MEHES JOURNAL (MEDICAL AND HEALTH SCIENCES JOURNAL) | ISSN:3023-5804
Arrival Date: 19/08/2026 | Published Date: 30/09/2026 | 2026 Vol: 4 Issue: 3 pp: 48 -58 |
DOI: https://doi.org/10.5281/zenodo.22901229

ARTICLE TYPE: RESEARCH ARTICLE

Geriatrik Yoğun Bakım Hastalarında Metabolik ve Hematolojik Değişikliklerle İlişkili Bir Biyobelirteç Olarak Serum Albümin

Serum Albumin as a Biomarker Associated with Metabolic and Hematological Alterations in Geriatric Intensive Care Patients

Veysel Ağan[1*]

[1*]Harran University-Health Services Vocational School-Pharmacy Services Prog. Şanlıurfa, Türkiye, aganveysel@gmail.com, ORCID: 0000-0003-0702-6249

ÖZET

Amaç: Bu çalışma, geriatrik yoğun bakım hastalarında serum albümin düzeyleri ile demografik, hematolojik ve biyokimyasal parametreler arasındaki ilişkileri araştırmayı ve hipoalbüminemi ile bağımsız olarak ilişkili faktörleri belirlemeyi amaçlamıştır.

Materyal ve Metot: Bu çalışma, Harran Üniversitesi Hastanesi Yoğun Bakım Ünitesine yatırılan 172 hastayı içermiştir. Hastalar hipoalbüminemi ve normal albümin gruplarına ayrılmıştır. Demografik özellikler ile hematolojik ve biyokimyasal parametreler karşılaştırılmış ve hipoalbümineminin bağımsız belirleyicilerini belirlemek için çok değişkenli lojistik regresyon analizi yapılmıştır.

Bulgular: Hipoalbüminemi 111 hastada (%64,5) mevcuttu. Hipoalbüminemi grubunda hematokrit ve serum kalsiyum düzeyleri anlamlı olarak daha düşük, kırmızı kan hücresi dağılım genişliği değerleri ise daha yüksekti. Cinsiyet dağılımı ve serum üre düzeyleri de gruplar arasında anlamlı farklılık gösterirken, yaş, glukoz, CRP, HDL ve LDL düzeylerinde anlamlı bir farklılık gözlenmedi. Çok değişkenli analizde, düşük serum kalsiyum ve ileri yaş bağımsız olarak hipoalbüminemi ile ilişkili bulundu.

Tartışma ve Sonuç: Düşük serum kalsiyum düzeyleri ve ileri yaş, geriatrik yoğun bakım hastalarında hipoalbüminemi ile bağımsız olarak ilişkilidir. Toplam serum kalsiyumunu yorumlarken serum albümini de dikkate alınması gerektiği kanaati oluştu.

Anahtar Kelimeler: Hipoalbüminemi, Geriatrik yoğun bakım, Lojistik regresyon, Biyomarkerlar

ABSTRACT

Objective: This study aimed to investigate the relationships between serum albumin levels and demographic, hematological, and biochemical parameters in geriatric intensive care patients and to identify factors independently associated with hypoalbuminemia.

Material and Methods: This study included 172 patients admitted to the Intensive Care Unit of Harran University Hospital. Patients were divided into hypoalbuminemia and normal albumin groups. Demographic characteristics were compared with hematological and biochemical parameters, and multivariate logistic regression analysis was performed to determine the independent determinants of hypoalbuminemia.

Results: Hypoalbuminemia was present in 111 patients (64.5%). In the hypoalbuminemia group, hematocrit and serum calcium levels were significantly lower, while red blood cell distribution width values were higher. While gender distribution and serum urea levels showed significant differences between the groups, no significant differences were observed in age, glucose, CRP, HDL, and LDL levels. In multivariate analysis, low serum calcium and advanced age were independently associated with hypoalbuminemia.

Discussion and Conclusion: Low serum calcium levels and advanced age are independently associated with hypoalbuminemia in geriatric intensive care patients. It was concluded that serum albumin should also be considered when interpreting total serum calcium.

Keywords: Hypoalbuminemia, Geriatric intensive care, Logistic regression, Biomarkers

Sorumlu Yazar/Corresponding Author: Veysel Ağan, Harran Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Eczacılık Hizmetleri Programı, Şanlıurfa, Türkiye.

