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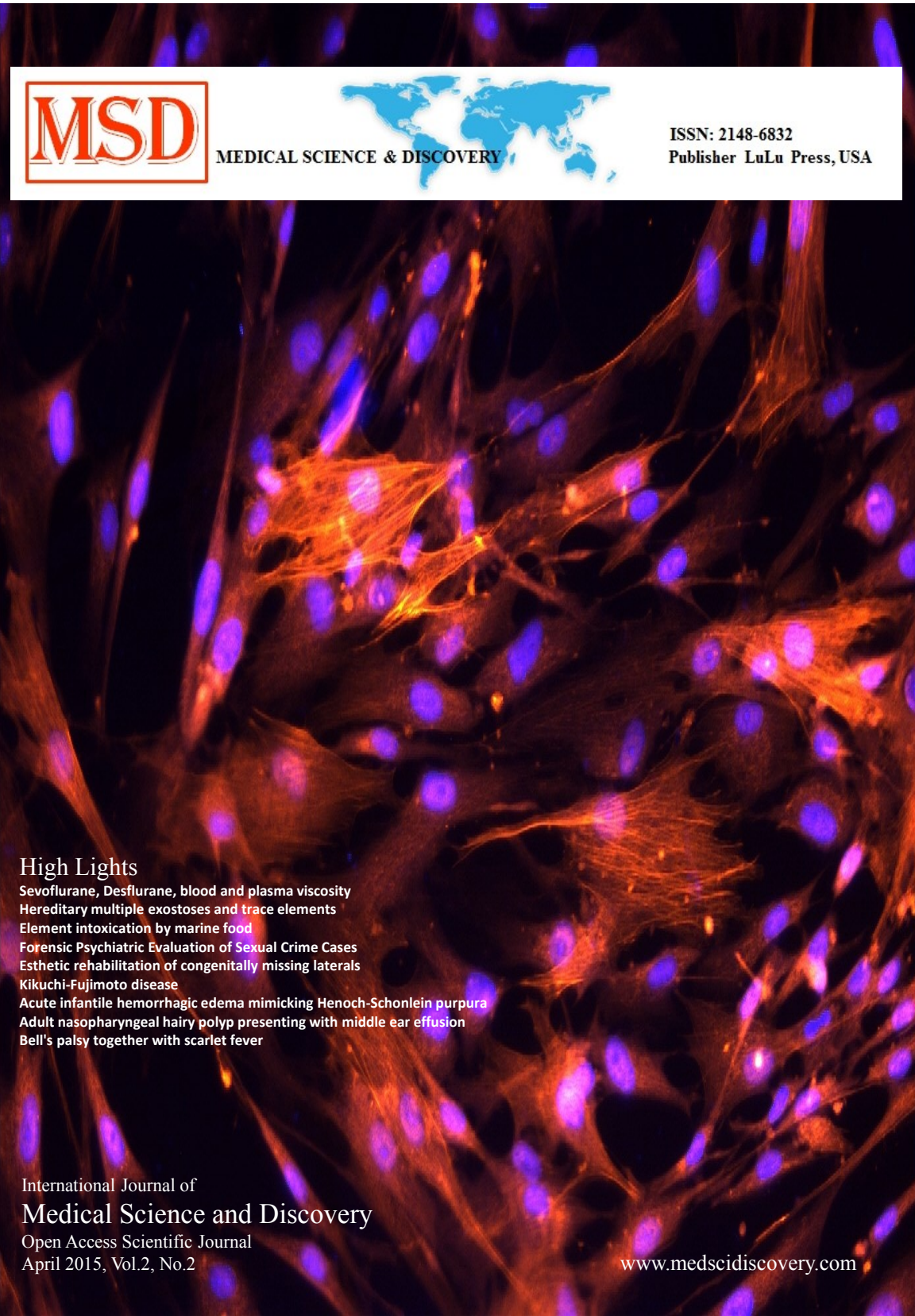

## High Lights

**Sevoflurane, Desflurane, blood and plasma viscosity**
**Hereditary multiple exostoses and trace elements**
**Element intoxication by marine food**
**Forensic Psychiatric Evaluation of Sexual Crime Cases**
**Esthetic rehabilitation of congenitally missing laterals**
**Kikuchi-Fujimoto disease**
**Acute infantile hemorrhagic edema mimicking Henoch-Schonlein purpura**
**Adult nasopharyngeal hairy polyp presenting with middle ear effusion**
**Bell's palsy together with scarlet fever**

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# Contents

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# Effects of sevoflurane and desflurane on the blood and plasma viscosity

Rauf Gul[1], Denizhan Karis[2], Guniz Meyanci Koksal[3], Cem Sayilgan[3], Murat Bolayirli[4], Huseyin Oz[3], Meltem Ercan[4]

**Abstract**

The purpose of present study was to compare the effects of desflurane and sevoflurane on blood viscosity in three different shear rates and plasma viscosity. Forty male patients, ASAI-II, undergone tympanoplasty were included in this study. Patients were randomly categorized as anaesthetized either with sevoflurane or desflurane. Anaesthesia was maintained with inspiratory concentrations of sevoflurane 1-1.5 MAC or desflurane. The samples were taken for hemorheological and biochemical examinations before induction of anaesthesia (initial time) and at 60$^{th}$ and 120$^{th}$ min of the operation. Blood viscosities were measured by rotational viscometer. Plasma viscosity was measured by capillary viscometer. Patients receiving desflurane showed steady decrease at 23 1/sec shear rate at 60$^{th}$ and 120$^{th}$ min and in blood viscosity at 115 1/sec shear rate in 120$^{th}$ min.

Statistically significant decrease in the level of plasma viscosity was observed in the patient group anesthetized with desflurane, between initial time vs 60$^{th}$ min ($p<0.01$), initial time vs 120$^{th}$ min. ($p<0.01$). Desflurane produced stable effects on the blood circulation. The differences in the blood viscosity should not be overlooked.

**Keywords**: Desflurane, Sevoflurane, Blood viscosity, Plasma viscosity

## Introduction

General anaesthesia is a medically combination of analgesia, loss of consciousness and protective reflexes resulting from the administration of one or more general anaesthetic agents. Inhalation or nonvolatile agents are used to induct and to maintain general anesthesia or to relieve pain or to suppress the response and to control the changes in breathing drastically.

General anasethtetic agents do not have a specific pharmacological structure, instead their effects can be also observed in other organs except central nervous system. General anaesthesia has different cardiovascular effects, including its partial effect on anaesthetics of heart and blood vessels [1]. Microcirculatory parameters are altered by the most anaesthetics agent used for induction and during the anaesthesia process. These parameters have effects on the vasoactivity [1-3], blood pressure [4, 5] cardiac output [6] and vascular resistance [7].

It is well known that systemic circulation regulates tissue blood flow and local tissue oxygen diffusion, and has a key role in the development of numerous disease and dysfunctions [8]. Blood flow characteristics, which are also defined as blood viscosity, are directly affected by the physical features of blood. The hemodynamic changes of blood have a significant effect on the vascular system. Blood viscosity is one of the major determinants of blood flow and can be directly related to cardiovascular disease. Since blood is a non-Newtonian fluid, the viscosity of blood depends on the factors such as shear force and shear rate of the blood. As the speed of blood flow decreases, blood viscosity increases. Mediators of blood viscosity include hematocrit, red blood cell deformability, red blood cell aggregation, and plasma viscosity [9, 10]. These mediators of blood viscosity differ according to diameters of vessels.

There are many studies that investigate the advantages or disadvantages of volatile anaesthetics to choose more appropriate and less harmful anaesthetics [11, 12]. The potent inhalation anaesthetics currently used in clinical practice have similar effects in regional tissue perfusion and microcirculation under stable anaesthetic conditions, but these effects may be different under pathophysiologic conditions such as hemorrhage, sepsis, or during surgical operations [13]. Anaesthetics have been studied by many different issues, but little has been written about the anaesthetics' hemoreological effects.

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Considering the wide use of anaesthetics' in daily practice importance of the study on desflurane and sevoflurane becomes more clear. Sevoflurane and desflurane are widely used clinical volatile anaesthetics that provide a greater degree of control of anaesthetic depth and a more rapid immediate recovery from anesthesia than is currently available with other inhaled agents because of their decreased solubility [14]. The aim of the study was to compare the effects of desflurane and sevoflurane on the changes of time dependent blood viscosity.

## Materials and Methods

This study was approved by the Human Studies Review Board of the Cerrahpasa Medical Faculty of Istanbul University, and informed consent forms were received from all patients. The cycle variations of women life may have effects over hormones and hemodynamic features. The hematocrit concentration, hormonal status and liquid/fat distribution are more standardized among men. Thus, forty male patient aged 20-45 year, ASA I-II, undergone tympanoplasty procedure were enrolled to this study. The decision of tympanoplasty procedure was chosen according to the fact of the limited chance of probable bleeding, and its minor effects on hemodynamic and hormonal status and the close amounts of liquid exchange. Patients were randomly selected as either anaesthetized with Group sevoflurane (Group S: n=20) or desflurane (Group D: n=20).

Exclusion criteria were performed for the patients with abnormal preoperative laboratory data (electrolyte imbalance, anemia, polycythemia, thrombocytopenia, leucopenia, and leukocytosis), chronic hypertension, diabetes, hematologic diseases, kidney diseases, anticoagulant and antiagregant treatment history and macro molecular fluid infusion. Moreover, the patients who were faced with major bleeding during the operation were also excluded from the study.

Premedication was done by midazolam 0.03 mg/kg IV (Dormicum, ROCHE). Monitoring consisted of continuous measurement of electrocardiogram (ECG), peripheral arterial oxygen saturation by pulse oxymetry ($sPO_2$), non invasive blood pressure (NIBP) and end-tidal $PCO_2$ ($ETCO_2$) and inhaled anaesthetic gas concentrations (Millenia 3500; Vital Signs, Parway, Orlando, FL, USA)

A 20 G IV cannula was inserted into a dorsum of hand for fluid infusion and another 18 G IV cannula was inserted into brachial vein (opposite side of the body) for blood sampling. Fluid balance of the patients was the supply of the continuous requirement and the loss of fluid (urine, hemorrhage and insensible loss) during operation. Thus, the tympanoplasty procedure was chosen as a study group to limit the hemorrhage probability and to minimalize the liquid loss. Balanced salt solutions were given intra-operatively (0.9 % NaCl, 2 mL/kg /h). Dehydrated and over-hydrated patients were excluded from the study. Central venous pressure was not assessed in our study. The total liquid concentrations were not included in the study.

In both groups, anaesthesia was performed with propofol 2 mg/kg, morphine 0.1 mg/kg intravenously, and orotracheal intubation was facilitated with cis-atracurium 0.2 mg/kg. Patients lungs were ventilated with 40% oxygen in air at a frequency of 12 breaths/min and tidal volume adjusted to maintain $ETCO_2$ at 4.6- 5.3 kPa ($V_T$, 6 - 8 mL/kg). Anaesthesia was maintained either with sevoflurane at an inspiratory concentration of 2-3% (1-1.5 minimum alveolar concentration (MAC)), or desflurane 6 - 9% (1-1.5 MAC). Minimum alveolar concentration is the concentration of the vapour in the lungs that is needed to prevent motor response in 50% of subjects in response to surgical stimulus. It is median value used to compare the strengths, or potency, of anaesthetic gasses. A lower MAC value represents more potent volatile anesthetic. Incremental cis-atracurium doses were administered regularly in order to maintain the neuromuscular block and MAC follow-up was held by means of percentages on the monitor in the operating room.

