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EDİTÖRE MEKTUP LETTER TO EDITOR

A NEW FRONTIER FOR IN VITRO BIOLOGY: RETRACING CELL CULTURE'S PATH TO ORGANS-ON-A-CHIP TECHNOLOGY

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ABSTRACT

This abstract reviews the transformative evolution within the field of Cell Culture, the fundamental bedrock of modern Medical Biology, tracing its history from Ross Harrison's pioneering the suspended droplet technique in 1907 to the sophisticated Organs-on-a-Chip (OOC) platforms of today. For over a century, traditional two-dimensional (2D) and static monolayer cultures served as the standard for drug discovery and basic research. However, the primary limitation of these simplistic models lay in their inability to accurately mimic in vivo tissue architecture and the dynamic cellular environment, which necessitated the development of more physiologically relevant three-dimensional (3D) culture systems. This evolution currently culminates in OOC technology, which integrates microfluidic systems to precisely replicate critical physiological parameters, including dynamic flow, mechanical strain, and complex cellular crosstalk. By successfully reconstructing living systems as microphysiological systems (MPS) in the laboratory, OOC offers the closest in vitro approximation of the in vivo state yet achieved. This technological leap holds groundbreaking potential for applications in toxicology screening, precise disease modeling, and personalized medicine, marking the dawn of a new era in biological research.Vaginal foreign bodies are more commonly observed in children according to the literature, however, they can also occur in adults due to multiple reasons.

Keywords: *Microphysiological Systems (MPS), In Vivo Fidelity, Human-Relevant Models, Tissue Engineering, Biomimicry*

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A NEW FRONTIER FOR IN VITRO BIOLOGY: RETRACING CELL CULTURE'S PATH TO ORGANS-ON-A-CHIP TECHNOLOGY

Koksoy H.

Dear Editor,

This letter presents a concise, retrospective analysis of the pivotal advancements that have profoundly redefined the methodology of cell culture, a foundational pillar of modern biomedical sciences. The discipline's origin traces back to Wilhelm Roux's (c. 1885) pioneering attempts to maintain chick tissue in vitro, subsequently affirmed by Ross Granville Harrison's (1907) landmark development of the hanging drop method, which established the technical feasibility of sustained tissue culture. Alexis Carrel's (c. 1912) influential studies on the long-term viability of cells further validated the technique's potential as a research tool (1-3).

The inherent limitations of conventional, static two-dimensional (2D) culture, specifically its failure to accurately recreate the native cellular microenvironment, necessitated a fundamental methodological shift (4). This transition toward three-dimensional (3D) culture was accelerated by innovators such as Johannes Holtfreter (c. 1940s), Aron Moscona (c. 1950s), and Joseph Leighton (c. 1950s), who introduced essential techniques for generating tissue-like structures (5).

A major scientific revolution followed with the discovery of induced pluripotent stem cells (iPSCs) by Takahashi and Yamanaka (2006). This breakthrough provided an unprecedented source of patient-specific cells, significantly enhancing the potential for personalized medicine and sophisticated disease modeling (6). The latest evolution culminates in Organs-on-a-Chip (OOC) technology. These advanced microphysiological systems (MPS) integrate microfluidics to mimic complex physiological stimuli, such as dynamic flow and mechanical strain, offering the highest level of in vivo fidelity achieved to date (5,7).

This letter meticulously examines the historical trajectory from the constraints of 2D models to the complexity of 3D techniques, illuminating the critical discoveries and engineering hurdles that have been overcome. In conclusion, I have explored future research directions that leverage these sophisticated platforms to accelerate the development of more effective, individualized therapeutic strategies.

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DERLEME REVIEW

RENAL CELL CYTOTOXICITY AND ACUTE KIDNEY INJURY: A CLINICAL-BIOLOGICAL EVALUATION OF MARAS POWDER (SMOKELESS TOBACCO) INDUCED NEPHROTOXICITY IN THE EMERGENCY SETTING

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ABSTRACT

A male patient who presented to the Emergency Department of Karaman Training and Research Hospital exhibited significantly impaired renal function following the use of Maras Powder (a form of smokeless tobacco). This clinical observation is consistent with literature reports indicating that Maras Powder is a highly cytotoxic substance, a finding confirmed by in vitro toxicity studies conducted specifically on renal cell lines. The global use of this product is rapidly expanding, driven by its low cost, easy accessibility, and ability to be consumed without smoke, resulting in its use by younger demographics, including those at the middle school level. Maras Powder poses a serious threat to public health, leading users to seek clinical care for a wide variety of serious conditions, such as oral and dental health problems, peripheral circulatory disorders, cardiovascular issues, withdrawal syndrome, esophageal diseases, pregnancy complications, erectile dysfunction, cognitive decline, and hepatic and renal function impairment. This case underscores the escalating public health risk associated with Maras Powder consumption.

Keywords: *Renal function, Maras powder, smokeless tobacco, emergency department, toxicity*

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INTRODUCTION

Maras Powder is the most widely used smokeless tobacco product globally, and in Turkey, it is particularly prevalent in the Southeastern Anatolia region. It is also known by local names such as “Deli Tütün” (Crazy Tobacco) and “Ağızotu” (Mouth Herb). In both the pure form of Maras Powder and the form mixed with oak charcoal, concentrations of heavy metals, including aluminum, manganese, copper, zinc, and lead, are dangerously high for human health. It is important to raise public awareness regarding Maras Powder, which is often perceived as a less harmful and cheaper alternative to cigarettes (1). Although tobacco is most commonly consumed globally in the form of cigarettes, its direct smokeless use is quite widespread; there are approximately 288 million adult smokeless tobacco users in the Southeast Asia Region. This rate is stated to represent about 77% of the global total (2).

Maras Powder, the most common smokeless tobacco product in Turkey, is primarily consumed around Kahramanmaraş and Gaziantep, and its nicotine content is 6–10 times higher than that found in cigarettes (1, 3). Maras Powder is still often viewed as a seemingly innocuous addictive substance today; yet, its easy accessibility and high nicotine levels can cause severe toxicities, particularly for younger age groups. Containing significantly more nicotine than cigarettes, Maras Powder is an extremely harmful substance that, due to its oral placement, leads to decay, recession, loss of sensation, and cancer risk in the mouth, teeth, and gums (4). Once absorbed into the bloodstream, it causes blood pressure irregularities, vascular obstruction, risk of myocardial infarction, and generalized circulatory disorders. In males, it can cause impotence and erectile problems. In pregnant individuals, it may lead to severe outcomes such as miscarriage, premature birth, and intellectual and developmental delay in the infant. It inflicts extensive damage on the digestive system, including gastric and intestinal issues, extending to liver and kidney damage, and these effects are often irreversible (5, 6).

CASE PRESENTATION

A thirty-one-year-old male patient presented to the Emergency Department with complaints of right flank pain and generalized leg pain. The patient's general condition was good; he was cooperative and oriented. Physical examination findings were normal except for tenderness in the right costovertebral angle (CVA). The patient's vital signs were as follows: Blood pressure 160/110

mmHg (hypertension), oxygen saturation 96%, pulse 91/min, and temperature 36.1 °C. A detailed history revealed that the patient, who had no known chronic diseases, had been regularly using Maras Powder for the last five years. Laboratory tests detected significant renal failure and metabolic disturbance.