Atıf /Cite: Ağan V. Serum Albumin as a Biomarker Associated with Metabolic and Hematological Alterations in Geriatric Intensive Care Patients. Mehes Journal. 2026Sep22;4(3):48–58. doi:10.5281/zenodo.22901229

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INTRODUCTION

With the increase in life expectancy worldwide, the geriatric population is rapidly growing, and consequently, the number of elderly patients monitored in intensive care units is also increasing. The decrease in physiological reserves, multiple comorbid diseases, chronic inflammation, malnutrition, and metabolic disorders frequently observed in geriatric individuals increase the need for reliable biomarkers in clinical evaluation. Therefore, determining laboratory parameters that can reflect the biological severity of the disease and the systemic metabolic status in elderly intensive care patients has become one of the important topics of current research (1, 2).

Serum albumin is an essential protein synthesized in the liver and constituting the majority of plasma proteins. Albumin has important physiological functions in maintaining plasma oncotic pressure, transporting many endogenous and exogenous molecules, antioxidant defense mechanisms, acid-base balance, and regulating various biological signaling pathways. In addition, albumin synthesis is directly affected by nutritional status, inflammatory response, liver functions, hormonal regulation, and catabolic processes. Therefore, serum albumin level is considered an important indicator not only of nutritional status but also of the organism's overall metabolic reserve and systemic physiological balance (3).

Recent research indicates that reduced serum albumin levels correlate with chronic inflammation, oxidative stress, sarcopenia, frailty, renal impairment, and metabolic dysregulation in older adults. Nevertheless, rather than assessing fluctuations in albumin concentration independently, analyzing them in conjunction with additional biochemical and hematological parameters is believed to offer a more comprehensive insight into patients' overall metabolic health (4).

Biologically, serum urea serves as a key biomarker for protein breakdown, kidney performance, and nitrogen balance. In a comparable manner, because a substantial fraction of circulating calcium is bound to albumin, variations in albumin concentration directly impact calcium regulation. Aging represents a primary physiological factor influencing albumin levels, driven by diminished protein synthesis capacity, persistent low-grade systemic inflammation, and the depletion of metabolic reserves. Conversely, C-reactive protein (CRP) stands out as a critical acute-phase reactant; given that inflammatory states downregulate albumin production, an inverse biological correlation typically exists between these two markers (5).

On the other hand, some laboratory markers reflecting hematological and lipid metabolism are also reported to be closely related to serum albumin levels. Beyond its clinical utility in hematological disorders, red blood cell distribution width (RDW) functions as a highly sensitive marker for systemic inflammation, oxidative stress, and nutritional deficits. Hematocrit (Hct) reflects tissue oxygenation and red blood cell mass, while high-density lipoprotein cholesterol (HDL) is considered one of the important components of systemic metabolic homeostasis due to its anti-inflammatory and antioxidant properties. The decrease in both HDL levels and serum albumin concentration, especially during chronic inflammation, suggests that these biomarkers may be related to common pathophysiological mechanisms (6).

However, studies evaluating serum albumin levels together with metabolic markers (age, urea, calcium, and CRP) and hematological/lipid markers (RDW, Hct, and HDL) in geriatric intensive care patients are limited. Most existing studies have considered albumin only as a prognostic or mortality indicator; they have not comprehensively examined the independent relationships of albumin with metabolic and hematological biomarkers (7).

The primary objective of this investigation is to evaluate the interactions between serum albumin concentrations and various metabolic and hematological parameters among critically ill elderly patients. It is believed that this approach will contribute to evaluating serum albumin not just as a single laboratory parameter, but as a holistic biomarker reflecting metabolic homeostasis, hematological balance, and inflammatory processes.

MATERIALS AND METHODS

Study Design and Patient Population

Designed with a retrospective, observational, and descriptive framework, this study evaluated the electronic health records of elderly patients managed in the Intensive Care Unit at Harran University Hospital from January 1, 2025, to January 1, 2026. Demographic characteristics along with biochemical and hematological laboratory results were extracted directly from the hospital information management system (HIMS).