In our study, patients' venous blood samples were withdrawn before (baseline) and $60^{th}$, $120^{th}$ min of the operation. Systolic artery pressure (SAP) and diastolic artery pressure (DAP) as mmHg of the patients recorded at blood sampling time. The duration of the operation did not have any importance, as the hemodynamic features were followed up for 120 minutes. On fasting venous blood for hemorheological measurements was sampled in (K+EDTA) tubes in resting conditions. Hemorheological (blood and plasma viscosity) parameters examinations were made in Istanbul University, Cerrahpasa Medical Faculty, Biophysics Department. Blood viscosity samples were measured by 'Wells-Brookfield cone-plate rotational viscometer, with CP-40 spindle (LVDV III Brookfield engineering LTD; USA) at three shear rates (23 1/sec, 115 1/sec, 230 1/sec).

Viscosity measurements were made according to "New guidelines for hemorheological laboratory techniques" [15]. Blood viscosity values were corrected to a hematocrit of 45% by a regression equation [16]. These adjusted blood viscosity values were termed as corrected blood viscosity, and were reported at shear rates of 23, 115, and 230 1/sec. Blood samples were centrifuged 15 min at 3000 rpm and divided into multiform element for plasma viscosity measurement. Derived plasma viscosity was measured by Harkness capillary viscometer (Coulter Electronics LTD England) [17].

Plasma viscosity does not vary with shear rate, as it behaves like a Newtonian fluid. Blood and plasma viscosity measurements were made at $37^{o}$ C and data were expressed as milipascal second (mPa.s). Biochemical studies were performed by routine laboratory procedures in Cerrahpasa Medical Faculty, Biochemistry Department, Fikret Biyal Laboratory. During the study, 4 - 5 ml blood (K+ EDTA) for hemogram, blood and plasma viscosity, total

cholesterol fibrinogen 3 ml blood (dry tube) for total protein and albumin was taken. Fibrinogen levels were measured with Dade Behring BCT optic Reader (Dade Behring Tech. Germany) and data were expressed as mg/dl. Hematocrit was measured with Beckmann-Coulter HMX apparatus and total protein and albumin were measured with Olympus Au 800 (MITSUCHI Olympus Tech, Japan) and the data were expressed as g/dl.

**Statistical Analyses**

Data are expressed as mean ± standard deviation (SD). Demographic and biochemical variables between the groups were compared using unpaired student t-tests. Hemorheological variables (Blood viscosity, corrected blood viscosity, plasma viscosity) were analyzed using two-way ANOVA with repeated measurement (Comparison of between two groups) and one-way ANOVA with repeated measurement (intra-group comparisons). For analysis of blood viscosity, univariate two-way analysis of covariance (ANCOVA) was done with three different shear rate and time as the covariates. Post hoc analysis was performed with the Bonferroni/Dunn correction. The values of $p < 0.05$ were considered significant. All statistical analysis was performed using the statistical analysis software package SPSS 11.0 for Windows.

## Results

This study consisted of two groups as Group S and Group D. There were no differences between two groups in demographic data (Table 1). Data from the sevoflurane and desflurane groups are given on Table 2 and Table 3, respectively. The hemorheological and biochemical parameters in the tables are expressed as mean values ± SD. Each groups' measurements were repeated in three certain times as initial time, 60$^{th}$ min. and 120$^{th}$ min., respectively.

**Table 1.** Patients characteristics

| Group | Age (yr) | Weight (kg) | Height (cm) |
|---|---|---|---|
| Group S (n=20) | 31 ± 5 | 71 ± 9 | 162 ± 5 |
| Group D (n=20) | 29 ± 3 | 70 ± 7 | 163 ± 4 |

Data tested by t-test: mean±SD, Group S; Sevoflurane Group, Group D; Desflurane Group.

In the patients who were received the sevoflurane, we observed a significant decrease in the value of SAP, DAP and MAP at initial time vs 60$^{th}$ min. ($p<0.001$, $p<0.001$ and $p<0.001$, respectively) and 120$^{th}$ min. ($p<0.001$, $p<0.001$ and $p<0.001$, respectively). Patients received desflurane showed significant decrease in the value of SAP, DAP and MAP at initial time vs 60$^{th}$ min. ($p<0.001$, $p<0.001$ and $p<0.001$, respectively) and 120$^{th}$ min. ($p<0.001$, $p<0.001$ and $p<0.001$, respectively).

When the blood viscosity was measured at its native hematocrit level in the patients anesthetized with sevoflurane, we noted that a significant reduction in the level of blood viscosity at 23 1/sec and 230 1/sec shear rates in the following time periods in both 60$^{th}$ min . ($p<0.001$ and $p<0.05$, respectively) and 120$^{th}$ min. ($p<0.01$ and $p<0.05$, respectively) samples (Table 2). Likewise, in the patients who were received the Group S, we observed a significant decrease in the level of blood viscosity in the shear rate is 115 1/sec at initial time vs 60$^{th}$ min. ($p<0.01$). After hematocrit 45% was standardized, there was no statistically significant in the level of blood viscosity at three shear rate (23, 115 and 230 1/sec) in patients anesthetized with Group S (Table 3).

Patients received desflurane showed a meaningful decrease at 23 1/sec shear rate in 60$^{th}$ min ($p<0.05$) and an important decrease at 120$^{th}$ min. ($p<0.01$) and also in the level of blood viscosity in 115 1/sec shear rate at 120$^{th}$ min. ($p<0.01$). There was no a statistically significant difference observed in the level of blood viscosity at 230 1/sec shear rate in patients anesthetized with desflurane (Table 3). After hematocrit 45% was standardized, there was only a meaningful reduction in blood viscosity in 23 1/sec shear rate at initial time vs 120 min. ($p<0.05$) in the patients anesthetized with desflurane (Table 3).

In our study, time-dependant changes of measured parameters were calculated by their division to initial values and the results were expressed as change ratio. To conclude that Group S had a decreased blood viscosity compared to desflurane, we calculated data on decrease rate of blood viscosity in both Group S and Group D. Rate of change was shown as percentage change from initial value. The decrease ratio of blood viscosity from the Group S and Group D is given on Table 4. When the decrease ratio of blood viscosity was calculated at its native hematocrit level in the patients anesthetized with Group S, we noted that meaningful decreases in the level of blood viscosity at the all shear rates (23, 115 and 230 1/sec) at initial time vs 60$^{th}$ min. ($p<0.05$, $p<0.05$ and $p<0.05$ respectively) (Table 4). There was no a statistically significant difference observed on the rate of blood viscosity in both native and corrected hematocrit (45%) at the all shear rates (23, 115 and 230 1/sec) are at initial time vs 60$^{th}$ min. and at initial time vs 120$^{th}$ min. in patients anesthetized with desflurane (Table 4).

Although the level of plasma viscosity remained the same during measuring period in the patients anesthetized with Group S, statistically important decrease in the level of plasma viscosity was observed between initial time vs. 60 min. ($p<0.01$), initial time vs 120 min. ($p<0.01$) in patients anesthetized with desflurane.

The value of hematocrit decreased in the patients anesthetized with Group S at 60$^{th}$ min. ($p<0.01$) and 120$^{th}$ min. ($p<0.001$).

**Table 2.** Hemorheologic and hematologic values for sevoflurane group

| | Initial Time | 60th. min | 120th. min |
|---|---|---|---|
| Hct (%) | 39.24 ± 3.20 | 37.84 ± 3.34 a** | 37.33 ± 3.26 a*** |
| BV (230 1/sec, mPa.s) | 4.10 ± 0.55 | 3.82 ± 0.39 a* | 3.89 ± 0.34 a* |
| BV (115 1/sec, mPa.s) | 5.95 ± 0.94 | 5.36 ± 1.10 a** | 5.58 ± 1.12 |
| BV (23 1/sec, mPa.s) | 7.07 ±1.30 | 6.15 ± 1.24 a*** | 6.33 ± 1.13 a** |
| **Corrected Hct (45%)** | | | |
| BV (230 1/sec, mPa.s) | 4.68 ± 0.45 | 4.82 ± 0.84 | 4.76 ± 0.23 |
| BV (115 1/sec, mPa.s) | 6.65 ± 0.81 | 6.35 ± 1.35 | 6.48 ± 1.08 |
| BV (23 1/sec, mPa.s) | 7.74 ± 1.22 | 7.16 ± 1.45 | 7.17 ± 0.95 |
| PV (mPa.s) | 1.23 ± 0.11 | 1.25 ± 0.11 | 1.22 ± 0.12 |
| SAP (mmHg) | 133.2 ± 21.56 | 107.15 ± 13 a*** | 103.6 ± 13.61 a*** |
| DAP (mmHg) | 82.45 ± 13.04 | 68 ± 7.49 a*** | 65.05 ± 9.29 a*** |
| MAP (mmHg) | 98.9 ± 1.76 | 81.25 ± 8.4 a*** | 79.1 ± 9.77 a*** |
| Fibrinogen (mg/dl) | 257.76 ± 89.34 | 316.46 ± 84.10a** | 294.07 ± 93.29 |
| Total protein (g/dl) | 7.00 ± 0.46 | 6.74 ± 0.54a** | 6.84 ± 0.56 |
| Albumin (g/dl) | 4.33 ± 0.35 | 4.14 ± 0.35a** | 4.18 ± 0.30 |
| Total Cholesterol (mg/dl) | 173.25 ± 48.33 | 174.55 ± 31.07 | 183.30 ± 44.73 |

Data are mean±SD, BV; Blood viscosity, PV; Plasma viscosity, Hct; Heamatocrit, SAP; Systolic Artery Pressure, DAP; Diastolic Artery Pressure, MAP; Mean Artery Pressure,[a] Initial time vs 60th min ., 120th min., * p<0.05, **p<0.01, ***p< 0.001.

**Table 3.** Hemoreologic and hematologic data for desflurane group

| | Initial Time | 60 th. min | 120 th. min |
|---|---|---|---|
| Hct (%) | 38.84±5.24 | 37.62±4.92 | 37.60±4.29 |
| BV (230 1/sec, mPa.s) | 4.20±0.98 | 4.18±0.75 | 4.17±0.68 |
| BV (115 1/sec, mPa.s) | 5.79±0.84 | 5.60±0.91 | 5.22±0.80 a** |
| BV (23 1/sec, mPa.s) | 6.70±1.20 | 6.20±1.29 a* | 5.92±1.31 a** |
| **Corrected Hct (45%)** | | | |
| BV (230 1/sec, mPa.s) | 4.72±0.20 | 4.89±0.46 | 4.82±0.54 |
| BV (115 1/sec, mPa.s) | 6.40±0.59 | 6.35±0.67 | 6.09±0.88 |
| BV (23 1/sec, mPa.s) | 7.39±0.85 | 7.03±0.91 | 6.52±1.65 a* |
| PV (mPa.s) | 1.24±0.86 | 1.21±0.11 a** | 1.23±0.11 a** |
| SAP (mmHg) | 127.65±26.91 | 106.4±12.81 a** | 103.85±12.63 a*** |
| DAP (mmHg) | 80±11.73 | 67.1±10.01 a*** | 64.4±9.68 a*** |
| MAP (mmHg) | 98.95±11.83 | 81.2±10.55 a*** | 77.9±8.58 a*** |
| Fibrinogen (mg/dl) | 304.51±73.41 | 309.25±64.13 | 309.05±43.63 |
| Total protein (g/dl) | 7.09±0.66 | 6.80±0.46 a** | 6.94±0.55 |
| Albumin (g/dl) | 4.36±0.40 | 4.18±0.26 a** | 4.20±0.29 |
| Total Cholesterol (mg/dl) | 165.42±57.13 | 167.10±55.15 | 170.10±60.40 |

Data are mean±SD, BV; Blood viscosity, PV; Plasma viscosity, Hct; Heamatocrit, SAP; Systolic Artery Pressure, DAP; Diastolic Artery Pressure, MAP; Mean Artery Pressure,[a] Initial time vs 60th min., 120th min, *p<0.05, **p<0.01, ***p<0.001.