Table 1. Patient's Laboratory Values at the Time of Emergency Department Presentation

Parameter	Admission Value	Unit
Acid-Base Status		
pH (Arterial Blood Gas)	7.29	
HCO3 (Bicarbonate)	15.9	mmol/L
Renal and Electrolytes		
Urea (BUN)	224.7	mg/dL
Creatinine (Cr)	12.17	mg/dL
Ca (Calcium)	6.38	mg/dL
Enzymes and Metabolism		
CK (Creatine Kinase)	1286	U/L
Lactate	7.7	mmol/L
Hematology		
WBC (White Blood Cell)	7.13	K/µL
Hemoglobin (Hb)	12.1	g/dL
Platelet	159	K/µL

Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Sodium (Na), and Potassium (K) values were within normal limits. Urinalysis revealed proteinuria. An abdominal computed tomography (CT) scan performed showed the appearance of hypodense cysts in the right and left kidneys.

TREATMENT AND FOLLOW-UP

Upon detection of acute renal failure (AKI), significant metabolic acidosis, and rhabdomyolysis, the patient was admitted to the Internal Medicine Service with an indication for dialysis. Following dialysis, the patient's Creatine Kinase (CK) levels demonstrated a trend toward normalization, and a decrease in creatinine levels was observed. The patient was subsequently scheduled for regular dialysis sessions over a period of one month.

Figure 1. Nicotiana Rustica linn (Kahramanmaraş, Photo: Hale Koksoy Mi 10 lite Camera, 2018)

CELL CULTURE STUDIES

Maras Powder (Nicotiana Rustica derivatives) is a smokeless tobacco product with significant cytotoxic and systemic toxicity potential due to its high nicotine and alkaloid content. The nicotine concentration in N. rustica is reported to be approximately 10–20 times higher than that in commercial cigarette tobacco (3, 6). This increased nicotine level leads to toxic effects even at low doses in both clinical and experimental studies. In in vitro models (HK-2, HEK-293), Maras Powder extracts have been shown to significantly reduce cell viability at concentrations of 10–50 ppm. At concentrations of 100 ppm and higher, apoptosis emerged as the predominant mode of cell death, evidenced by increased caspase activity and nuclear changes detected by DAPI staining. The toxic ppm value of Maras Powder extracts can be determined by probit analysis (7). The same studies also reported changes in oxidative stress markers (MDA↑, GSH↓) and elevated expression of IL-6 and TNF-α, confirming that the observed toxicity develops via inflammation and oxidative stress pathways. These laboratory findings are consistent with the systemic toxicity profile observed clinically.

N. rustica exposure in living organisms is associated with severe effects such as acute cardiotoxicity, hypertension, arrhythmia, neurological symptoms, respiratory depression, and peripheral circulatory disorders (8–10). Because it can be consumed without smoke, high and continuous nicotine loading is particularly common in younger age groups, which consequently increases emergency department presentation rates. The most frequent symptoms of acute nicotine poisoning observed in patients admitted to the emergency department are tachycardia/bradycardia, hypertensive states, nausea and vomiting, dizziness, sweating, agitation, and, in severe cases, respiratory depression. In cases involving renal impairment, an increase in creatinine-urea and oliguria are notable findings. The immediate treatment approach is symptomatic, as there is no specific antidote. Patient's airway and circulatory stability must be ensured, IV fluid therapy should be initiated, atropine administered for bradycardia, and appropriate cardiovascular medications used for hypertension/tachycardia. If renal function impairment develops, fluid management and dialysis evaluation are essential. Both the clinical findings and the cellular level demonstration of increased oxidative stress and inflammatory response indicate that Maras Powder is more than just a local oral tobacco product; it is a serious public health concern leading to multi-organ toxicity (11, 12).

DISCUSSION

This case clearly demonstrates that the chronic use of Maras Powder can lead to severe organ system damage. The findings in the patient—high-grade hypertension (Blood Pressure: 160/110 mmHg), severe acute kidney injury (Creatinine: 12.17 mg/dL), metabolic acidosis (pH: 7.29), and rhabdomyolysis (CK: 1286 U/L)—strongly suggest the long-term systemic effects of nicotine toxicity or other toxic substances within the tobacco product. The renal damage may have been exacerbated by myoglobinuria resulting from rhabdomyolysis. Concurrently, severe hypocalcemia (Ca: 6.38 mg/dL) developed, likely due to phosphate release that frequently accompanies rhabdomyolysis. This case is one of the rare reported examples of Maras Powder (Nicotiana rustica Linn) toxicity in an adult patient, indicating that the product possesses a multifaceted toxicity profile attributable to its high nicotine content, alkaline composition, and heavy metals (such as copper and cadmium) carried by the wood ash component (12).

A study conducted on the oral mucosa examined genotoxic damage by performing micronucleus (MN) counts in a cohort of 100 subjects, divided into groups of conventional tobacco, reverse smoking, electronic cigarette, cannabis users, and non-smokers (n=20 in each group). Analysis results revealed that the MN count was significantly higher in conventional, reverse, and electronic cigarette users compared to the non-smoking control group ($P < 0.001$) (14). The high prevalence of smokeless tobacco use, reaching 2.4% of US adults (approximately 5.9 million people) and being particularly common among men, indicates that oral lesions and potential malignant transformation caused by these products threaten a large segment of the population. This wide usage underscores the necessity for dentists and physicians to increase their efforts in early diagnosis and management of such lesions (15). Smokeless tobacco is reported to harbor numerous chemical carcinogens, including tobacco-specific N-nitrosamines such as N′-nitrosonornicotine. These carcinogens have been linked to cancers of the oral cavity, esophagus, and stomach (16). In India, the widespread use of smokeless tobacco, encompassing approximately 21% of adults (with Khaini, a tobacco-lime mixture, being used by over 50%), highlights the product's impact on public health and the urgent need for regulation. It is noted that health warning labels on packages are often too small or absent (17). Furthermore, a comprehensive analysis was conducted by the Cross Cohort Collaboration Tobacco Working Group, harmonizing data from 15 prospective US cohorts spanning 1948–2015 to evaluate the long-term systemic risks of non-cigarette tobacco products. The

study examined the effects of non-cigarette tobacco use on significant cardiovascular outcomes, including myocardial infarction, stroke, heart failure, and atrial fibrillation. The median follow-up time of 13.8 years for all-cause mortality provides strong evidence for long-term risk assessment (18). In a reported case, the risk of acute nicotine toxicity associated with high-concentration nicotine pouches was clearly demonstrated. A 21-year-old male, who consumed 15 extra-strength nicotine pouches (10.9 mg of nicotine per pouch) over 12 hours while studying, presented to the emergency department with bizarre behavior, persistent confusion, and nausea. Although symptoms resolved within 24 hours, this case serves as an important warning that the ease of use and high nicotine content of these products can push users toward the threshold of acute toxicity, potentially necessitating emergency intervention, especially during periods of stress or dose escalation (19). In a separate context, clinical research on obesity has reported a 5–6% loss in patients' starting total body weight, alongside marked improvements in metabolic health indicators. Moreover, this process of weight management is suggested to enhance female fertility capacity by supporting conditions like Polycystic Ovary Syndrome (PCOS) and endometriosis, and by concurrently reducing the drive for alcohol and smoking (20).