The study cohort comprised 172 patients. Individuals lacking required laboratory results were omitted from specific comparative evaluations, with statistical testing executed strictly according to the available data points for each parameter.

Before the study began, the necessary ethical committee approval was obtained from the Harran University Clinical Research Ethics Committee (Decision No: 2026-00215 Date: 13.07.2026). The research was conducted in accordance with the principles of the Helsinki Declaration, and patient data were evaluated after anonymization.

Inclusion and Exclusion Criteria

Inclusion Criteria

Eligibility for study participation was defined by the following criteria: Admission to the intensive care unit within the designated study timeframe. Chronological age of 65 years or above. Availability of baseline serum albumin measurements taken upon initial intensive care admission. Complete accessibility of all required clinical and laboratory records via the hospital information management system.

Exclusion Criteria

Individuals presenting with any of the following parameters were omitted from the analysis: Being under 65 years of age. Lack of serum albumin measurement during intensive care unit admission. Not being suitable for evaluation due to incomplete clinical or laboratory data.

Study Groups

Cohort stratification was based on serum albumin levels, dividing subjects into two distinct groups. Individuals presenting with values under 3.5 g/dL were assigned to the hypoalbuminemia category, whereas those with concentrations of 3.5 g/dL or higher were categorized into the normoalbuminemic group. Clinical and laboratory differences between the groups were compared.

Parameters Evaluated

Demographic variables encompassed age and sex. Laboratory parameters analyzed included serum albumin, C-reactive protein, glucose, urea, creatinine, uric acid, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, alkaline phosphatase, lactate dehydrogenase, creatine kinase, calcium, magnesium, potassium, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, serum iron, vitamin B12, and folate concentrations.

Statistical Analysis

Data processing and statistical evaluations were executed utilizing IBM SPSS 25 (IBM Corp., Armonk, NY, USA) Statistics software. Continuous data were presented as mean standard deviation (SD), whereas categorical variables were reported as frequencies and percentages [n (%)]. Distributional normality for numerical parameters was evaluated through a combination of graphical inspection and formal statistical normality tests. Intergroup comparisons of continuous metrics between two cohorts were conducted using the independent samples t-test. Equality of variances was verified via Levene's test, with Welch's adjusted t-test applied whenever the assumption of variance homogeneity was violated. To determine factors independently associated with hypoalbuminemia, variables

that were found to be significant in univariate analyses or considered to be clinically important were evaluated. To mitigate the risk of model overfitting—considering collinearity among predictors, clinical relevance, biological plausible mechanisms, and the available sample size—age, sex, and serum calcium levels were selected for inclusion in the final multivariable logistic regression analysis. The regression outcomes were detailed in terms of regression coefficients (B), standard errors (SE), odds ratios (OR) with corresponding 95% confidence intervals (CI), and two-tailed p-values. Statistical significance across all analytical tests was defined at a two-tailed probability threshold of $p < 0.05$.

RESULTS

The study population comprised 172 patients. Among them, hypoalbuminemia (serum albumin < 3.5 g/dL) was identified in 111 individuals (64.5%), whereas 61 patients (35.5%) exhibited normal serum albumin concentrations (≥ 3.5 g/dL).

Table 1 outlines the baseline demographic and laboratory profiles of both patient cohorts. As anticipated, individuals in the hypoalbuminemia cohort exhibited markedly reduced serum albumin concentrations relative to those in the normoalbuminemic group (2.81 ± 0.42 vs. 3.82 ± 0.34 g/dL, $p < 0.001$).

Table 1. Baseline demographic profiles and clinical laboratory parameters of the enrolled patient population.

Variable	Hypoalbumin	Normal Albumin	p
Number of patients (n)	111	61	—
Albumin (g/dL)	2.81 ± 0.42	3.82 ± 0.34	<0.001
Age (years)	77.54 ± 8.99	74.43 ± 7.39	0.079
Gender (F/M)	60/51	22/39	0.048
Hematocrit (%)	31.10 ± 6.22	34.68 ± 8.49	0.007
RDW (%)	19.31 ± 10.83	17.50 ± 10.07	0.004
Glucose (mg/dL)	154.89 ± 96.70	223.18 ± 169.75	0.056
Urea (mg/dL)	135.87 ± 80.85	217.72 ± 100.04	0.009
Calcium (mg/dL)	7.75 ± 0.75	8.58 ± 1.60	<0.001
CRP (mg/L)	17.53 ± 18.92	18.07 ± 39.46	0.179
HDL (mg/dL)	38.07 ± 36.26	50.78 ± 62.75	0.084
LDL (mg/dL)	66.42 ± 37.06	83.13 ± 42.37	0.097

While patients in the hypoalbuminemic cohort presented with a higher mean age compared to those in the normoalbuminemic group, this disparity did not reach statistical significance (77.54 ± 8.99 vs. 74.43 ± 7.39 years, p=0.079).