**Table 4.** The percentage of the blood viscosity changes in sevoflurane and desflurane group

| | Group S | | Group D | |
|---|---|---|---|---|
| | $P_1$(%) | $P_2$(%) | $P_1$(%) | $P_2$(%) |
| **Native Hct (%)** | | | | |
| BV(230 1/sec, mPa.s) | 0.941±0.107* | 0.957±0.082 | 1.005±0.104 | 0.986±0.131 |
| BV(115 1/sec, mPa.s) | 0.900±0.113* | 0.944±0.159 | 0.968±0.091 | 0.909±0.125 |
| BV(23 1/sec, mPa.s) | 0.874±0.106* | 0.904±0.119 | 0.930±0.125 | 0.886±0,136 |
| **Corrected Hct (45%)** | | | | |
| BV(230 1/sec, mPa.s) | 1.037±0.190 | 1.026±0.102 | 1.038±0.007 | 1.022±0.108 |
| BV(115 1/sec, mPa.s) | 0.957±0.184 | 0.977±0.124 | 0.994±0.084 | 0.955±0.134 |
| BV(23 1/sec, mPa.s) | 0.931±0.158 | 0.936±0.109 | 0.957±0.116 | 0.881±0.211 |
| PV (mPa.s) | 1.018±0.003 | 0.991±0.008 | 0.988±0.017** | 0.991±0.016 |
| SAP (mmHg) | 0.807±0.033 | 0.780±0.024 | 0.844±0.079 | 0.824±0.076 |
| DAP (mmHg) | 0.829±0.041 | 0.790±0.012 | 0.838±0.002 | 0.805±0.003 |
| MAP (mmHg) | 0.820±0.070 | 0.798±0.084 | 0.820±0.891 | 0.787±0.007 |

Data are mean±SD, Group S; Sevoflurane Group, Group D; Desflurane Group, BV; Blood viscosity, PV; Plasma viscosity, SAP; Systolic Arterial Pressure, DAP; Diastolic Arterial Pressure, MAP; Mean Arterial Pressure, $P_1$(%); 60 min/initial time, $P_2$(%); 120 min/initial time, * p < 0.05, ** p< 0.01.

Also the value of hematocrit showed meaningful decrease at 60th ($p<0.05$) and 120th min. ($p<0.05$) in the patients anesthetized with desflurane. The level of fibrinogen in patients anesthetized with Group S at 60th min. ($p<0.01$) increased significantly. Unlike the results of the patients anesthetized with Group S, there was no a difference in the level of fibrinogen observed in the patients anesthetized with desflurane at any time. In addition, the level of albumin and protein in patients anesthetized with sevoflurane and desflurane at 60th min. importantly decreased ($p<0.01$).

When we compared both the patients anesthetized with sevoflurane and desflurane, we did not find any statistical evidences for significant changes in the level of blood viscosity at three different shear rates, total protein, albumin, fibrinogen, total cholesterol at both 60th min. and 120th min.

## Discussion

The aim of our study is to investigate the effects of desflurane and sevoflurane on blood viscosity in different shear rates. Both anaesthetics agents have effects over blood viscosity via sympathetic blockade due to decreased hematocrit. The authors found that Group S had a negative effect on the blood viscosity, whereas desflurane produced stable effects on the blood circulation.

Sevoflurane and desflurane are the newly volatile anesthetics commonly used for the general anesthesia before the surgery. General anesthesia results in significant changes in the microvasculature involving primarily changes in the diameters of the arterioles and venules and combined changes in arterial pressure and the cardiac output [4,5]. The peripheral vascular effects of the anesthetics may influence the choice of anesthesia and may alter the results of experimental investigations performed in anesthetized animals. For this reason we have previously investigated the effects of these two volatile anesthetics on the deformability of erythrocytes which performed in young and old animals. These results revealed that even the desflurane anesthesia [18] and the sevoflurane anesthesia [2] has improved the deformability of erythrocytes in young animals, whereas it has impaired it in elderly animals [14].

Inhalation anaesthetics has several effects on different organ systems, like cardiovascular system, central nervous system, respiratory system, liver and kidney metabolism and neuromuscular pathways. Most studies have evaluated different characteristics of anaesthetic agent, and their comparisons of clinical manifestations over the organism. However, to our knowledge there has been no too many studies linking with the hemorheologic and hemostatic effects of volatile anaesthetic agents [19, 21].

Hemorheologic alternations are also important in term of anaesthesia. It is known that hemorheology is affected by many factors such as applied anaesthesia techniques, general or local use of anaesthetic agents, operation duration, duration and quantity of hemorrhage, infusion of crystalloid and macromolecular fluid, pain, hypothermia etc. [22-24]. In our study, we selected all the patients from those who had not any comorbidity and to undergo tympanoplasty, in order to provide patient standardization. Only one patient in Group S was ASA II because of Down syndrome. We tried to keep the parameters constant that might affect intraoperative rheology (MAC value, temperature, the amount of the intravenous fluid administered and bleeding quantity, etc.). In addition, all patients were received midazolam premedication that has been reported not to affect the blood viscosity in order to minimize the patients' anxiety [25].

Magora et al. [23] observed the effects of halothane, cyclopropane, thiopental and ketamine on blood viscosity. Their study showed that in patients who were exposed to the halothane and the cyclopropane, a significant decrease in the level of blood viscosity -especially in the 230 1/sec hematocrit and fibrinogen concentration is observed. During the thiopental anaesthesia, there was significant reduction in blood viscosity at 230 1/sec and in the level of hematocrit. During the ketamine anaesthesia, they did not found any statistically significant changes at the level of hematocrit, total protein, fibrinogen and blood viscosity at the different shear rates vs initial level. All those changes were explained with the effects of medicines to the sympathetic nervous system activity.

Hematocrit was one of the most important factors determining blood viscosity [9, 10, 22]. However the vessels smaller than 100 µm (arteriole, capillary) are affected less than large vessels [8, 9]. In a review written by the guidance of these studies, Gordon et al. [22] reported that the most important parameters affecting blood rheology are peripheral vessel tone and hematocrit level as well as plasma viscosity and levels of fibrinogen and albumin, thus hematocrit alterations are inversely related to plasma volume. However, especially increase of the levels of hematocrit and fibrinogen has been reported to increase the predisposition to thrombosis [22].

In our study, we observed a decrease in blood viscosity at 23 1/sec in both groups. There was a decrease observed at 230 1/sec in Group S group alone, and although no statistically significant difference was found between the groups in terms of capillary vessel viscosity, decrease in Group S compared to baseline value suggests that Group S is more effective on the capillary vessel viscosity. Whereas, effects of plasma viscosity is more determinant in the small vessels [8, 9, 22]. In addition, we believe that the differences found in inter-group comparison of the corrected hematocrit viscosities compared to the baseline values might have been resulted from the changes in plasma viscosity. These data of Yerer et. al. [19] are in compliance with ours, because considering the corrected viscosity values and the decrease in viscosity at the capillary level compared to baseline values.

When our data are evaluated in the light of these findings, main cause of the decrease in the blood viscosity can be shown as anaesthetic agents to suppress the sympathetic nervous system activity. Viscosity decrease seen with both agents' results from sympatholytic effect differs in these agents. Desflurane has been reported to less suppress sympathetic activity, even induced it in high doses [4, 26]. Decrease in hematocrit value has been reported in the previous studies to be resulted from the peripheral congestion due to vasodilatation caused by sympathetic blockade [23, 24].

Plasma viscosity is a crucial determinant of whole blood viscosity [27]. Plasma is principal interface with the blood vessel wall because of the axial migration of RBCs in flowing blood. Consequently, it is possible to think that plasma viscosity directly affects endothelium [28, 29]. In many cohorts fibrinogen has been established as the major protein determinant of plasma viscosity. It is well known that plasma viscosity depends especially on plasma fibrinogen concentration, but also is affected by the concentration of other macromolecules, cholesterol and triglycerides [27, 30]. Microvascular blood flow is actively regulated in response to change in viscosity as a consequence of the level of shear stress developed in the endothelium [31]. Increased plasma viscosity restores shear stress in the microcirculation. Shear stress increases the rate of production of vasodilators (nitric oxide and prostacyclin) via mechanotransduction and has been associated with increased microvascular flow and capillary pressure [32]. Plasma viscosity in Group S increased by 1.02 % at 60 minutes from baseline level with a significant degree, but decreased at 120 minutes by 0.99 % in spite of the disappearance of significance. We can evaluate this statistical significant increase as increased plasma viscosity restores shear stress in the microcirculation. This change can be explained possibly with the change in plasma fibrinogen concentration. The decrease in plasma viscosity of Group D were 1.2 % at 60 minute ($p<0.05$) and 0.9 % at 120 minute. Although there is no change statistically by means of plasma fibrinogen concentration, this change may be due to total protein and albumin levels. However, we did not observe a significant difference between the plasma viscosities. Nevertheless, we believe this is still a subject to be studied. When SAP, DAP and MAP values were investigated in accordance with the role of plasma viscosity in the regulation of systemic circulation and microcirculation, no statistical significance was found in two groups, but the changes among the groups in time were statistically significant. The change ratio of Group S and Group D at baseline and 60 min were calculated as %19.3 and %15.6 for SAP, %17.1 and %16.2 for DAP and %18 and %18 for MAP. The change ratio of Group S and Group D at baseline and 120 min were calculated as %22 and %17.6 for SAP, %21 and %19.5 for MAP and %20.2 and %21.3 for MAP. In the review of Salazar et al. [33] stated that a negative correlation between whole blood viscosity and systolic blood pressure in the strong Heart Study. The evaluated data by considering the changes in plasma viscosity values are in the direction of lesser effect of desflurane over arterial pressure changes, in this way desflurane can facilitate the stabilization easily. Our study is consistent with the results of Ozarslan et al. [34].

In conclusion, decrease was found in the blood viscosity with both anaesthetic agents, mainly due to decreased hematocrit. This effect was primarily caused by the sympathetic blockade. The effects of potent volatile agents, specifically focusing on macrohemodynamics, have been investigated in clinical studies. In general, the decrease in blood pressure caused by volatile anesthetics is a direct result of the vasodilatation and depression of myocardial contractility and an indirect of the attenuation of sympathetic nervous system activity. The authors found that Group S had a negative effect on the blood viscosity, whereas desflurane produced stable effects on the blood macrocirculation [34]. In our opinion, desflurane might be a preferable anaesthetic agent. Further research is necessary to ascertain the effects on anaesthetics on the macro-microcirculation

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**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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# The relation of Hereditery Multiple Exostoses and trace elements

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**Abstract**

**Introduction:** Hereditary multiple exostoses (HME) is a rarely autosomal dominant bone tumoral disorder; which is characterized by abnormal ossification especially at long bones. The common symptoms are bone pain, joint movement limitation, malign degeneration, vessel and neuron impression and asymmetry of extremities.

**Material and Methods:** The association of a group of trace elements of the HME patient was analysed at the Department of Biophysics. A 26-year-old male patient (weight 60 kg, height 170 cm) who admitted to Department of Orthopaedics Out-patient Clinic at Cerrahpasa Medical Faculty in July 2013 had been suffering from bone pain and prominences in different parts of his body for 20 years. Other individuals diagnosed with HME were reported in his family history.

**Results:** When the values of serum Ca (134.5 ppm), P (173.3 ppm), Fe (1.104 ppm), Se (1.119 ppm) and as (0.647 ppm) levels in patient were compared with reference ranges, all these elements had showed higher values. However, Zn (0.562 ppm) levels had a lower value than reference ranges. Residual trace elements that were determined in patient were found in physiological ranges. Ni level was too low to be measured

**Conclusion:** Until this time there has been no investigation about the association of HME and trace elements. The level of trace elements that play crucial roles in all systems especially bone and renal metabolism should be kept in mind in evaluation of HME patients. For this purpose, familial and environmental trace element level determination would be one of our projects in this study.