As confirmed by cell culture and cytotoxicity studies, Maras Powder extracts lead to significant cytotoxicity, increased oxidative stress, and activation of an inflammatory response in kidney cells, even at low doses (8, 9, 13). These experimental findings support the underlying cellular mechanisms responsible for the severe acute kidney injury (Creatinine: 12.17 mg/dL) observed in our patient. Clinically, acute nicotine poisoning can manifest as a wide spectrum of symptoms, including cardiovascular instability, neurological symptoms, and renal function impairment. This case report demonstrates that Maras Powder (Nicotiana rustica L.) use leads to a multifactorial systemic toxicity that cannot be attributed to a single mechanism due to its complex chemical components. The severe clinical picture observed in our patient (acute kidney injury, rhabdomyolysis, and metabolic acidosis) is closely linked not only to the high nicotine level but also to the product’s overall chemical composition. The toxic profile of Maras Powder results from the simultaneous effects of three main components: high nicotine load, its alkaline pH composition, and its heavy metal content.

The significantly higher nicotine concentration in N. rustica compared to traditional tobacco types, combined with its prolonged contact with the oral mucosa (the traditional usage method), results

in rapid and high absorption (12). The pharmacological consequence of this is that nicotine triggers the release of catecholamines, leading to systemic vasoconstriction. This vasoconstriction and subsequent tissue hypoperfusion are the primary clinical mechanisms explaining the Type A Lactic Acidosis observed in our patient, indicated by a Lactate level of 7.70 mmol/L. The alkaline composition of the product (often derived from wood ash) not only facilitates nicotine absorption but also causes chemical irritation and increased permeability in the oral mucosa; the "burning sensation" reported by users is a clinical reflection of this effect (12). Additionally, heavy metals (specifically cadmium and copper) introduced to the product via the wood ash or absorbed by the plant are considered primary causes of long-term renal damage. In this context, the severe acute kidney injury observed in our patient (Creatinine: 12.17 mg/dL) is supported by in vitro (cell culture) studies (9, 13). These experimental findings definitively show that Maras Powder extracts have significant cytotoxic effects, particularly on renal tubular cells. Cytotoxicity is linked to oxidative stress, where components increase the production of Reactive Oxygen Species (ROS) within the cell, leading to lipid peroxidation. Furthermore, cytotoxic exposure activates transcription factors like NF-κB, triggering an inflammatory response and inducing apoptosis (cell death) at high doses, contributing to the rapid deterioration of organ function (13).

Clinically detected rhabdomyolysis (CK: 1286 U/L) develops either from the direct toxic effect of high-dose nicotine and heavy metals on myocytes or from ischemic damage secondary to severe vasoconstriction. Myoglobinuria resulting from rhabdomyolysis exacerbates kidney damage, while hyperphosphatemia resulting from muscle damage and breakdown is the key physiopathological trigger leading secondarily to severe hypocalcemia (Ca: 6.38 mg/dL). The concordance of these comprehensive clinical and fundamental scientific findings indicates that the toxic effects of Maras Powder are robust, both experimentally and clinically. Early dialysis treatment is vital for patients with advanced renal damage, as observed in this case.

Clinicians should remain vigilant that Maras Powder use may be among the causes of unexplained hypertension, acute kidney failure, and rhabdomyolysis in young patients. For patients with advanced renal damage, as seen in this case, early dialysis treatment is vital. The consistent corroboration of cellular-level cytotoxic findings with the broad clinical picture observed in the emergency department demonstrates that the toxic effects of Maras Powder are robust both experimentally and clinically. This outcome reveals that Maras Powder possesses a multifactorial toxicity

profile stemming not only from nicotine but also from heavy metal content and chemical irritation linked to its alkaline pH. The complex toxicity profile demands that clinicians, particularly in regions where Maras Powder is prevalent, approach patients with a high degree of suspicion and take a detailed history. More comprehensive clinical and experimental studies are needed in this area to optimize the mechanisms of intoxication and treatment strategies. Overall, the molecular-level cytotoxic effects and the extensive clinical presentation observed in the emergency department reaffirm that Maras Powder poses a serious public health risk.

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VAKA TAKDİMİ CASE REPORT

A NOVEL HETEROZYGOUS SI GENE MUTATİON (C.1783G>T; P.G595X) İN A CHİLD WİTH CLİNİCAL FEATURES OF CONGENİTAL SUCRASE-ISOMALTASE DEFİCİENCY: A CASE REPORT

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ABSTRACT

Congenital sucrase–isomaltase deficiency (CSID) is increasingly recognized across a broad clinical spectrum, including milder presentations associated with heterozygous SI variants.

***Case:** In this report, a child with chronic abdominal pain, bloating, frequent loose stools and recurrent perianal dermatitis is presented. Genetic testing identified a novel heterozygous nonsense SI variant, c.1783G>T (p.Gly595X). Cascade testing revealed the same variant in his father, who had intermittent loose stools, postprandial bloating, recurrent oral aphthae and IBS-like symptoms, suggesting a mild phenotype. Initiation of oral sacrosidase resulted in marked improvement in stool frequency, abdominal symptoms and perianal dermatitis.*

***Conclusion:** This case illustrates the clinical relevance of heterozygous SI variants and expands the mutational spectrum of CSID. The findings underscore the importance of considering SI-related carbohydrate malabsorption in children with chronic loose stools and functional gastrointestinal symptoms when routine investigations are unrevealing.*

***KEYWORDS;** Sucrase-isomaltase deficiency, SI gene, Carbohydrate malabsorption, Chronic diarrhea, Nonsense mutation, Sacrosidase therapy*

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INTRODUCTION

Congenital sucrase–isomaltase deficiency (CSID) is a disorder caused by impaired function of the sucrase–isomaltase (SI) enzyme complex in the brush-border membrane of the small intestine. Defects in SI lead to reduced hydrolysis of sucrose and starch-derived oligosaccharides, resulting in variable degrees of carbohydrate malabsorption (1,2). Although classically described in infancy with watery diarrhea, abdominal distension and poor weight gain after the introduction of complementary foods, recent studies have broadened the recognized clinical spectrum. Milder presentations in older children and adults, often resembling functional gastrointestinal disorders such as irritable bowel syndrome (IBS), appear to be more common than previously appreciated (3–6).

More than 40 SI gene variants have been associated with CSID, including missense, nonsense and frameshift mutations that differ in their effects on folding, trafficking or catalytic activity of the enzyme (2,7,8). In addition to the well-described biallelic pathogenic variants, increasing evidence suggests that heterozygous or hypomorphic SI variants can produce clinically relevant symptoms in some individuals, particularly those with IBS-like complaints or chronic loose stools (5,6,9–11). Residual enzymatic activity, dietary sucrose and starch exposure, and host-specific factors are thought to contribute to the wide variability in symptom severity among carriers (4,10).

In this report, a child with chronic gastrointestinal symptoms is presented, in whom genetic analysis revealed a novel heterozygous nonsense SI variant, c.1783G>T (p.Gly595X). The same variant was identified in his father, who had a long-standing history of intermittent loose stools, postprandial bloating, IBS-like symptoms and recurrent oral aphthae, suggesting a mild but clinically meaningful phenotype. To our knowledge, this variant has not been previously described in the literature. This case contributes to the expanding understanding of heterozygous SI deficiency and illustrates the phenotypic variability within affected families.