A statistically significant variation was observed between the two cohorts regarding sex distribution ($p = 0.048$). Specifically, female subjects predominated within the hypoalbuminemic group, whereas male patients constituted a higher proportion of the normoalbuminemic cohort.

When hematological parameters were evaluated, the hematocrit level was found to be significantly lower in the hypoalbuminemia group (31.10 ± 6.22 vs. 34.68 ± 8.49%, p=0.007). In contrast, the erythrocyte distribution width (RDW) was significantly higher in the hypoalbuminemia group (19.31 ± 10.83 vs. 17.50 ± 10.07%, p=0.004).

Regarding metabolic parameters, serum glucose concentrations were elevated in the normoalbuminemic cohort; however, this intergroup variation failed to achieve statistical significance (223.18 ± 169.75 vs. 154.89 ± 96.70 mg/dL, p=0.056). Regarding renal function metrics, serum urea concentrations were markedly elevated in the normoalbuminemic cohort (217.72 ± 100.04 vs. 135.87 ± 80.85 mg/dL, p=0.009).

Assessment of mineral metabolism revealed that serum calcium concentrations were significantly diminished in the hypoalbuminemic cohort (7.75 ± 0.75 vs. 8.58 ± 1.60 mg/dL, p<0.001).

Regarding the inflammatory marker C-reactive protein (CRP), no statistically meaningful divergence was detected between the two groups (17.53 ± 18.92 vs. 18.07 ± 39.46 mg/L, p=0.179).

Evaluation of the lipid panel indicated that while high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol concentrations were elevated in the normoalbuminemic cohort, these disparities fell short of statistical significance (p = 0.084 and p = 0.097, respectively). To elucidate independent determinants of hypoalbuminemia, a multivariable logistic regression model was constructed incorporating age, sex, and serum calcium concentrations (Table 2). The resulting model demonstrated overall statistical significance (Omnibus test, p < 0.001) alongside adequate goodness-of-fit (Hosmer–Lemeshow test, χ^2= 8.757, p = 0.363). The Nagelkerke R^2 value indicated an explanatory coefficient of 0.294.

Table 2. Multivariable logistic regression analysis of independent determinants associated with hypoalbuminemia.

Variable	B	SE	OR	(95% CI)	p
Age	-0.052	0.027	0.949	(0.901–1.000)	0.049
Sex	-0.512	0.392	0.599	(0.278–1.291)	0.191
Calcium	1.338	0.277	3.810	(2.212–6.561)	<0.001

B: Beta coefficient, SE: Standard Error, OR: Odds Ratio, 95% CI: 95% Confidence Interval

Multivariable logistic regression revealed serum calcium concentrations as the primary independent predictor of hypoalbuminemia (OR = 3.81, 95% CI: 2.21–6.56, p < 0.001).

Additionally, age demonstrated a statistically significant independent association with hypoalbuminemia (OR = 0.949, 95% CI: 0.901–1.000, p = 0.049). Conversely, sex lost its independent significance within the multivariable framework (OR = 0.60, 95% CI: 0.28–1.29, p = 0.191). Figure 1 depicts the forest plot illustrating the calculated odds ratios alongside their corresponding 95% confidence intervals derived from the regression model.

