions of the *BChE* gene and exon-intron linkage regions of coding exons from genomic DNA isolated from the patient's EDTA peripheral blood sample. As a result of the analysis, BChE (NM\_000055.4) c359 G>C, p. (Cys 120 Ser) variant was detected as heterozygous. Although the variant detected was previously reported in databases (rs1164843733), it was classified as a likely pathogenic (LP) variant because it fulfilled the criteria of PP3, PM2, and PP2 according to the American College of Medical Genetics and Genomics criteria.<sup>[9]</sup> It was observed that the variant detected in the database searches was not reported in the literature and ClinVar database in individuals with low pseudocholesterase levels (affected). The proband was accepted as a carrier for BChE deficiency. The genetic map of the patient is given in Figure 1.

## DISCUSSION

Pesticides are an important class of environmental chemical pollutants and have become a major public health concern. OPs account for more than 50% of pesticide use worldwide and it is estimated that their use will increase further until 2030 and will lead to harmful consequences for human health and the

environment.<sup>[10]</sup> Since BChE is abundant in plasma, changes in the enzyme are considered as an indicator of intoxication with OPs and carbamates and changes in this enzyme are used as a biomarker of exposure to OPs.<sup>[7]</sup> Since our patient was an agricultural engineer, pesticide exposure was considered in the foreground at first glance, and it was assumed that the current pseudocholesterase level was due to his occupation. However, when the occupational anamnesis was deepened, it was found that the patient did not work in active production

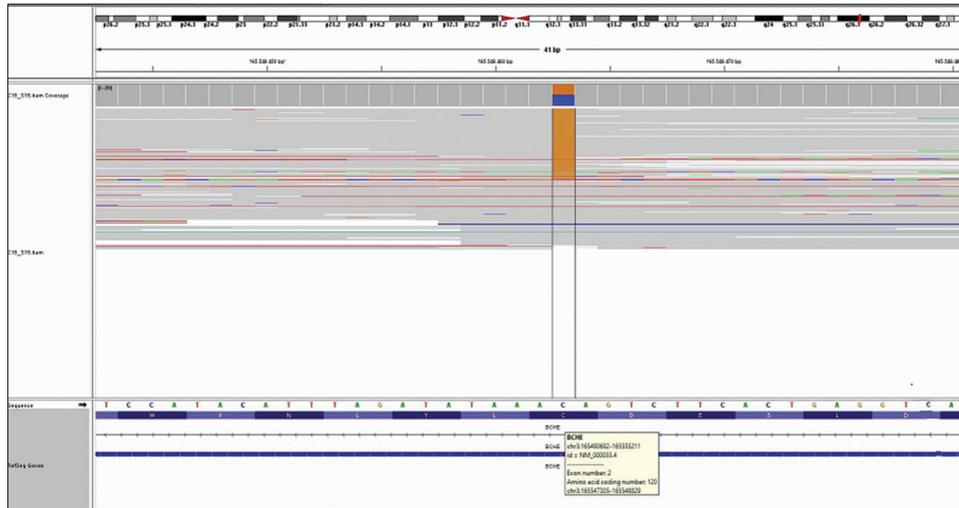
**Table 1:** Pseudocholesterase levels.

Date	Psödokolin level U/L (4900–11900)
November 13, 2024 (private hospital)	3004
November 21, 2024 (private laboratory)	2869
December 04, 2024 (hospital)	3178

**Table 2:** Hematological and biochemical data.

Variable	On presentation	Reference range
Hemoglobin g/dL	13.5	12–16
Hematocrit %	39.8	36–46
Mean corpuscular volume (fl)	86.8	78–98
WBC×10 <sup>3</sup> /uL	8.08	4.5–11
Neutrophil×10 <sup>3</sup> /uL	4.33	2–8
Lymphocyte×10 <sup>3</sup> /uL	3.04	0.6–34
Basophils×10 <sup>3</sup> /uL	0.05	0–0.2
Monocytes×10 <sup>3</sup> /uL	0.41	0–0.9
Eosinophils×10 <sup>3</sup> /uL	0.13	0.02–0.5
Thrombocyte×10 <sup>3</sup> /uL	359	150–450
Glucose mg/dL	97	74–106
Urea	30	20–50
Creatinine mg/dL	0.8	0.5–11
AST U/L	17	13–40
ALT U/L	17	10–49
ALP U/L	68	46–116
GGT U/L	9	<38
Total bilirubin mg/dL	0.46	0.3–1.2
Direct bilirubin mg/dL	0.15	0–0.3
Indirect bilirubin mg/dL	0.31	
HBsAg index	<0.10 (Negative)	0–0.99
Anti-HBs mIU/mL	15.9 (Positive)	0–11.99
Anti-HCV index	0.05 (Negative)	0.8–0.99
Anti-HIV index	<0.05 (Negative)	0–0.999

WBC: White blood cell, HBsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, AST: Aspartate aminotransferase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, HBs: Hepatitis B surface antibody



**Figure 1:** Genetic map of the patient.

departments, was not present in the agricultural lands where pesticides were sprayed, and only sold packaged products in the sales department in the store, and other causes of low levels were considered. Chronic liver disease, kidney disease, and additional medication use were investigated and after they were evaluated as normal, genetic causes were started to be investigated. Inherited hereditary deficiency occurs due to mutations in the *BChE* gene located on chromosome 3, 3q26.1–q26.2 between nucleotides 165.490.692 and 165.555.260. More than 20 genetic variants in the *BChE* gene have been found to be associated with this type of disease.<sup>[8]</sup> However, in our case, to the best of our knowledge, a LP that had not been reported in the literature in affected individuals was detected, and enzyme activity was found to be 60%.

At the start of the job, it should be ensured that the characteristics of the person who will be working and the characteristics of the job he/she will be doing are suitable. The examinations conducted for the purpose of placing in a suitable job are called pre-employment examinations. The examinations conducted for the purpose of determining whether there is an effect despite the precautions taken, early diagnosis and treatment are called periodic examinations.<sup>[11]</sup> In those working with pesticides and their products, the enzyme pseudochochine esteraseserterase is inhibited,<sup>[7]</sup> and in those working in this sector, pseudochochine esterase levels should definitely be checked both at the start of the job and during the intermittent control examinations to place a suitable job and to evaluate whether there is an effect. In our case, although she has been in this sector for 7 years, the pseudochochine esterase level was not checked during the start of the job and during the intermittent control examinations until the period when she changed jobs.

## CONCLUSION

The most common causes of low pseudochochine esterase levels are postnatal diseases, medications, and occupational exposures. Even in cases where occupational exposure is considered in the foreground, it should not be forgotten that the occupational anamnesis should be deepened and genetic deficiency may be in the back of our minds. Our case was identified as an affected individual with a low level of pseudochochine esterase, and although genetic counseling was given to the patient, we wanted to emphasize that the patient should be more careful about protective measures while working in his/her profession, which he/she will continue throughout his/her life due to this genetic deficiency, and that genetic changes should be kept in mind in those working in risky jobs.

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