CASE PRESENTATION

A 3-year-old boy was evaluated for recurrent abdominal pain, abdominal distension, excessive gas, and frequent loose stools occurring three to five times daily. His parents also reported persistent perianal dermatitis that fluctuated with stool frequency. Symptoms worsened after intake of sweets and starchy foods. There was no history of vomiting, fever, nocturnal diarrhea, or rectal bleeding.

He was born at 37+3 weeks' gestation via an uncomplicated vaginal delivery, weighing 2750 g. Early infancy was notable for marked infantile colic and a period of suspected allergic proctocolitis, which improved with dietary elimination. Recurrent oral aphthous ulcers had been present since the toddler period. Growth parameters at presentation were within normal ranges for age: weight 14.5 kg (25–50th percentile) and height 93 cm (10–25th percentile). Physical examination showed a mildly distended abdomen without tenderness and erythematous perianal irritation consistent with chronic dermatitis.

Baseline laboratory evaluation—including complete blood count, metabolic panel, inflammatory markers and immunoglobulins—was unremarkable. Stool cultures and parasitologic studies were negative, and celiac serology (tTG-IgA with total IgA) was normal. Abdominal ultrasonography showed no intestinal or hepatobiliary abnormalities.

Given the persistent loose stools, abdominal distension and negative routine investigations, a carbohydrate digestion defect was considered. Because disaccharidase testing via small-bowel biopsy was not readily available, targeted next-generation sequencing for suspected CSID was performed. This identified a heterozygous nonsense mutation in the SI gene, c.1783G>T (p.Gly595X), predicted to introduce a premature stop codon and cause loss of normal enzyme function.

Cascade testing showed that the patient's father carried the same heterozygous variant. On detailed history, he reported intermittent loose stools, postprandial bloating, IBS-like abdominal discomfort, and recurrent oral aphthae since adolescence. These symptoms had never prompted medical attention and were viewed as normal variations.

The child was started on oral sacrosidase therapy along with practical dietary guidance to reduce sucrose-rich foods. Within weeks, stool frequency improved to one to two formed stools per day, abdominal pain resolved, and perianal dermatitis disappeared. Symptomatic control remained stable during follow-up.

Table 1. Clinical Characteristics of the Patient

Parameter	Findings
Age	3 years
Sex	Male
Birth history	37+3 weeks, 2750 g, normal vaginal delivery
Early infancy findings	Infantile colic, suspected allergic proctocolitis
Current symptoms	Abdominal pain, bloating, excessive gas, 3–5 loose stools/day
Associated findings	Recurrent oral aphthae, persistent perianal dermatitis
Growth parameters	Weight 25–50th percentile, height 10–25th percentile
Laboratory tests	Normal CBC, metabolic panel, inflammatory markers, Ig levels
Celiac serology	Negative (tTG-IgA normal)
Abdominal ultrasound	Normal, no steatosis
Genetic testing	*SI* c.1783G>T (p.Gly595X), heterozygous
Treatment	Oral sacrosidase + sucrose reduction
Response to therapy	Improved stool frequency, resolution of abdominal pain, perianal dermatitis cleared

Clinical characteristics of the affected child, summarizing presenting gastrointestinal symptoms, associated findings, baseline investigations, genetic results and treatment response.

Table 2. Clinical Features of the Father Carrying the Same Variant

Parameter	Findings
Genetic result	*SI* c.1783G>T (p.Gly595X), heterozygous
GI symptoms	Intermittent loose stools, postprandial bloating
IBS-like features	Yes
Oral aphthae	Recurrent
Growth / weight issues	None
Prior workup	None
Dietary triggers	Sweets, high-starch meals
Overall phenotype	Mild, intermittent symptoms consistent with partial SI deficiency

Clinical features of the father carrying the same heterozygous SI c.1783G>T (p.Gly595X) variant, demonstrating a mild IBS-like phenotype with intermittent symptoms consistent with partial SI deficiency.

DISCUSSION

This case highlights several important aspects of SI-related disease. First, the child's presentation—with chronic loose stools, abdominal discomfort and perianal dermatitis despite normal growth—is consistent with the increasingly recognized mild or atypical CSID phenotype. Such cases may not fit the classical infantile picture and are often initially attributed to functional gastrointestinal disorders (3–6).

Second, the identification of a novel heterozygous nonsense SI variant suggests a pathogenic mechanism through partial loss of enzyme activity. Nonsense mutations leading to premature termination codons typically result in nonsense-mediated mRNA decay or production of a truncated, non-functional protein (2,7,8). Based on its premature stop codon and predicted loss of full-length SI protein, the c.1783G>T (p.Gly595X) variant most closely fits the phenotype I category of SI mutants, characterized by retention in the endoplasmic reticulum and absence of enzymatic activity, as defined by Gericke et al. Loss-of-function variants in SI are a well-established cause of CSID, and even single-allele defects have been associated with symptomatic disease in certain individuals (5,9–11). The excellent clinical response to sacrosidase therapy further supports the functional relevance of this variant in our patient.

Table 3. Predicted Functional Impact of the SI c.1783G>T (p.Gly595X) Variant

Feature	**Interpretation**
Mutation type	Nonsense (premature stop codon)
Genomic/protein position	c.1783G>T → p.Gly595X
Location within protein	Early truncation within luminal domain of SI
Expected molecular consequence	Nonsense-mediated mRNA decay or a severely truncated non-functional protein
Predicted intracellular trafficking	Retention in the endoplasmic reticulum (ER)
Predicted enzyme activity	Absent sucrase activity; minimal or absent isomaltase activity
Corresponding phenotype category*	Phenotype I — “Blocked in the ER, enzymatically inactive”
Clinical implication	Consistent with significant loss of SI function; compatible with CSID spectrum even in heterozygous carriers

Predicted molecular and functional consequences of the SI c.1783G>T (p.Gly595X) variant. Given the premature termination codon and expected degradation of the transcript, the variant most closely aligns with phenotype class I in the established SI mutant classification system, characterized by ER retention and absent enzymatic activity.

Third, the father's history of intermittent loose stools, IBS-like symptoms and recurrent oral aphthae, combined with his carrier status, underscores the concept of variable expressivity among heterozygous SI variant carriers. Previous studies have shown that heterozygous pathogenic or hypomorphic SI variants may predispose to IBS-like symptoms, carbohydrate intolerance, or mild chronic diarrhea (5,6,9–11). Environmental influences, dietary habits and residual enzymatic activity likely contribute to differences in severity among family members. The intrafamilial variability observed here aligns with earlier reports of families exhibiting a spectrum of symptoms despite sharing the same SI mutation (4,6).

Finally, the novelty of the c.1783G>T (p.Gly595X) variant is notable. Existing mutation databases and published series of SI variants do not include this change, suggesting that it has not been previously reported in association with CSID.

Overall, this case contributes to the expanding recognition that heterozygous SI variants can produce meaningful clinical symptoms, and that genetic testing can play a valuable role in evaluating children with chronic loose stools and unexplained abdominal complaints when conventional investigations are unrevealing.

CONCLUSION

This case highlights the expanding phenotypic range associated with sucrase–isomaltase deficiency and reinforces that **heterozygous loss-of-function *SI* variants can produce clinically significant symptoms**, even in the absence of a second pathogenic allele. The identification of a **novel nonsense variant, c.1783G>T (p.Gly595X)**, in both the affected child and his mildly symptomatic father demonstrates clear intrafamilial variability and supports the growing recognition that partial SI deficiency may contribute to chronic loose stools, abdominal discomfort and IBS-

like features. The child's rapid response to sacrosidase therapy further affirms the functional relevance of this variant. Clinicians should consider *SI*-related carbohydrate malabsorption in pediatric patients with persistent gastrointestinal symptoms when standard evaluations are non-diagnostic, and genetic testing may provide a valuable non-invasive pathway to diagnosis.