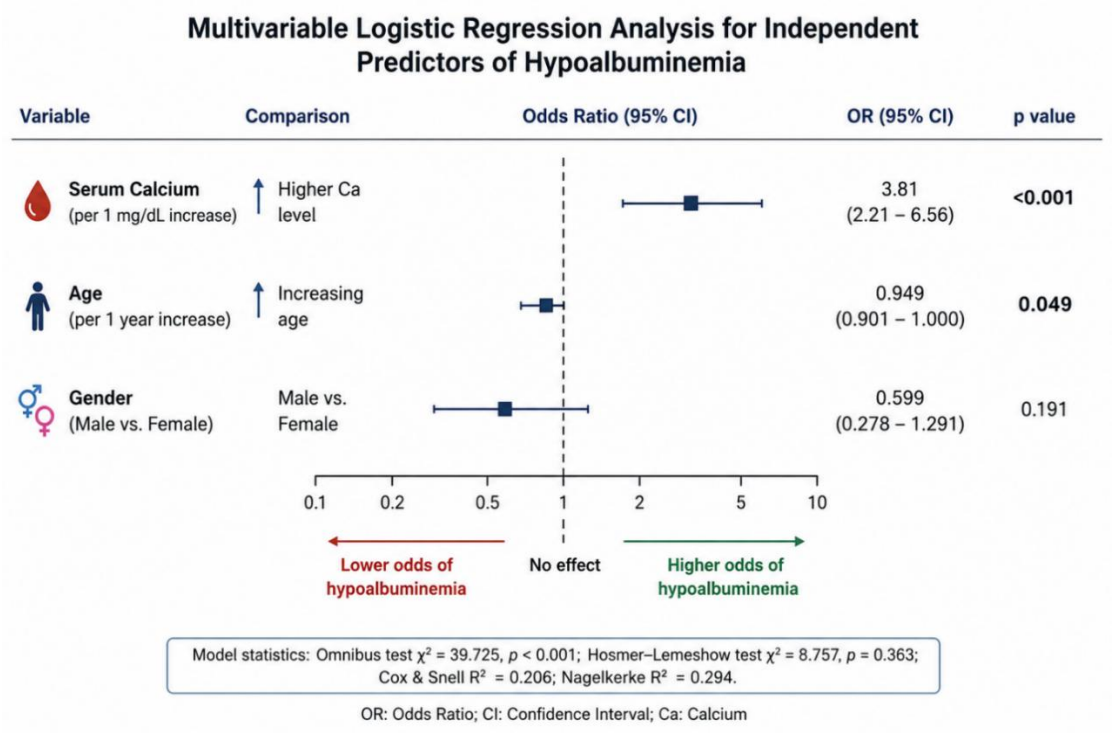

Figure 1. Independent factors associated with hypoalbuminemia identified by multivariable logistic regression analysis.

DISCUSSION

In this study, demographic and biochemical factors associated with hypoalbuminemia were evaluated, and multivariate logistic regression analysis showed that serum calcium level, along with age, was an independent predictor of hypoalbuminemia. In contrast, although gender, hematocrit, RDW, glucose, urea, CRP, HDL, and LDL levels differed in univariate analyses, they did not maintain their independent significance in the multivariate model. These findings suggest that the decrease in serum albumin levels is closely related to calcium homeostasis.

Although our univariate group comparisons revealed a higher mean age among patients with hypoalbuminemia, this divergence was not statistically significant. Nonetheless, the retention of age as an independent determinant in the multivariable logistic regression model suggests

that the aging process may exert an effect on albumin status distinct from co-occurring biochemical parameters. Decreased protein intake in advanced age, sarcopenia, chronic inflammation, and decreased liver protein synthesis capacity are among the main mechanisms contributing to the decrease in serum albumin levels. Although gender distribution differed significantly between the two groups, the disappearance of this relationship in multivariate analysis suggests that the observed difference may be due to age and biochemical variables. This indicates that gender may be an indirect variable related to other clinical characteristics rather than a direct risk factor (8, 9).

Notably, hematocrit levels were markedly lower in the hypoalbuminemic group. Depressed hematocrit values often reflect underlying pathologies, including anemia of chronic disease, protein-energy malnutrition, systemic inflammation, or bone marrow suppression. Given that serum albumin similarly serves as a surrogate for nutritional adequacy and overall systemic disease burden, a concomitant decline in both markers is biologically plausible. Nevertheless, the lack of independent predictive capacity for hematocrit in multivariable regression modeling indicates that this co-association is primarily mediated through confounding or co-varying clinical parameters (10, 11).