**Key words:** Hereditary Multiple Exostoses, Osteochondroma, Trace element

## Introduction

Hereditary multiple exostoses (HME) is an autosomal dominant bone tumoral disorder; which is characterized by abnormal ossification especially from the metaphysis of long bones [1, 2]. HME, which includes growth retardation and osteochondromas; is a rarely seen disorder. Onset of the disease is from early childhood (2–3 years) to puberty, with 40% of patients were affected before 10 years of age. The lesions can be present at birth and continue to appear and grow throughout childhood and into puberty. Nevertheless, the diagnosis of HME at birth has been rarely described [3]. Bones formed via intramembranous formation are not involved. The prevalence of HME has been estimated to be at least 1/50 000 in the general population, and penetrance is estimated to be 96%. Most published instances of non-penetrance have occurred in females.

Osteochondromas may cause complications, including osseous and cosmetic deformities, fracture, bursa formation and impingement on adjacent structures (tendons, nerves, vessels) and malignant transformation. Osteochondromas that are located at pelvis, knee and shoulder are prone to malign transformation [4, 5, 6]. Growing of osteochondromas cause defects around perichondrium; this is called as Ranvier cycle and covers epiphyseal plaque. This perichondrial defect allow the growing of cartilage to sides and it binds to growing plaque with 90 degree angle and generate the typical appearance of osteochondroma. The common symptoms are bone pain, joint movement limitation, malign degeneration, vessel and neuron impression, asymmetry of extremities [7].

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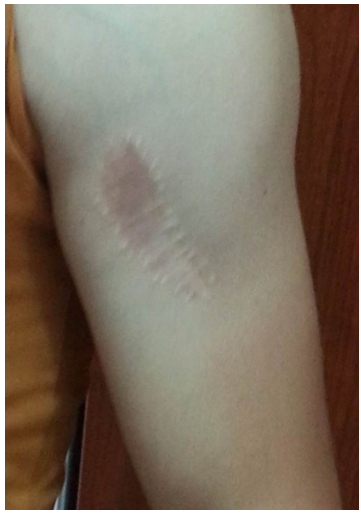
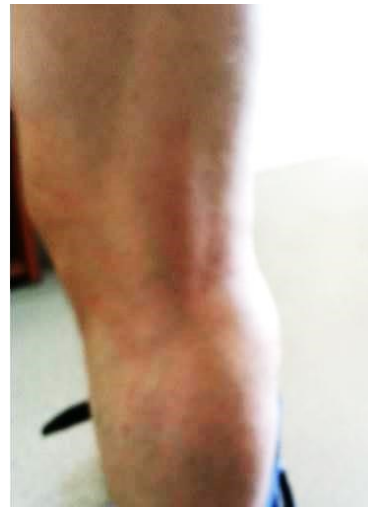


Picture 1: HME patient had operations on his left arm



Picture 2: Swelling located at left leg resulted from osteochondromas

HME is genetically heterogeneous, and three loci have been identified so far: EXT1, on chromosome 8q23–q24; EXT2, on 11p11–p12; and EXT3, on the short arm of chromosome 19 [8, 9, 10, 11]. Loss of heterozygosity at the EXT1, EXT2 and EXT3 loci has been observed among patients with EXT-related and unrelated chondrosarcomas, suggesting that EXT genes are tumour suppressors in chondrosarcomas [12, 13, 14].

Trace elements are cofactors in enzymatic reactions. Deficiency of trace elements (such as zinc or selenium) and excessive of potentially harmful trace elements (such as lead or arsenic) are both known to have adverse consequences in general population [15, 16, 17]. Despite the excess number of studies, we have not encountered studies with HME and trace elements. In present study, we aim to evaluate the association of some trace elements in the patient with HME disease who admitted to Orthopedics Out-patient Clinic at Cerrahpasa Medical Faculty.

## Material and Methods

A 26-year-old male patient (weight 60 kg, height 170 cm) who admitted to Orthopaedics Out-patient Clinic at Cerrahpasa Medical Faculty had been suffering from bone pain and prominences in different parts of his body for 20 years in July 2013. Other individuals diagnosed with HME were reported in his family history.

The diagnosis of HME in postoperative pathology report revealed that our patient had been operated on his left arm, elbow and wrist. Difficulties in movement were found out because of these deformities [Picture 1]. In addition, a swelling on right leg was visible [Picture 2]. Left proximal humerus and meta-diaphysis of left tibia were hypertrophic in radiological examination with new bone formations.

The concentrations of calcium, phosphor, chrome, iron, copper, magnesium, manganese, selenium, zinc, boron, silicon, nickel, arsenic and cobalt elements in serum were analysed by Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES - Thermo - iCAP 6000) in Trace Element Laboratory at Biophysics Department.

## Results

When the serum values of Ca (134.5 ppm), P (173.3 ppm), Fe (1.104 ppm), Se (1.119 ppm) and as (0.647 ppm) levels in patient were compared with reference ranges, all these elements showed higher values. However, Zn (0.562 ppm) levels had a lower value than reference ranges. Residual trace elements that were determined in patient were found in physiological ranges. Ni level was too low to be measured [Table 1]

**Table 1.** Trace element levels of patient with HME

| Concentrations (ppm) | Results (ppm) | References (ppm) |
|---|---|---|
| **Ca** | 134.5 (↑) | 85 - 115 |
| **P** | 173.3 (↑) | 25 - 45 |
| **Cr** | 0.011 | 0.05 - 0.5 |
| **Fe** | 1.104 (↑) | 0.9 - 1.2 |
| **Cu** | 1.046 | 1 - 2 |
| **Mg** | 27.90 | 17 - 30 |
| **Mn** | 0.022 | 1.9 - 5.8 |
| **Se** | 1.119 (↑) | 0.0005 - 0.0015 |
| **Zn** | 0.562 (↓) | 0.7 - 1.2 |
| **B** | 0.05 | 0.033 - 0.191 |
| **Si** | 0.670 | 0.4 - 10 |
| **Ni** | (-) | $0.05\ 10^{-3}$ - $1.1\ 10^{-3}$ |
| **As** | 0.647 (↑) | 0.001 - 0.004 |

**(↑):** higher than reference values, **(↓):** lower than reference values, **(-):** too low to be detectable

## Discussion

HME is a genetically heterogeneous disease located at the locus for the genes of $EXT_1$ and $EXT_2$. Pannier S et al. reported that EXT1 and EXT2 may have tumour suppressing activity. Some studies have concluded that mutations in either the EXT1 or the EXT2 genes are responsible for most cases of multiple exostoses. However in Caucasian and Japanese patients, mutations were detected in EXT1 genes more than in EXT2 genes. Premature terminations of the EXT proteins were caused by most of the mutations in the two genes [12, 18].

After performing sequencing analysis in some families, it was not possible to detect the disease-causing mutation. The presence of a third gene (EXT3 gene) that is a minor disease locus for HME could be a possibility [14, 19, 20]. Symptomatic lesions are because of complications, which include fracture, osseous and cosmetic deformities, impingement on adjacent structures (nerves, vessels and tendons), bursa formation and malignant complications such as spinal cord compression resulting from HME. Number of osteochondromas of each patient may change significantly, even within families. The osteochondromas may range from a few lesions to a thousand. The exibility cause of clinical variability could not be still explained, although various mutations are identified in HME [1, 6, 21].

Trace elements have an important role in skeletal and muscular system, nerve transmission, and many biological processes such as kidney metabolism. In this study, we analysed that the serum selenium, calcium, iron, arsenic and phosphorus values in the patient were higher than normal values. Selenium, arsenic and phosphorus and particularly calcium and iron elements, playing a role in bone metabolism, were found to be high in our study. We think that the evaluation of patients with HME should be taken into consideration by means of the level of trace elements that play crucial role on the whole system particularly in bone and kidney metabolism. We suggest that trace element levels have to be considered for diagnosis and treatment of HME patients. In near future, our main goal is to determine familial and environmental trace element level.

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# Element intoxication by marine food

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**Abstract**

**Introduction:** Pollution is deformation of natural condition of earth with physical, chemical and biological factors. Environmental pollution suppresses life balance and has negative effect on living and ecosystem with its effects on the food chain. Toxic metal pollution easily enters to food chain and accumulates in the living body. Marine species are intensely exposed to toxic metals, because of its habitats and feeding habits, and metals accumulate in their body.

**Material and Methods:** A 56 year-old obese male patient attended to Ortakent-Yahsi Family Health Center (Bodrum, Mugla, Turkey) with the symptoms of palpitation, constipation, long-term muscle contraction in January 2014. VEGA test resulted in toxic load accumulation. The pre-treatment and inter-treatment blood/serum levels of a group of trace/toxic elements were measured with Inductively Coupled Plasma Optical Emission Spectrometer (ICP - OES) at Istanbul University Cerrahpasa Medical Faculty, Biophysics Department. Neural therapy and chelation therapy were initiated to the patient by his doctor at Yahsi Family Health Center in February 2014.

**Results:** The pre-treatment values of blood/serum phosphor, selenium, nickel, arsenic and aluminium levels were analyzed higher than reference ranges. The inter-treatment blood/serum levels of selenium, nickel and aluminium decreased by November 2014, however blood/serum levels of phosphor and arsenic were still higher than reference values. The patient is still under medical supervision and treatment by his general-practitioner

**Conclusion:** There is limited data related with the trace/toxic contamination of marine food in humans. The evaluation of trace and toxic elements might have significant value in diagnosis, treatment and follow-up of the individuals in contaminated environment and especially in seafood consumers.

**Key words:** Marine food, trace element, toxicity, VEGA test, chelation therapy.

## Introduction

Environmental pollution deteriorates life balance and has negative effects on living organisms and ecosystems in Turkey, as well as in all over the world. Toxicity resulting from toxic elements and chronic toxicity of trace elements have been the highlight environmental problem in recent years in Turkey. Toxic element pollution originated from various sources infiltrates easily through food chain and accumulates in living organisms. Thus, toxicity of elements acts as the leading factor among other chemical pollutes. Urbanisation, tourism, coastal population, agriculture, maritime traffic and the influence of fisheries augment the risks of coastal and marine degradation in regions of semi-enclosed seas such as the Mediterranean Sea [1].

Marine food especially fish has high protein content and low saturated fatty acids such as omega fatty acids, thus it is an important food resource for human consumption in healthy diet being at the the top of the aquatic food chain [2,3].

Elements can be divided into two groups; trace and toxic elements. Trace elements are dietary elements that are needed in very minute quantities for the proper growth, development, and physiology of the organism. Toxic elements can bioaccumulate in the body and in the food chain. Therefore, a common characteristic of toxic element is the chronic nature of their toxicity. Marine food is intensely exposed with toxic elements by means of their habitat and dietary habit and transmits the toxication to human beings. Although many elements found in marine food are essential for human life in low doses, these elements may have negatoroius effects even with low doses. Thus, elements in marine food may be hazardous for consumers and may be a good indicator for toxic metal contamination in aquatic systems [4]. Fish is gradually exposed to toxic elements and chemicals through water and food resulting in bioaccumulation in different fish organs [5, 6].

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The concentrations of toxic elements in fish alter in various species and different aquatic systems [7]. The toxic elements uptake from polluted water may vary according firstly to the grade of water, food and sediment accumulation; secondly to the ecological needs and metabolism of the system and thirdly to the biological and environmental factors such as size, age, feeding habit, temperature and dissolved oxygen [8, 9]. Toxic elements tend to accumulate in target organs like liver, gonads, kidney and gills in high concentration. Muscle is not an active tissue for bioaccumulation of toxic elements [10]. Gills are the first organ of the fish in contact with the sea water, thus they can readily reflect the concentrations of toxic elements in the ecosystem [11, 12]. Due to the fact that of short distance between blood and sea water, toxic elements may directly pass through the gills [13]. Besides, gills can exchange toxic elements between the fish and the aquatic environment via its osmoregulation and gas exchange metabolism [11]. Moreover, crustacean seafood such as mullets, crabs and etc. can accumulate much higher levels of toxic elements than in the water [9].

Various ways of bioavailability of toxic elements include discrimination against the uptake of the toxic metal, incorporation of toxic elements within their bodies, distribution of toxic elements to tissues and organs and excretion via kidneys and digestive tract. Despite the excretion ability, chronical low-metal exposure may result in impaired functioning and chronic disease [14, 15].