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VAKA TAKDİMİ CASE REPORT

CYTOTOXIC LESION OF THE CORPUS CALLOSUM IN THE EMERGENCY DEPARTMENT: CASE REPORT

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ABSTRACT

The corpus callosum is the primary commissural area formed by white matter tracts that provides interhemispheric communication between the two cerebral hemispheres.

In recent years, cytotoxic lesions observed in the splenium of the corpus callosum have been identified by Magnetic Resonance imaging (MRI). These lesions which are called cytotoxic lesions of the corpus callosum, are rare radiological findings that can be seen secondary to a wide range of diseases.

We present a case of a patient presenting to the Emergency Department with left leg pain and numbness on the left side of the face, who had a cytotoxic lesion of the corpus callosum

Case:*A 31-year-old male patient presented to the emergency department with complaints of pain in his left leg and numbness in the left side of his face. The physical examination is normal. Vital signs are normal. The patient's diffusion MRI showed a cytotoxic lesion of the corpus callosum as a well-defined, oval lesion with hyperintense diffusion restriction in the central part of the corpus callosum, corresponding to a hypointense lesion on ADC. The patient was admitted to the neurology clinic for follow-up*

Discussion and conclusion *Cytotoxic lesions of the corpus callosum are secondary lesions associated with drug therapy, malignancies, infections, subarachnoid hemorrhage, metabolic diseases, head trauma, and more recently, Coronavirus disease 2019 (COVID-19) Cases are usually asymptomatic, but may present with symptoms such as headache, confusion, seizures, and delirium.Although cerebrovascular disease is primarily considered when interpreting imaging in patients presenting to the emergency department with neurological complaints, cytotoxic lesions of the corpus callosum should be kept in mind, too*

KEYWORDS; *Corpus Callosum, numbness, emergency service, magnetic resonance (MR), cytotoxic lesion*

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INTRODUCTION

The corpus callosum is the primary commissural area formed by white matter tracts that provides interhemispheric communication between the two cerebral hemispheres(1). Anatomically, the corpus callosum is divided into four distinct parts: rostrum, genu, body, and splenium. These components connect the corresponding centers of the right and left cerebral hemispheres and provide comprehensive neural coordination.(1)

In recent years, cytotoxic lesions observed in the splenium of the corpus callosum have been identified by Magnetic Resonance imaging (MRI). These lesions which are called cytotoxic lesions of the corpus callosum, are rare radiological findings that can be seen secondary to a wide range of diseases.(3)

We present a case of a patient presenting to the Emergency Department with left leg pain and numbness on the left side of the face, who had a cytotoxic lesion of the corpus callosum. When interpreting MRI images in patients presenting to the emergency department with neurological complaints, cytotoxic lesions of the corpus callosum should also be considered.

CASE REPORT

A 31-year-old male patient presented to the emergency department with complaints of pain in his left leg and numbness in the left side of his face. He was routinely taking hydroxychloroquine, which had been initiated by the rheumatology department. Patient's vital signs:blood pressure 120/60 mmHg, pulse 80 beats/min, oxygen saturation 98%, temperature 36.6°C.

Neurological examination of the patient revealed a Glasgow Coma Scale score of 15, the patient was conscious, cooperative, oriented, and had bilateral positive light reflexes. There was no nuchal rigidity. Muscle strength was 5/5 in the upper extremities and 5/5 in the lower extremities. The patient's vision and hearing were normal. The patient's facial nerve examination was normal. Speech was normal. The patient only reported numbness on the left side of his face.

The patient's pulses were palpable in the extremities, but there was no discoloration. There was no difference in circumference in the lower extremities. The patient's other system examinations were normal. The patient's complete blood count and routine biochemistry tests were normal.

A computed tomography (CT) scan of the brain was performed to explain the patient's complaints. No pathology was detected on the CT scan. A diffusion brain MRI (magnetic resonance imaging) scan was requested for the patient.

The patient's diffusion MRI showed a cytotoxic lesion of the corpus callosum as a well-defined, oval lesion with hyperintense diffusion restriction in the central part of the corpus callosum, corresponding to a hypointense lesion on ADC (Figures 1, 2). We consulted with the neurology clinic. The patient was admitted to the neurology clinic for follow-up. Symptomatic treatment was provided at the neurology clinic. During two days of observation, the patient's symptoms completely resolved. Since no new pathology was detected in the patient's follow-up imaging, the patient was discharged.

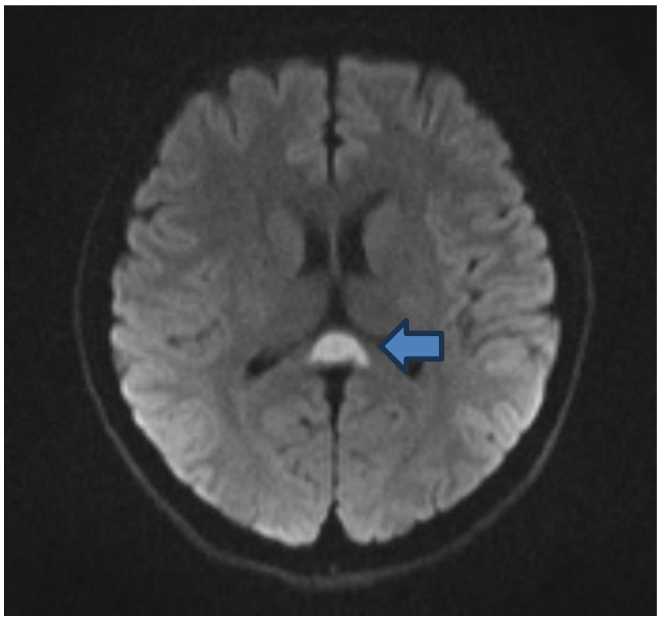

Figure 1. Hyperintense oval, well-defined lesion in the corpus callosum

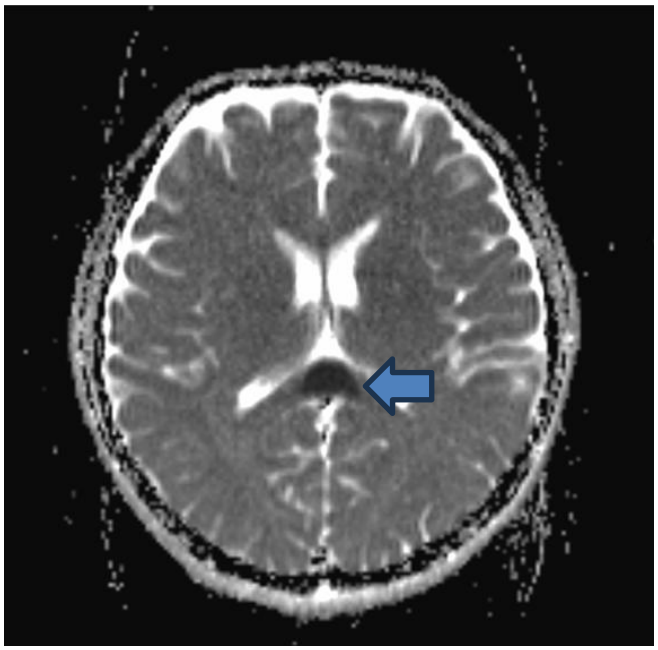

Figure 2. Hyperintense lesion's hypointense counterpart in the ADC

DISCUSSION

Cytotoxic lesions of the corpus callosum are secondary lesions associated with drug therapy, malignancies, infections (adenovirus, aseptic meningitis or encephalitis, Epstein-Barr virus, Escherichia coli, herpes, influenza virus A, influenza, Legionella, malaria, measles, Mycoplasma, mumps, rotavirus, Salmonella, Staphylococci, Streptococci, tick-borne encephalitis, varicella-zoster virus), subarachnoid hemorrhage, metabolic diseases, head trauma, and more recently, Coronavirus disease 2019 (COVID-19).(,3,4,5,6).