Hypoalbuminemic patients exhibited significantly elevated RDW values. In recent years, RDW has been shown to be a biomarker reflecting not only hematological diseases but also chronic inflammation, oxidative stress, malnutrition, and increased mortality risk. High RDW values indicate impaired erythropoiesis and increased heterogeneity in the erythrocyte population. Although the relationship between RDW and hypoalbuminemia was significant in the univariate analysis in our study, it could not maintain its independence in the multivariate model. This suggests that RDW reflects the underlying systemic disease burden rather than directly the albumin level (12, 13).

Although serum glucose concentrations were elevated in the normoalbuminemic cohort, this disparity did not attain statistical significance. Likewise, HDL and LDL cholesterol levels were higher among individuals with normal albumin levels, yet these differences similarly failed to reach the threshold for statistical significance. Since albumin is an important indicator of liver protein synthesis, changes in lipoprotein metabolism can also be expected to be related to serum albumin levels. However, the results in our study show that lipid parameters are not sufficient to independently explain hypoalbuminemia (14, 15).

The significantly higher urea levels found in the normal albumin group may seem unexpected at first glance. The main reason for this may be that patients in the normal albumin group have more pronounced renal dysfunction or more protein catabolism. Nevertheless, the

exclusion of urea as an independent predictor in multivariable logistic regression modeling is likely attributable to its multifactorial nature; serum urea concentrations are strongly influenced by renal perfusion, systemic hydration status, and dietary protein turnover, rather than demonstrating a direct physiological link to albumin homeostasis (16, 17).

CRP concentrations showed no statistically significant variation between the cohorts. Given that serum albumin functions as a negative acute-phase reactant, the comparable CRP levels across both groups imply that hypoalbuminemia in our study cohort cannot be solely attributed to acute systemic inflammation. Especially in the elderly population, malnutrition, chronic diseases, and decreased hepatic protein synthesis can affect serum albumin levels independently of inflammation (18, 19).

The most prominent observation of our investigation is that serum calcium concentrations were not only markedly reduced in univariate cohort comparisons but also emerged as the primary independent determinant of hypoalbuminemia in multivariable logistic regression modeling. Since serum albumin binds approximately 40–45% of the total calcium in circulation, a decrease in albumin level also causes a decrease in total serum calcium concentration. Therefore, low total serum calcium in the presence of hypoalbuminemia is an expected physiological result. The approximately 3.8-fold odds ratio obtained in the regression analysis indicates that the change in serum calcium is strongly associated with hypoalbuminemia. This finding supports that total serum calcium should be interpreted carefully when evaluating albumin levels (20, 21).

The research was conducted retrospectively and does not allow establishing a causal relationship. In addition, the lack of parameters that can evaluate ionized calcium, parathormone, vitamin D and nutritional status in more detail is an important limitation. However, the fact that multivariate analysis was applied in a homogeneous patient group and serum calcium was shown as an independent determinant can be considered among the strengths of the study.

Despite these limitations, our study revealed that although various hematological and biochemical alterations were observed in patients with hypoalbuminemia, serum calcium was the laboratory parameter most strongly and independently associated with hypoalbuminemia together with age. These findings indicate that serum albumin should be considered when interpreting total serum calcium concentrations, particularly in older adults.

CONCLUSION

In summary, hypoalbuminemia among geriatric intensive care unit patients exhibited an independent association with advancing age and reduced serum calcium concentrations.

Among the evaluated laboratory parameters, serum calcium showed the strongest independent association with hypoalbuminemia. These findings emphasize that serum albumin should be considered when interpreting total serum calcium concentrations and support the use of corrected or ionized calcium measurements in patients with suspected hypoalbuminemia.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Ethics Approval and Consent

Before the study began, the necessary ethical committee approval was obtained from the Harran University Clinical Research Ethics Committee (Decision No: 2026-00215 Date: 13.07.2026). The research was conducted in accordance with the principles of the Helsinki Declaration, and patient data were evaluated after anonymization.

Conflict of Interest

No conflict of interest was declared by the authors.

Author Contributions

Veysel Ağan; analysis and writing/hypothesis, calculating.

Financial Support/Funding

The authors declared that this case has received no financial support.

Acknowledgments

I would like to thank Assistant Professor Dr. Fatma Zehra Ağan for her help in providing patients dataset.

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