Symptoms of energy imbalance in functional disturbances occur long before any pathological morphology is evident. The first sign of pathology in the body is an electrical charge. VEGA test which is a non-invasive method of electro-dermal screening measures these bio-energetic phenomena by recording the change in skin conductivity after application of a small voltage. VEGA test can be held to investigate the toxic load accumulated in living organism; intestinal flora status; digestive disturbances; food sensitivity and vitamin, mineral and hormonal imbalance [16, 17].

Chelation therapy is a medical procedure that involves the administration of chelating agents to remove toxic elements from the body. It should only be used in people who have a diagnosis of metal intoxication [18]. Neural therapy is a medical approach of diagnosing and treating local pains and disturbances of the autonomic nervous system of the body's electrophysiology [19].

The aim of our study is to evaluate the relationship between trace/toxic element levels in blood and serum specimens and clinical findings of a 56 year-old male patient suffering from palpitation, constipation, long-term muscle contraction within a diet enriched with marine food.

## Material and Methods

A 56 year-old obese male patient was in follow-up of the general-practitioner at Ortakent - Yahsi Family Health Center (Bodrum, Mugla, Turkey) with the diagnoses of hypothyroidism, diabetes mellitus, hyperlipidemia, peripheric venous insufficiency, chronic obstructive pulmonary disease, gasto-oesefageal reflux, chronic sinusitis, backache. He attended to the health center suffering from palpitation, constipation, long-term muscle contraction within a diet enriched with marine food in January 2014. His biochemical evaluation was analyzed between physiological ranges. VEGA test resulted in toxic load accumulation. The pre-treatment and inter-treatment blood/serum levels of calcium, phosphor, chromium, iron, copper, magnesium, manganese, selenium, zinc, bor, silicium, nickel, arsenic, lead, cadmium, cobalt, aluminium were measured with Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES) to evaluate the treatment efficacy at Istanbul University Cerrahpasa Medical Faculty Biophysics Department. Neural therapy and chelation therapy were initiated to the patient by his doctor with the aim of regulation the toxic element excretion in February 2014. The patient is still under medical supervision and treatment by his general-practitioner.

## Results

The pre-treatment values of blood/serum phosphor, selenium, nickel, arsenic and aluminium levels were analyzed higher than reference ranges. The inter-treatment blood/serum levels of selenium, nickel and aluminium decreased by November 2014, however blood/serum levels of phosphor and arsenic were still higher than reference values (Fig 1, Fig 2). Pre- and inter-treatment blood/serum values of manganese were lower than reference ranges (Fig 3). Inter-treatment blood/serum lead level was analyzed higher than pre-treatment level by November 2014 (Fig 4). Pre-treatment and inter-treatment blood/serum values of calcium, chromium, iron, copper, magnesium, zinc, bor, silicium, cadmium and cobalt were analyzed between reference ranges (Fig 5) (Table1).

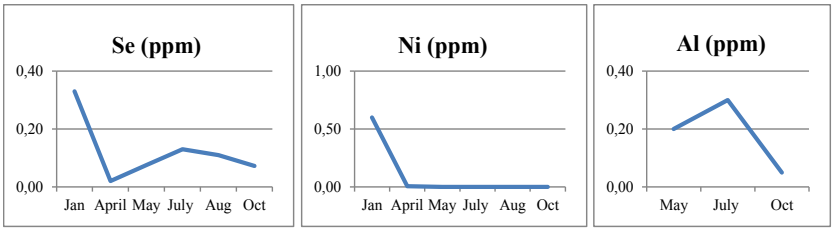


**Figure 1:** Blood/serum levels of pre-treatment elements levels higher than reference value, tending to decrease during inter-treatment.

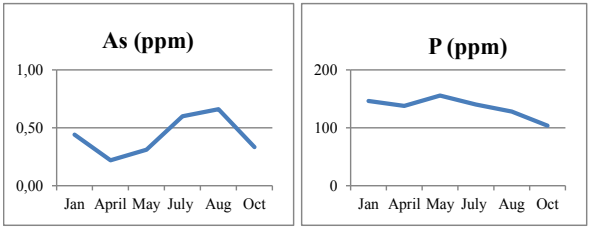


**Figure 2:** Blood/serum levels of pre-treatment and inter-treatment elements levels higher than reference values.

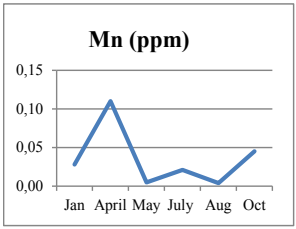


**Figure 3:** Blood/serum levels of pre-treatment and inter-treatment elements levels lower than reference values.

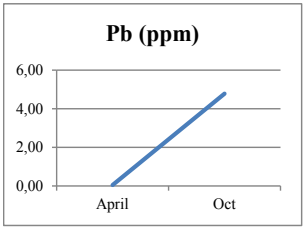


**Figure 4:** Blood/serum level of pre-treatment and inter-treatment element tending to increase.

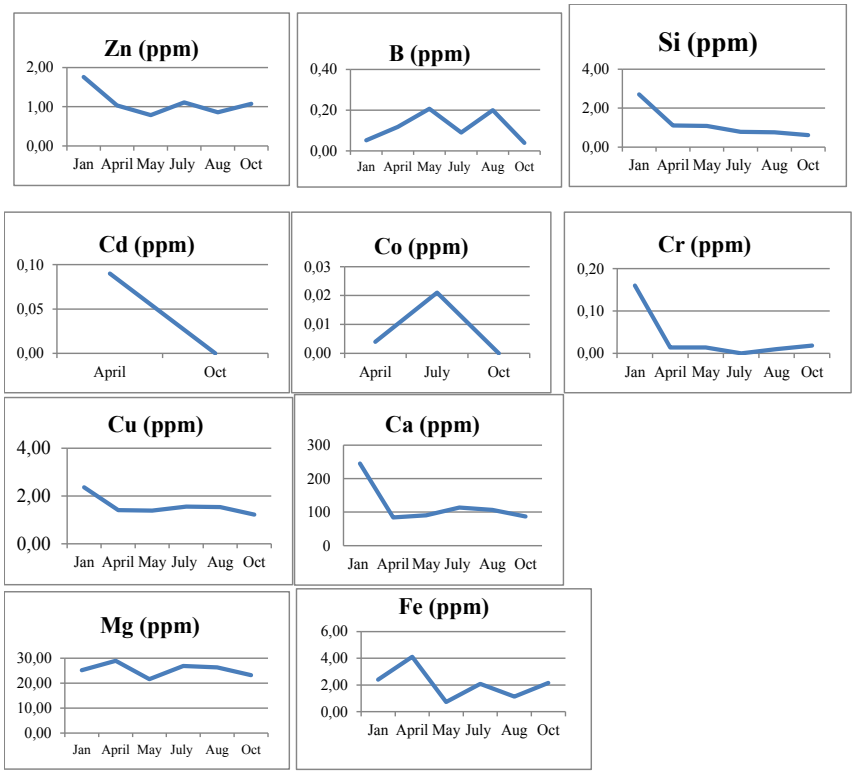


**Figure 5:** Blood/serum levels of pre-treatment and inter-treatment elements levels between reference values.

**Table 1.** Blood/serum values of the trace and toxic elements. ((-): Not measured.)

| Element | January (ppm) | April (ppm) | May (ppm) | July (ppm) | August (ppm) | October (ppm) | Reference Range (ppm) |
|---|---|---|---|---|---|---|---|
| **Ca** | 245.2 | 84.1 | 90.8 | 114 | 107 | 87.3 | 85 - 115 |
| **P** | 146.2 | 137.9 | 155.7 | 140.2 | 127.9 | 103.4 | 25 - 45 |
| **Cr** | 0.160 | 0.014 | 0.014 | 0 | 0.010 | 0.018 | 0.05 – 0.5 |
| **Fe** | 2.40 | 4.11 | 0.72 | 2.08 | 1.12 | 2.15 | 0.9 – 1.2 |
| **Cu** | 2.36 | 1.41 | 1.39 | 1.55 | 1.53 | 1.22 | 1.0 – 2.0 |
| **Mg** | 25.20 | 28.91 | 21.62 | 26.89 | 26.28 | 23.18 | 17 - 30 |
| **Mn** | 0.028 | 0.110 | 0.005 | 0.021 | 0.004 | 0.045 | 1.9 – 5.8 |
| **Se** | 0.33 | 0.02 | 0.08 | 0.13 | 0.11 | 0.07 | 0.0005 – 0.0015 |
| **Zn** | 1.76 | 1.03 | 0.79 | 1.11 | 0.86 | 1.07 | 0.7 – 1.2 |
| **B** | 0.052 | 0.118 | 0.207 | 0.090 | 0.200 | 0.039 | 0.033 – 0.191 |
| **Si** | 2.70 | 1.11 | 1.08 | 0.78 | 0.76 | 0.61 | 0.4 - 10 |
| **Ni** | 0.600 | 0.006 | 0 | 0 | 0 | 0 | 0.00005 – 0.0011 |
| **As** | 0.44 | 0.22 | 0.31 | 0.60 | 0.66 | 0.33 | 0.001 – 0.004 |
| **Pb** | (-) | 0.055 | (-) | (-) | (-) | 4.780 | 0 – 0.04 |
| **Cd** | (-) | 0.09 | (-) | (-) | (-) | 0 | 0 – 0.01 |
| **Co** | (-) | 0.004 | (-) | (-) | 0.021 | 0 | 0 - 900 |
| **Al** | (-) | (-) | 0.20 | (-) | 0.30 | 0.05 | 0.001 – 0.002 |

## Discussion

The excess consumption of marine food in which toxic elements highly accumulate is estimated to cause varied metabolic disorders. Trace/toxic elements can be hazardous for organisms even with low doses. Our patient had consumed excess amount of marine food including various fish, crustacean seafood such as mullets crabs and etc. resulting in various symptoms. The analysis of pre- and inter-treatment serum values of trace/toxic elements revealed different results including rises, reductions or steadiness. Neural therapy and chelation therapy were initiated to the patient. Trace/toxic elements are excreted from the body via urine, faeces, sweating, and exhalation in chelation therapy. The blood/serum fluctuations within reference ranges and increase of trace / toxic elements in chelation therapy might be due to the fact that elements are mobilized from tissues to blood circulation [20, 21].

In addition to chelation and neural therapy, the patient was advised to have a diet excluding refined wheat products and refined sugar and including well-balanced consumption of food with the possibility of sensitivity. Physical exercise was suggested accompanied with water consumption. The complaints and signs of our patient have ameliorated with ongoing treatment.

In conclusion, correlation between the complaints of the patient treated with chelation therapy and neural therapy and the decrease in the serum trace element levels revealed that treatment might ameliorate toxic element accumulation.

The contamination of the biological environment is a crucial issue related with the health of both aquatic animals and seafood consumers. Despite the inevitable industrialization, the main target of all human beings has to be the preservation of fresh and sanitated food for good health. The assessment of trace and toxic elements might have significant value in diagnosis, treatment and follow-up of the individuals in contaminated environment and especially in seafood consumers.

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# Forensic psychiatric evaluation of sexual crime cases

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**Abstract**

**Objective:** Sexual crimes are one of the most offensive crimes committed against individuals. Given that individuals from every age and both genders are affected from this action. In the USA, 20% of women and 5–10% of men exposes to sexual violence. It appears as a serious problem that threatens society and preventive measures have to be taken against it. It is an undeniable fact that; mental health seriously affected by sexual assaulted or abuse. In this study, we aimed to evaluate forensic psychiatric examination reports of the cases that are sending to examine whether or not any permanent psychiatric impairment after sexual assault or abuse.

**Methods:** Findings from examination of cases which are sent to Department of Forensic Medicine, Medical Faculty of Celal Bayar University between October 2012 and February 2014 for determining permanent psychiatric impairment were evaluated.