Cases are usually asymptomatic, but may present with symptoms such as headache, confusion, seizures, and delirium.(8) Our patient presented with symptoms of leg pain and facial numbness. In their series of four cases, Büyükşerbetçi et al. reported patient complaints including fever, blurred vision, fatigue, headache, tinnitus, focal seizures, and confusion.(1) In the case presented by Durmuş et al., it was reported as temporary vision loss.(7) In a series of studies, Barburoğlu et al. identified neurological symptoms such as dysarthria, altered consciousness, ataxia, syncope, epileptic seizures, and headache. (8) In the same study, it was determined that lesions developed due

to the direct or indirect effect of various infections on the central nervous system as an etiological factor. The study also identified metabolite decompression due to uremia in diabetic patients, subarachnoid hemorrhage, asthma attacks, trauma, high-dose lithium-levetiracetam intake, and antiepileptic drug interactions.(8) We were unable to identify the etiological factor in our case.

CONCLUSION

Although cerebrovascular disease is primarily considered when interpreting imaging in patients presenting to the emergency department with neurological complaints, cytotoxic lesions of the corpus callosum should be kept in mind when the emergency physician detects a well-defined, oval lesion showing T2 hyperintense and diffusion restriction in the central part of the corpus callosum.

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VAKA TAKDİMİ CASE REPORT

WHEN CEMENT MEETS THE EYE: A CASE REPORT

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ABSTRACT

Ocular injuries from cement dust are rare but can result in significant corneal damage and visual impairment. We present a case of acute exposure to a large amount of cement dust, leading to corneal opacity and reduced visual acuity. Management included immediate irrigation, careful removal of particles and topical medications for pain control and infection prevention. Despite these measures, corneal transplantation may be required if no improvement occurs. This case highlights the serious ocular risks caused by cement dust and shows the importance of rapid assessment, systematic evaluation, and multidisciplinary management. Preventive strategies, especially the use of protective eyewear in occupational settings, are essential to minimize the risk of such injuries and to protect visual function.

KEYWORDS; *Eye trauma, Ocular Emergencies, Foreign body in the eye*

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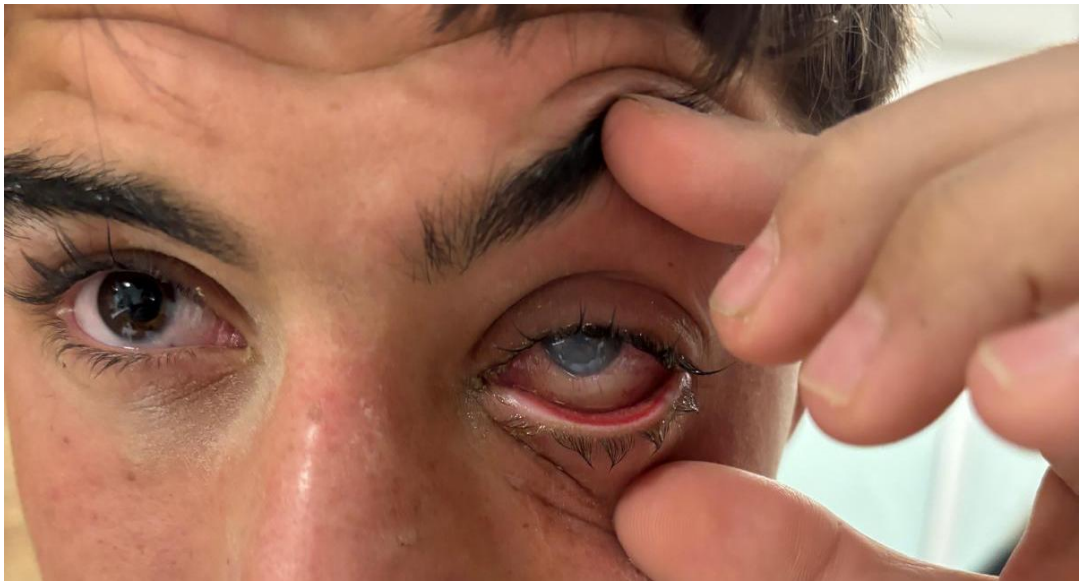
INTRODUCTION

Foreign body trauma to the eyes is a common reason for emergency room visits. The majority of these patients are male, while the most common foreign bodies are metal objects and dust (1,2). Foreign bodies cause damage in two ways: firstly, these objects can cause penetration leading to related complications, and secondly, they can result in infections and toxicity in the eye. In particular, perforation cases can lead to permanent vision loss depending on the size and type of the object (3). When encountered with these cases in the emergency department, ruling out open globe injuries is crucial. Penetrating injuries should be referred to an ophthalmologist without removal of the foreign body. If the foreign body is superficial, it can be removed by the emergency physician with saline irrigation or with a cotton-tipped applicator under direct visualization using a topical anesthetic (4).

In this case, we present a 15-year-old male patient whose left eye was exposed to cement/hardened sand.

CASE REPORT

A 15-year-old male with a medical history of only attention deficit and hyperactivity disorder presented to the emergency department with exposure to cement/hardened sand to the left eye. The exact mechanism of the injury was uncertain. The patient complained of pain and blurry vision in the left eye. On examination, the left cornea was completely opaque, and there was cement/hardened sand on the upper and lower eyelids. Visual acuity was decreased. Direct and indirect pupillary reflexes were present in both eyes.



The patient was consulted with ophthalmology with a differential diagnosis of perforation. An examination by the ophthalmologist revealed no perforation but widespread cement particles in the conjunctiva, eyelids, and cornea. Eye irrigation was performed with approximately 1000 cc of saline. A judicial notification was made considering the age and mechanism of the case. The patient was admitted to the eye department for observation and evaluation for surgery. Larger fragments were extracted under a microscope. After an observation period of 4 days with cyclopentolate hydrochloride drops, artificial tear drops, and prednisolone acetate drops, it was not possible to examine and clear the area under the patient's eyelid due to severe pain. Therefore, an operation was planned under general anesthesia, and all eyelids and fornixes were cleared of the particles. The opacity of the cornea had decreased compared to the first visit. However, the patient was referred to another center because of the possible necessity of corneal transplantation.