**Results:** Number of examined cases was 55 and number of diagnosed cases was 33. The age range of cases were from 7 to 77 years (SD=20.39±13.17). Of the cases; 57.6% (n=19) were younger than 18, 87.9% (n=29) were women, 63.7% (n=21) were simple sexual assaulted or abused, in the 72.8% offender was known by cases, in the 30.3% (n=10) crime happened at the home of offender or case. As a result of forensic psychiatric evaluation, in the %30.3 of cases (n=10) were detected permanent psychiatric impairment.

**Conclusion:** Examination of cases has to be performed scrupulously because, permanent psychiatric impairment by sexual crimes, not only negatively affect case his/her social environment but also it is a country's laws punishment-enhancing factor.

**Key words:** Sexual assault, sexual abuse, mental health, forensic psychiatry

## Introduction

Sexual crimes are one of the most offensive crimes committed against individuals. Given that individuals from every age and both genders are affected from this action. It is the most rapidly increasing kind of crime among violent crimes (1, 2). In a study, it was reported that 32,3% of women and 14,2% of men are exposed to sexual assault and in this study, under 18 year of age 39,9% of women and 32% of men are exposed to sexual assault (3).

It has been reported that in the majority of sexual assault cases, physical finding were not present, and hence psychological examination is of importance both for diagnosis and at the rehabilitation stage of the cases (4). Following sexual assaults, many psychiatric disorders including post-traumatic stress disorder (PTSD) and depression may occur (5). The prevalence of PTSD was found to be between 8–16% in general population studies (5).

It was determined that the highest risk of PTSD was seen after completed rape with a rate of 57.1% (6). It was stated that events such as rape and torture led to a higher risk of psychological disorder than natural disasters or traffic accidents (7). However, in some people who experienced the worst events, psychological disorder may not develop (8). In addition, only in some people who have psychological problems immediately after trauma, the problem becomes chronic (8). Factors such as the specific characteristics of each event, its influence on the case, its interpretation by the case, how the event is perceived, support given to the case by people close after the event are extremely effective in the development of the disorder (5).

Turkish Penal Law No. 5237, which came into effect in June 1, 2005 Article 102/5 on sexual crimes in adults, and article 103 on those in children state that if psychological health is impaired due to sexual assault, punishment will be more severe because of each sexual crime will

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create a psychological trauma for the case. However, the concept of 'the impairment of psychological health' necessitating the increase in punishment was not mentioned in detail in the law (8). In June 18, 2014 The Law changed because of the problems. Every sexual crime (assault or abuse) cases have accepted as psychiatric impairment so punishment has made of highest level. But our research is related to the previous event to the new law, cases have been subjected to psychiatric evaluation.

In this study, we aimed to evaluate forensic psychiatric examination reports of the cases that are send to examine whether or not any permanent psychiatric impairment after sexual assault or abuse

## Material and methods

This investigation is a retrospective analysis of forensic-psychiatric examinations in sexual crime cases. The examinations were performed at the Department of Forensic Medicine, Medical Faculty of Celal Bayar University between October 2012 and February 2014. Findings from examination of cases who were sent to determining permanent psychiatric impairment. Cases were investigated according to age, gender, crime type and psychiatric evaluation. Age groups are divided to two subgroups (under 18 years, upper 18 years) because of age of legal consent to sexual relationship is upper 18 years in Turkey.

SPSS (IBM SPSS Statistics Version 20 Software) program was used for data analysis. Distribution percentile, frequencies, means and standard deviations were used for statistical analysis

## Results

Numbers of examined cases were 55 and numbers of diagnosed cases were 33. The minimum age was 7 years whereas the maximum age was 77 years (mean 20.39±13.17). Of the cases; 57.6% (n=19) were younger than 18 years. Relationship between age and gender are shown in Fig.1. It was established that 12.1% of the cases were male (n=4) and 87.9% (n=29) were female and all accused were male. In 63.7% cases (n=21) were simple sexual assaulted or abused in 36.3% cases (n=12) were qualified sexual assault or abuse (Fig.2). Offender was familiar by cases in case of 72.7% (Fig.3). In the cases, 30.3% (n=10) crime happened at the home of offender or cases (Fig.4). As a result of forensic psychiatric evaluation, in the 39.4% of cases (n=13) were detected permanent psychiatric impairment (Fig.5)

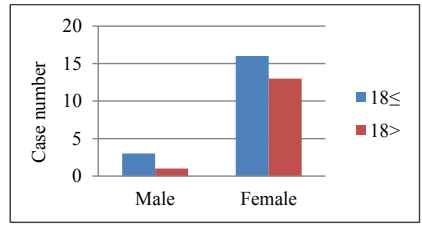


**Figure 1:** Case number, gender and age groups

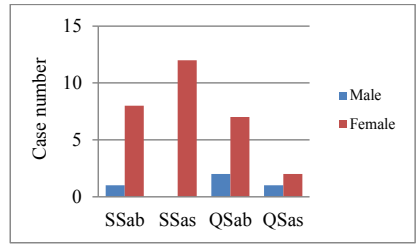


**Figure 2.** Grade of crime. SSab: Simple Sexual abuse, SSas: Simple Sexual assault, QSab: Qualified Sexual Abuse, QSas: Qualified Sexual assault

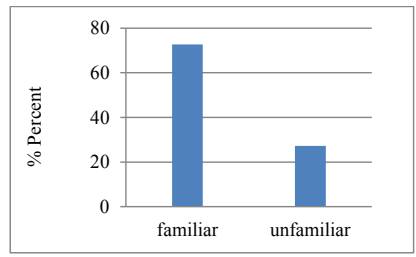


**Figure 3:** Relationship of the offenders and victims

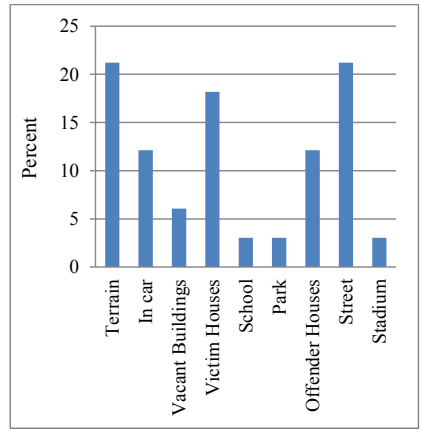


**Figure 4:** Scene of crime

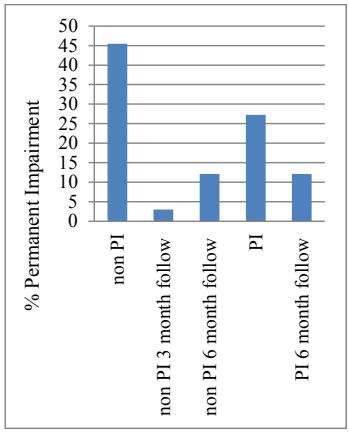


**Figure 5:** Psychiatric examination results of Permanent Impairment (PI: Permanent Impairment)

## Discussion

In the USA, 20% of women and 5–10% of men experience sexual violence (9). The 2009/2010 British Crime Survey reported that one in five females and one in fifty males had experienced some form of sexual assault (including attempts) at least once since the age of 16 (10). In the year prior to the survey, 2% of women and <1% of men had experienced an incident of sexual assault (11). The 2010 UNICEF child abuse and family violance research reported that 3% of children aged 7-18 years are exposed to sexual abuse in Turkey (12). According to Turkey Statistical Institute data, nearly 100,000 women has been the victims of sexual assault in the period of 2005-2010 (13).

In covenant with other studies (9,14,15), the majority of the sexual crime cases were female (87.9%) in this study. However, it should be kept in mind that male cases report a sexual crime less often (15). The majority of the cases resided of children and adolescents (57.6% were younger than 18), like Grossin et al (14).

Consistent with the current literature, the suspect was someone known by the case in the majority of cases (72.8%) (14,15). The high percentage of suspects, which are known by the cases, can explain the high rate of repeated abuse, because it is more likely to be a repeated case, if the alleged perpetrator lives in the same household or is frequently in the case`s home (15). Saint-Martin et al. (4) also documented that the majority of rape incidents occurred in the case's or offender's home, which can be explained by the fact that the offender is often someone known to the case. In this study in 30.3% cases crime happened at the home of offender or case and in 72.7%, offender was known by cases.

In a study of Janish et al. only 26.8% diagnostic findings were observed in the anal-genital region (15). Considering the low rate of genital injuries, it should be taken into account that penetration presents only certain group of sexual crime (15). Difficulties in finding biological evidence, and lack of penetration is some events like fondling, kisses and or any other forms or cases not being virgins at the time of the event, evaluation of psychological health may sometimes be only or the most important evidence both for diagnosis and at the rehabilitation stage of the cases (4,16). In our study, 63.7% cases were simple sexual assaulted or abused like touching, kisses or any other form without vaginal, oral or anal penetration (penile/digital/instrumental). In this study, the psychological finding looks more important than physical findings.

Many psychiatric disorders including PTSD, anxiety and depression may occur at sexual crimes (5, 17, 18). In the 179/3 article of German Penal law, it is stated that in case there is a serious threat to the health of the case due to sexual assault, or it causes physical or emotional disturbance, a prison sentence varying between 6 months and 10 years will be the punishment (16). Similarly, in Finnish Penal Law, in the 20/2 article, it is stated that in cases when assault causes severe physical and psychological disturbance, a prison sentence of at least 2 to at most 10 years will be the punishment (16). In Turkish Penal Law 102/5 whether case physical or psychological health of the adult case is impaired after sexual assault, a prison sentence not less than 10 years and if the case is a child, a prison sentence not less than 15 years (Turkish Penal Law 103/6) will be given as punishment (19).

Our cases which were sent to examine whether or not any permanent psychiatric impairment after sexual assault or abuse were evaluated and consulted with psychiatry, child psychiatry and forensic medicine specialists. In this study as a result of forensic psychiatric evaluation, in %30.3 of cases were detected permanent psychiatric impairment (depression, anxiety or PTSD).

Examination of cases has to be performed scrupulously because, permanent psychiatric impairment by sexual crimes, not only negatively affect case his/her social environment but also it is a country's laws punishment-enhancing factor.

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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# Esthetic rehabilitation of congenitally missing laterals and deciduous canines with direct restorative approach: A case report

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**Abstract**

Congenitally missing lateral incisors and persistent deciduous canines severely compromise esthetic appearance due to their strategic positions in the smile. Several treatment procedures have been proposed to rehabilitate this esthetic deficiency. With the recent improvements in adhesive dentistry and dental resin composites, the material is successfully used to restore anterior teeth in which the esthetic is primarily important. This case report illustrates the dental esthetic rehabilitation of an adolescent patient with diastemata resulted from hypodontia of upper lateral incisors and persistent upper decidious canines via direct composite veneers. In 12-month clinical follow-up, all restorations were preserving their integrity and no notable discoloration was observed.

This article presents that direct composite veneers are the most conservative, low cost, achievable in one-session treatment option for the rehabilitation of dental esthetics disfigured by both diastemata depending on hypodontia of lateral incisors and persistent decidious canines.

**Keywords**: composite dental resin, dental esthetics

## Introduction

Hypodontia is a term used for defining the developmental absence of one or more teeth except third molars in both dentitions [1]. The population studies have revealed that mandibular second premolars and maxillary lateral incisors are the most frequent congenitally absent teeth [2-6]. However, missing maxillary lateral incisors compromise dental esthetics due to their strategic position in the smile [7].Orthodontic movement of canine to its correct position followed by restoring lateral incisor either with a single-tooth implant supported restoration or a fixed crown-bridge restoration is one of the treatment options to overcome this esthetic problem. But the mentioned interdisciplinary approach is invasive, high cost and requires long treatment period. The ideal treatment should be conservative together with corresponding patient's esthetic and functional requirements [8]. Conservative veneer technique is described as the application of resin composite onto the tooth without doing any preparation on tooth surface [9]. Enlargement of maxillary central incisors to close diastemata and reconstruction of maxillary canines in the shape of lateral incisors with direct composite veneers is the most conservative and cheapest treatment option.

This case report represents a direct restorative treatment approach to rehabilitate dental esthetics that was disfigured by diastemata associated with missing maxillary lateral incisors and persistent canines.

## Case

A 16-year-old female patient who was complaining of diastemata in both maxillary and mandibular anterior teeth, was referred to the Department of Operative and Restorative Dentistry in Istanbul University to have her dental esthetics rehabilitated.

Prior to clinical oral examination, dental and medical histories of the patient had been obtained. In clinical oral examination, we observed immoderate diastemata between maxillary anterior teeth depending on both missing lateral incisors and narrow sizes of the persistent canines in the position of first premolars. Nevertheless, moderate diastema was observed between mandibular anterior teeth. We predicted that the diastemata between mandibular anterior teeth were resulted from discrepancies between tooth-size and dental arch space in consideration of no tooth was missing [Figure 1].

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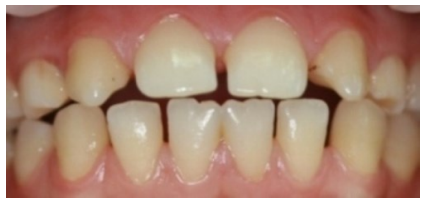

Figure 1: Intra-oral view of anterior diastemata before treatment

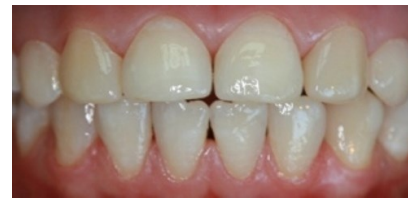

Figure 3: Intra-oral view of anterior diastemata after treatment

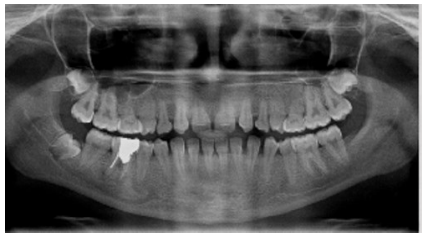

Figure 2: Panoramic radiography. Note that neither maxillary lateral incisors nor maxillary canines are impacted

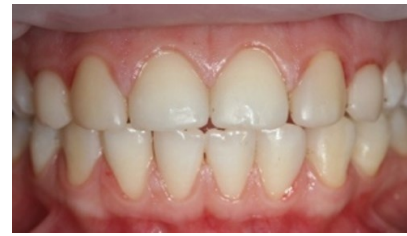

Figure 4: Intra-oral view of the restorations in 12-month follow-up

We confirmed with panoramic radiographs that maxillary lateral incisors and maxillary first premolars were congenitally missing [Figure 2]. The patient was informed about the possible treatment strategies and both advantages and disadvantages of each. We decided to rehabilitate her dental appearance with direct composite restorations considering the periodontal health status, oral hygiene habits, age and economic situation of the patient. Before pre-treatment on enamel surfaces, shade selection of the composite we would use was performed under daylight utilizing the manufacturer's shade scale. In order to confirm if the shade selected matched with the shade of tooth after polymerization of the composite, we put a small amount of composite onto enamel without any pre-treatment and light-cured. We determined that A2 was the most appropriate shade.

We didn't make any preparation on the enamel surfaces except acid etching. Since it's necessary to etch the enamel for providing higher bonding strength for the composite resin, a total-etch bonding system was used. Isolation was achieved with OptraGate (IvoclarVivadent, Schaan, Liechtenstein) instead of rubber dam in order to build the gingival margins of the restorations better. All the enamel surfaces to be restored were etched with 35 % phosphoric acid gel (Scotchbond Etchant; 3M ESPE, St. Paul, MN, USA) for 30 seconds prior to the application of the bonding agent. The etched surfaces were rinsed to send etchant gel completely away, and then the teeth were air-dried.

One-bottle bonding agent (Adper Single Bond 2 Adhesive; 3M ESPE, St. Paul, MN, USA) was applied to all etched surfaces with a brush, air blow-dried with air spray and polymerized with a LED curing unit (LEDemetron I; Kerr Manufacturing Inc., Orange, CA, USA) for 10 seconds. The restorations were performed using a light-cure nanofill composite resin (Clearfil Majesty Esthetic; Kuraray, Osaka, Japan) with incremental technique. Composite was placed on both mesial and distal surfaces of maxillary centrals to close diastemata, while only the mesial of maxillary canines were restored in the form of lateral incisors. Considering crown-root proportion of the persistent deciduous canines together with oral and radiographic examinations, the cuspal 1/3 of them were built up with direct composite resins in the form of first premolar. Because there was no missing tooth in the mandibular arch, the diastemata were treated placing the composite on mesial and distal surfaces of laterals and canines. Celluloid bands were used to form both mesial and distal contours of the restorations and to avoid adhering of the neighbouring restorations as well. A2 shade was used primarily to restore the teeth, however, in order to mask darkness of oral space OA2 was placed onto the A2 lingual layer excluding the incisal margins. Labial surfaces of the restorations were finished with placing another layer of A2. Each composite layer was polymerized with the LED curing unit (LEDemetron I; Kerr Manufacturing Inc., Orange, CA, USA) for 20 seconds. After polymerization process, the celluloid bands were moved away and the occlusion was

checked. Premature contacts during lateral and protrusive movements of the mandibular were eliminated with yellow-banded, egg-shaped diamond abrasive (#16). The restorations were contoured and polished with aluminium oxide finishing-polishing discs (Sof-Lex; 3M ESPE, St. Paul, MN, USA) which were used from the coarsest to the finest, respectively. In order to contour gingival margins of the restorations ideally as well as sending residuary of the restorative materials away and removing the oxygen inhibition layer on the composite resin, sandpaper strips were used in contact areas of the restorations [Figure 3]. To prolong the durability of restorations as clinically acceptable, the patient was informed about the importance of oral hygiene and how to protect the restorations from trauma. In 12-month clinical follow-up, no fracture or notable discoloration of the restorations was observed [Figure 4]. Conversely, the patient's oral hygiene deteriorated with build-up of bacterial plaque and associated marginal inflammation. Despite the fact that we had hardly advised her against performing daily oral hygiene procedures, she mentioned that she neglected brushing her teeth in last few weeks because of her changing working hours.

## Discussion

Tooth agenesis is one of the most common congenital anomalies occurring in the permanent dentition [10]. If the number of congenitally missing teeth is six or less excluding third molars, the situation is termed hypodontia [10]. whereas the situation that more than six teeth are congenitally missing is termed oligodontia [10-11]. In this case, maxillary lateral incisors and first premolars are congenitally absent, however decidious canines are existing in the positions of permanent first premolars.

Either congenitally missing teeth or discrepancies between tooth-size and dental arch space or both can cause diastemata that disfigure dental appearance of the patient [12]. In cases with diastemata due to congenitally missing teeth, the interdisciplinary approaches including prosthetic and orthodontic treatments can be the best choice for long-term durability of the restorations as well as for the satisfaction of the patient [13-14]. Following the extraction of persistent decidious canines, permanent canines can be moved distally into the correct positions in dental arch with orthodontic treatment while missing lateral incisors and first premolars can be restored prosthodontically either with fixed crown-bridges or dental implants. Nevertheless, this treatment option is costly and requires long treatment period. Correspondingly, in patients with insufficient space for prosthodontic treatment or dental implants, anterior diastemata can be rehabilitated either with indirect restorative techniques like full-porcelain crown restorations and porcelain veneers or direct composite veneers. In such cases, the diastemata can be closed directly with direct or indirect restorations without the need of orthodontic treatment. However, all these techniques have both advantages and disadvantages. Since both full-porcelain crown restorations and porcelain veneers require tooth preparation that can damage gingival tissues, they are not appropriate restorative options especially for teenagers. Long duration of treatment, high cost, abrasion of antagonistic teeth and technical sensitivity requirement for intra-oral repairmentare considered as disadvantages [12]. On the other hand, optimum esthetic properties like colour stability, minimal surface roughness associated with high surface abrasion resistance are considered as advantages of these restorative treatment techniques compared to direct composite veneers [15]. In the case of non or minimal tooth preparation limited to enamel tissue, local anesthesia is not needed in direct composite veneers [9-12]. In this case, the diastemata in maxillary anterior teeth were resulted from congenitally missing lateral incisors and persistent decidious canines instead of first premolars while the diastemata in mandibular anterior teeth were as the result of discrepancies between tooth-size and dental arch space. As the patient in this case refused rehabilitation of maxillary anterior esthetics via interdisciplinary approach including orthodontic treatment followed by dental implants because of high cost and long duration of treatment, we used conservative direct composite veneers to eliminate the diastemata both in maxillary and mandibular anterior teeth. The maxillary diastemata could also be treated with fiber-reinforced composite bridges. As this technique requires to make preparations on centrals and canines we preferred the direct composite veneers considering the patient's age and reversible nature of this procedure that allows other treatments in the future.

In cases where estheticapperance of the patient is rehabilitated with direct composite veneers, type of composite and bonding system used affects long-term clinical performances of the restorations as well as satisfaction of the patient [16]. Over the years, several changes have been made in the filler particles of dental composites to enhance the colour stability, surface characteristics and wear resistance [17].One of the recent composites introduced contains nano-sized fillers in the inorganic part of resin. It's reported that nanofill composites can be used to restore high-stress bearing areas due to their excellent mechanical properties as well as in the restorations of anterior teeth due to the excellent optical properties and high initial polish [17-18]. Polishability is of importance not only for esthetics but also for marginal consistency of the restorations and health of the oral soft tissues [18]. As the aesthetics was primarily important in this case, direct composite veneers were performed using a nanofill composite resin. Even though most manufacturers of dental

adhesives offer both a total-etch adhesive and a self-etch adhesive for the direct composite veneers [19], it was reported that the highest mean bond strengths to enamel were obtained with total-etch adhesives [20]. Thus we preferred to use a total-etch bonding system instead of a self-etch one in order to obtain high strength to enamel and to achieve clinical durability of the restorations.

In conclusion, this case report describes esthetic rehabilitation of a teenager, who was complaining about diastemata with direct composite veneer technique. Although such cases could be managed with several treatment options, especially in young patients conservative veneer technique is more advantageous compared to indirect restorative techniques such as fixed crown-bridge restorations and porcelain veneers. However direct composite veneers might not be as durable as porcelain veneers. Last but not least, if composite restoration procedures are strictly followed and the patient performs oral hygiene procedures properly, satisfying long-term clinical results can be achieved.

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**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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# Kikuchi-fujimoto disease: histopathological and clinical review of a case

Belma Pehlivan[1], Muammer Karagoz[2], Şeyda Belli[1], Fatma Tokat[3], Yesim Saglican[3]

**Abstract**

Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is an idiopathic, benign, self-limited, rare disease. This disease is mostly encountered in Asia and in young adult. Cervical lymph node involvement is the most common symptom. In addition, fever, fatigue, increase in erythrocyte sedimentation rate, and leukocytopenia may also occur. A specific diagnosis and treatment for this disease has not been defined. The diagnosis of this disease however can be diagnosed with excision of lymph node and histopathological examination. KFD can often resolve spontaneously. If there is no spontaneous regression, oral corticosteroid therapy can be applied. In this case report, we were referred a rare case of Kikuchi-Fujimoto disease, presented with the cervical lymphadenopathy, increased erythrocyte sedimentation rate, and fever.

**Keywords:** Kikuchi-Fujimoto disease (KFD), histiocytic necrotizing lymphadenitis, cervical lymph node

## Introduction

Kikuchi-Fujimoto disease (KFH) or histiocytic necrotizing lymphadenitis (HNL) is a rare, benign self-limited disease with unknown etiology [1, 2]. The disease was first described in 1972 by Fujimato and Kikuchi [3]. The disease is most common in late 20s and early 30s among Asian women [3]. It commonly presents with posterior cervical lymphadenopathy, fever and night sweats [2, 4]. It typically has a benign course and 1-6 months after the diagnosis, it usually resolves spontaneously [ 3]. Microscopically, lymph node demonstrates par cortical coagulation necrosis, focal histiocytic proliferation, and karryorrhexis. There is currently no specific treatment for the disease [2].