DISCUSSION

Ocular traumas require a systematic approach to ensure proper diagnosis and management. Following a detailed patient history, visual acuity should be assessed, and both eyes should be examined, including evaluation of pupillary reflexes and extraocular movements. Information regarding contact lens use should be obtained, and any suspicion of orbital fractures should be excluded. Additionally, a prophylactic tetanus shot should be administered if indicated (5). Corneal abrasions caused by foreign bodies are frequently encountered in emergency departments. For superficial

abrasions, treatment typically focuses on pain control and infection prevention. Topical NSAIDs and artificial tears may be prescribed, while topical antibiotics are commonly prescribed as a precaution (6).

In contrast, chemical injuries can result in extensive damage to the ocular surface epithelium, cornea, and anterior segment, potentially causing permanent visual impairment and necessitating immediate irrigation (7). Cement dust represents a particular occupational hazard, as chronic exposure has been shown to induce corneal dehydration and progressive deterioration of vision in exposed workers (8). In the present case, the patient experienced acute exposure to large quantities of cement dust, leading to significant corneal involvement and reduced visual acuity, highlighting the severity of such injuries.

Penetrating ocular injuries are also common and typically present with hyphema, abnormal pupil or uveal changes, and decreased visual acuity. These injuries may result in long-term complications such as visual loss, traumatic cataract, or secondary infection. Urgent referral to ophthalmology is essential to optimize outcomes and prevent further damage (9).

In our patient, if no improvement is seen with treatment, corneal transplantation is considered as a final therapeutic measure. Corneal blindness remains one of the leading causes of reversible vision loss and can often be successfully treated through keratoplasty. Modern techniques now allow for selective replacement of diseased corneal layers, achieving favorable visual outcomes. Advances in customized component corneal replacement technologies and eye banking methods have further enhanced the success rates of corneal transplantation procedures (10).

This case highlights the rarity of ocular injuries caused by cement dust in the literature, emphasizing the importance of rapid assessment, early intervention, and a multidisciplinary approach. Furthermore, it shows the need for preventive measures, including protective eyewear, particularly in occupational settings where exposure to cement and other hazardous materials may occur.

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VAKA TAKDİMİ CASE REPORT

INTRAOCULAR FOREIGN BODY AND OPEN GLOBE INJURY: A CASE REPORT
İNTRAOKÜLER YABANCI CİSİM VE AÇIK GLOB YARALANMASI: VAKA SUNUMU

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ABSTRACT

This case report describes a 23-year-old male patient admitted to the emergency department following a motor vehicle accident, presenting with an open globe injury and intraocular foreign body in the right eye. Physical examination was limited due to anterior chamber hemorrhage, but bedside ultrasonography and orbital CT revealed globe contour disruption, vitreous hemorrhage, and a foreign body. The patient also had multiple facial and extremity lacerations, as well as maxillary and nasal bone fractures. Facial wounds were primarily sutured, and the patient was referred to a tertiary center for retinal surgery. The discussion highlights classification systems for ocular trauma, prognostic zones, major complications (endophthalmitis, retinal detachment, sympathetic ophthalmia), and the critical importance of timely primary repair. In conclusion, early diagnosis and appropriate surgical intervention are essential to reduce complications and improve visual and functional outcomes.

KEYWORDS; *Open globe injury, Intraocular foreign body, Ultrasonography, Orbital CT, Sympathetic ophthalmia*

ÖZET

Bu olgu sunumunda, araç içi trafik kazası sonrası acil servise başvuran 23 yaşında erkek hastada sağ gözde açık glob yaralanması ve intraoküler yabancı cisim saptanmıştır. Fizik muayene ön kamara hemorajisi nedeniyle sınırlı kalmış, ancak yatakbaşı ultrasonografi ve orbita BT ile glob kontur bozukluğu, vitreus hemorajisi ve yabancı cisim varlığı gösterilmiştir. Hastada eş zamanlı yüz ve ekstremite laserasyonları ile maksiller ve nazal kemik fraktürleri de bulunmuştur. Yüz kesileri primer sütüre edilmiş, hasta retina cerrahisi yapılabilen ileri merkeze sevk edilmiştir. Tartışmada, açık glob yaralanmalarının sınıflandırılması, prognoz belirleyici zonlar, komplikasyonlar (endoftalmi, retina dekolmanı, sempatik oftalmi) ve primer onarımın zamanlamasının önemi vurgulanmıştır. Sonuç olarak, erken tanı ve uygun cerrahi müdahale görsel ve fonksiyonel sonuçların iyileştirilmesinde kritik rol oynamaktadır.

ANAHTAR KELİMELER; *Açık glob yaralanması, İntraoküler yabancı cisim, Ultrasonografi, Orbita BT, Sempatik oftalmi*

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GİRİŞ

Açık glob yaralanmaları; patlama, künt ya da kesici travma sonrası oluşabilir ve intraoküler yabancı cisimler ile termal veya kimyasal hasarlar eşlik edebilir. Kesici travmalar genellikle laserasyon veya penetran yaralanmalara, künt travmalar ise rüptürlere yol açar. Giriş ve çıkış yarası bulunan lezyonlar perforan yaralanma olarak tanımlanır (1).

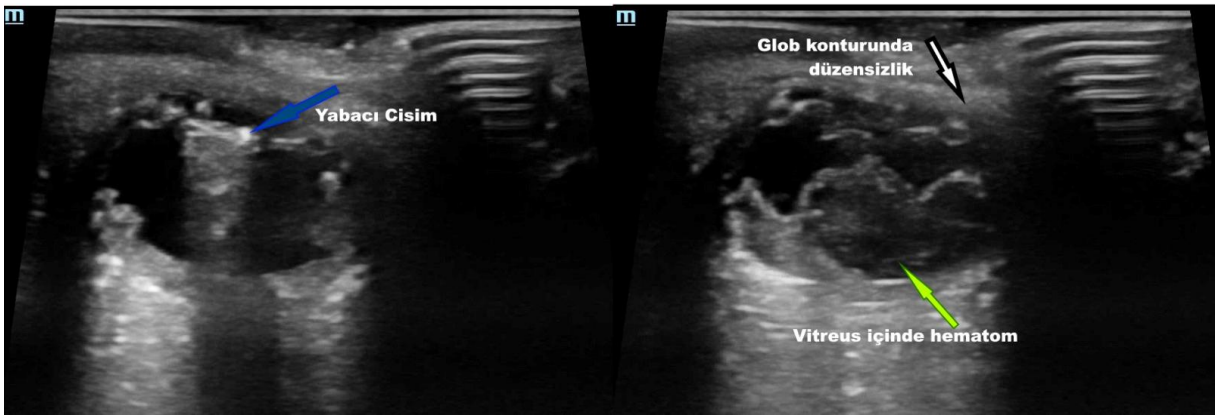
Açık göz yaralanmaları çoğunlukla erkeklerde görülür. Genellikle iş yeri yaralanmaları ve cisimle oluşan travmalarla meydana gelirler. Ancak yaşlı ve kadın popülasyonda düşmeye bağlı yaralanmaların da sık görüldüğü bildirilmektedir (2). Göz duvarının tam kat defektleriyle oluşan açık göz yaralanmaları ciddi görme kayıplarına ve morbiditeye yol açabilir; erken tanı ve tedavi, oluşan hasarın geri döndürülebilmesinde kritik öneme sahiptir (3).

VAKA SUNUMU

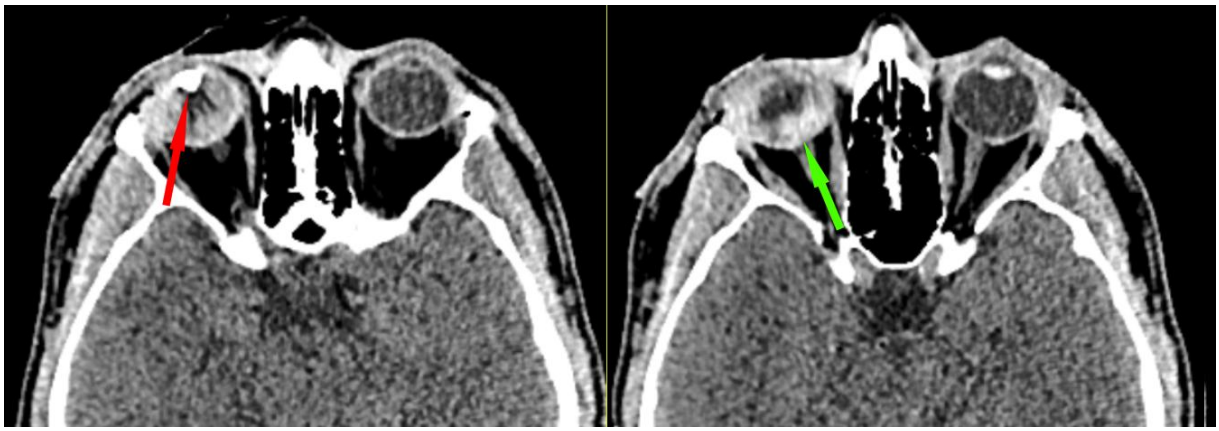
23 yaş erkek hasta araç içi trafik kazası sonrası 112 ile acil servise başvurdu. Hastanın vital bulguları stabildi (TA: 110/60 mmHg, Nabız: 75/dk). İlk değerlendirmede yüzde birden fazla bölgede dermisi içeren doku kayıpları mevcut olup yüzde belirgin bir asimetri saptanmadı.

Sağ gözünü ağrı nedeniyle açmakta zorlanan hastanın oftalmolojik değerlendirmesinde, sağ gözde korneal perforasyon saptandı; ancak ön kamara hemorajisi nedeniyle ayrıntılı muayene yapılamadı. Göz hareketleri her iki gözde de serbestti. Sol göz kapağında cilt kesisi mevcuttu. Fizik muayenenin sınırlı kaldığı bu tür yaralanmalarda, erken dönemde yapılan ultrasonografi (USG) önemli tanısal katkı sağlamaktadır. Nitekim yatakbaşı USG'de göz küresinin şeklinin bozulduğu, vitreus içinde heterojeniteye neden olan hematom ve göz içinde yabancı cisimle uyumlu akustik gölge yapan hiperekojen odak tespit edildi. Bu bulgular, açık glob yaralanmasının kapsamını ve eşlik eden patolojileri erken dönemde ortaya koyarak tedavi planlamasında yol gösterici oldu **(Figür 1).**

Yapılan orbita BT'de, sağ glob içinde anterior yerleşimli yabancı cisim, vitröz boşlukta yoğunluk artışı ve glob konturunda bozulma saptandı. Bulgular, sağ gözde ciddi glob yaralanması ile uyumluydu **(Figür 2).**



Figür 1. Okuler içinde akustik gölge yapan hiperekojen yabancı cisim imajı (mavi ok). Okuler konturda düzensizlik (beyaz ok) ve vitreus içinde hemorajı (yeşil ok)



Figür 2. Orbita BT de okuler içinde hiperdens yabancı cisim imajı (kırmızı ok) ve okuler perforasyona bağlı konturda düzensizlik ve vitreus içi hematom (yeşil ok)

Hastada okuler yaralanmanın yanı sıra, alın ve kaş bölgesi doku kayıpları, glabella ve çene-alt dudak hattında derin kesiler ve laserasyonlar, göz çevresinde kesiler, dudak çevresinde abrazyonlar, sağ yanakta yüzeysel yaralanmalar ile her iki dirsek ve el bileklerinde çoklu laserasyonlar eşlik etmekteydi.

Yüz kemiklerinde yapılan görüntülemede maksiller kemikte üst dudak seviyesine doğru uzanan orta hat fraktürü ve nazal kemikte anterior fraktür saptandı. Plastik cerrahi ile yapılan değerlendirme sonucunda yüz kesileri primer suture edildi. Sonrasında hastanın retina cerrahisi yapılabilen ileri merkeze sevki gerçekleştirildi.

TARTIŞMA

Göz travmalarının sınıflandırılmasında en sık kullanılan iki sistem Birmingham Eye Trauma Terminology System (BETTS) ve International Globe and Adnexal Trauma Epidemiology Study (IGATES) olup, bu sistemler yaralanmayı mekanizma, tip ve yaralanma bölgesine göre kategorize eder. Travma mekanizması kesici, künt, karışık (patlama gibi yüksek enerjili) veya intraoküler yabancı cisimle ilişkili olabilir. Yaralanma tipi ise göz duvarının tam kat etkilenip etkilenmediğine göre kapalı veya açık glob şeklinde ayrılır. (4).

Yaralanmanın zonu prognoz açısından belirleyicidir. Zone I kornea ve limbusu, Zone II limbusun 5 mm posteriorunu, Zone III ise daha posterior bölgeleri ifade eder. Posterior yaralanmalar, özellikle Zone III retinal hasar olasılığı ve kötü prognostik sonuçlar açısından en yüksek riskli grubu oluşturur (5).

Açık glob yaralanmalarından sonra anatomik ve fonksiyonel sonuçları olumsuz etkileyen başlıca ikincil komplikasyonlar arasında ekspulsif hemoraji, endoftalmi, korneal skar, proliferatif vitreoretinopati (PVR) ve retina dekolmanı yer alır (6).

Primer onarımın uygun zamanda yapılması, özellikle endoftalmi ve ekspulsif hemoraji gibi ciddi komplikasyonların riskini azaltmak açısından kritiktir. Mevcut literatür 24 saatten sonraya planlanan primer onarımların savunulabilir olmadığını göstermektedir (7).

Açık glob yaralanmalarının en korkulan komplikasyonlarından biri, nadir görülen ancak diğer gözde görme kaybına yol açabilen sempatik oftalmidir (SO). Bazı çalışmalar, primer onarım sonrası SO oranını %0,15, göz alınması sonrası ise %0–0,21 olarak bildirmektedir; bu fark minimal olup primer tamire göre göz çıkarılması ile SO önlendiğine dair net bir kanıt bulunmamaktadır. Mevcut kanıtlar, mümkünse gözün onarılmasının en uygun yaklaşım olduğunu göstermektedir (8).

Sunulan olguda da çoklu travma ile birlikte intraoküler yabancı cisim mevcuttu; literatür ve vaka serileri, mümkün olan durumlarda gözün anatomik olarak onarılmasının en uygun yaklaşım olduğunu ortaya koymaktadır. Ayrıca fizik muayenenin yetersiz kaldığı bu tür kompleks olgularda, yatakbaşı ultrasonografinin (USG) erken dönemde yabancı cisim varlığını ve glob şekil bütünlüğündeki bozulmayı göstermesi, tanı ve yönetim sürecine anlamlı katkı sağlamaktadır. Erken ve uygun müdahale, komplikasyon risklerini azaltarak görsel ve fonksiyonel sonuçların iyileştirilmesinde belirleyici rol oynamaktadır.

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