In this report, we discussed a 21 year old woman with Kikuchi-Fujimoto disease (KFD) who had had painful cervical lymphadenopathy and fever for 3 months, and resolved under treatment with prednisolone

## Case

A twenty-one year old female patient applied to our outpatient clinic with painful neck mass and fever, which had first appeared 3 months earlier. She was a non-smoker with no past-medical history of chronic diseases (e.g. diabetes, hypertension, etc.). She had multiple painful conglomerate palpable masses on her neck at levels of C2, C3, C4 and C5, of which the largest one had a diameter of 1.5 cm. At the same time, patient had a low grade fever. A prior fine needle aspiration biopsy performed in an outside facility was non-diagnostic. The patient had no symptoms regarding respiratory system. She had no other complaints including fatigue, night sweats, skin rash, significant weight loss, and decrease in appetite. Past-medical and family histories were insignificant for tuberculosis or anti-tuberculosis medication use. The mass had been recently noticed by the patient.

Her pulse was 98 beats/minute, respiratory rate was 20 breaths/minute, axillary temperature was 37.8 °C, and arterial blood pressure was 110/65 mmHg. Neck examination showed multiple masses on the left side at zones 2, 3, 4, and 5, which were painful, mobile, ovoid, rubbery, conglomerate masses with 2.5 cm in greatest dimension. She also had left supraclavicular lymphedema. Swelling was not fixed to the skin or subcutaneous tissues and the mass did not have fluctuation, fistulization or change in color of overlying skin. Patient had normal nasopharynx, oropharynx and larynx with no signs of pathologies. Respiratory system and other systems were normal on examination. The patient was not icteric and had no hepatosplenomegaly.

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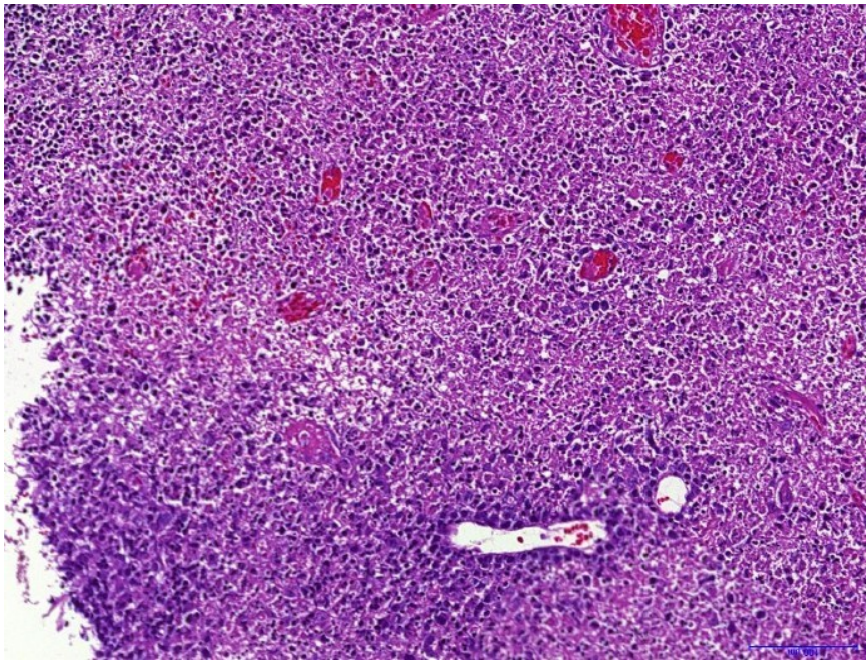

**Picture 1:** Necrosis, abundant karyorrhectic debris, distributed fibrin deposits and mononuclear cells

The patient had normal complete blood count and blood chemistry. Erythrocyte sedimentation rate was 49 mm/hour. Mantoux test was negative (induration was 5 cm/72 hours). The levels of anti-HIV, anti-Ebstein Barr virus (EBV), anti-cytomegalovirus (CMV), anti-Toxoplasma gondii and anti-Bartonella henselae titers were all negative. The levels of C-reactive protein (CRP), antinuclear antibodies (ANA), and angiotensin converting enzyme (ACE) were normal.

Cervical ultrasonography (USG) revealed conglomerate lymphadenopathies at levels 2 and 5 on the left side of the neck, of which the largest was at level 4 with 15x9 mm in dimensions. Echogenic hilus were not clearly visualized and they were suspicious for malignancy. Bilateral parotid, submandibular and thyroid glands had normal echogenicity. Abdominal USG and chest X-ray were normal. Fine needle aspiration biopsy performed in an outer facility was consistent with reactive lymphoid hyperplasia. She received cefuroxime for 10 days at a dose of 500 mg bid and did not resolve. Excisional lymph node biopsy was planned with a preliminary diagnosis of lymphoma.

Histopathological evaluation showed apoptotic cells at sites of necrosis, together with semilunar histiocytes which had phagocytosed nuclear debris. Neutrophils were absent at sites of necrosis and other sites had immunoblastic transformed cells and focal monocytoid B cell hyperplasia, lymphocytes, and rare histiocytic cells constituting inflammatory infiltration (Figure 1). Immunohistochemical staining showed increased proliferation (45-50%) with ki-67, positivity with CD3 and CD8, positive reaction with CD68 in histiocytic cells, and partial CD4 and CD20 reactivity in lymphocytic cells. ALK-1 and CD30 were negative. Pathological diagnosis was necrotizing histiocytic lymphadenitis (Kikuchi-Fujimoto disease) (KFD).

Prednisolone was started at a dose of 25 mg/day and gradually tapered after 2 weeks of therapy. The patient was afebrile at day 2 and free of relapse at 6 months follow-up at outpatient clinic.

## Discussion

KFD is a rare disease which is relatively more common in Asia and its etiology is unclear. Most of the current reports demonstrated a female/male ratio of 1/4 while some of the current data showed equal ratios [4]. The disease is characterized by cervical lymph node involvement (i.e. especially in the posterior triangle) in young adults at second and third decades [2, 3].

There are several theories to explain its etiology which includes viral infections and autoimmune phenomenon [5]. In addition to cervical lymphadenopathy, patients might have

fever, myalgia, leukopenia, and elevated erythrocyte sedimentation rate (ESR]. Some of the reports in current literature discuss liver, spleen, kidney and skin involvement [5, 6]. However, our patient did not have any additional signs or symptoms other than cervical lymph node involvement, mildly elevated ESR and subfebrile fever. The duration of symptoms were longer than 2 months and the recurrence rate was 2-3% [5]. The duration of symptoms was 3 months in our patient as well. Some patients might have panuveitis, arthritis, aseptic meningitis, amygdalitis, or atypical symptoms with pneumonia and renal failure caused by opportunistic infections [5, 7]. Current literature reported a rare association between KFD and heart failure-related death, need for transplantation, febrile syndrome, and hemophagocytic syndrome [4, 5, 7].

The diagnosis of KFD can only be made with lymph node biopsy and histopathological analysis [4, 5]. Histopathological findings of this disease include paracortical coagulative necrosis with abundant karyorrhectic debris which distorts normal architecture of the lymph node. Abundant histiocytic and plasmacytoid monocytic infiltration and relative absence of neutrophils are common at sites of necrosis. The predominant lymphocyte type at lymph nodes is T cells and they stain positively with CD8 [2]. These results are consistent with histopathological and immunohistochemical findings of our patient.

Findings on computerized tomography and USG are similar to lymphoma [4, 5]. There are no specific radiological imaging findings in KFD [5]. Our preliminary diagnosis after ultrasonography was lymphoma and we confirmed the diagnosis only after histopathological analysis.

Differential diagnosis of this disease includes infectious agents including EBV, CMV, tuberculosis, Herpes Simplex virus (HSV), and HIV; and systemic lupus (SLE) [4, 7].

KFD has an excellent prognosis with minimal risk of death and it has a benign course. Early diagnosis of this disease is important to distinguish it from lymphoma and other diseases in order to avoid expensive and excessive diagnostic tests. Pathologists and clinicians should have a high index of suspicion to avoid wrong diagnosis. We aimed to increase awareness on this rare disease by presenting this case.

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# Acute infantile hemorrhagic edema mimicking henoch-schonlein purpura

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**Abstract**
Acute infantile hemorrhagic edema is an acute cutaneous leucocytoclastic vasculitis that can be seen in infancy and characterized by fever, palpable purpura, and edema. Although it presents with severe symptoms, the clinical course is benign and the disease resolves in a short time. In this report, we present a 17-month-old infant who was admitted with cutaneous purpuric rash and edema of the extremities and subsequently diagnosed as acute infantile hemorrhagic edema.

**Key words:** Edema, Infant, Vasculitis

## Introduction

Acute infantile haemorrhagic edema (AIHE) is characterized by rosette-shaped purpuric lesions ranging from 1 to 5 cm in diameter, predominantly on the cheeks, ears, and extremities [1, 2]. Although the ethology remains unknown, AIHE constitutes 12% of leukocytoclastic vasculitis (LCV) cases and is mostly seen during 4 months to 2 years of age, with no gender difference, and generally follows an upper respiratory tract infection [3].There is no specific treatment for AIHE. Steroids and antihistamines have been used without an effect on the clinical course of the disease [4, 5]. Patients with a history of infection should receive treatment. A male patient who underwent steroid treatment and recovered completely has been recently reported [1]. Treatment response to antihistamines has also been reported in the literature [4]. We report a 17-month-old male infant who presented with AIHE accompanied by acute tonsillopharyngitis without systemic involvement

## Case

A 17-month-old male infant with a one-week history of fever and a two-day history of rashes and swellings on the ears was admitted to our clinic with rashes on the ears, hands, and legs.

In the physical examination, the temperature was 37.2 °C, blood pressure was 100/60 mm/Hg, body weight was 11.3 kg (10-25 percentile), and height was 85 cm (10-25 p). Physical examination also revealed widespread ecchymotic lesions with differing diameters over the hands, dorsal aspects of the feet, and both ears. The remainder of the physical examination was normal. Laboratory parameters were as follows: leucocyte count: 11,000/mm$^3$, thrombocyte count: 350,000/mm$^3$, Hb; 9.8gr/dl, erythrocyte sedimentation rate:18 mm/hr, and C-reactive protein : 18 mg/L. The coagulation test results revealed normal. The blood biochemistry, urinalysis, and serum immunoglobulins were in normal limits. The stool samples were negative for parasites and occult blood. The cerebrospinal fluid (CSF) analysis revealed normal. Viral cultures were negative, and there was no growth in blood, urine, throat, and CSF cultures. The diagnosis of LCV was confirmed by the findings of the skin biopsy. Antibiotic therapy was commenced for acute tonsillopharyngeal infection, and systemic and local steroids, and antihistamines for the skin manifestations. Over the following 10 days, the patient recovered completely.

## Discussion

AIHE is considered by some scholars as a cutaneous variant of Henoch-Schönlein purpura (HSP) [1], whereas the others regard it as a distinct entity [6]. Although the etiology of AIHE remains vague, 75% of AIHE patients present with a history of recent upper respiratory or urinary tract infection [6]. The onset of acute infantile hemorrhagic edema is earlier than HSP. Acute infantile hemorrhagic edema is observed mostly at the age of 4 months-2 years while; HSP is observed at 4-7 years [7]. Unlike HSP, systemic symptoms (joint pain, gastrointestinal bleeding, kidney involvement) are rarely observed in AIHE. The palpable purpura is observed on the lower legs and buttocks in HSP, but the purpura in AIHE has a wider extension and observed on the face and close to the distal extremities accompanied by edema [8].

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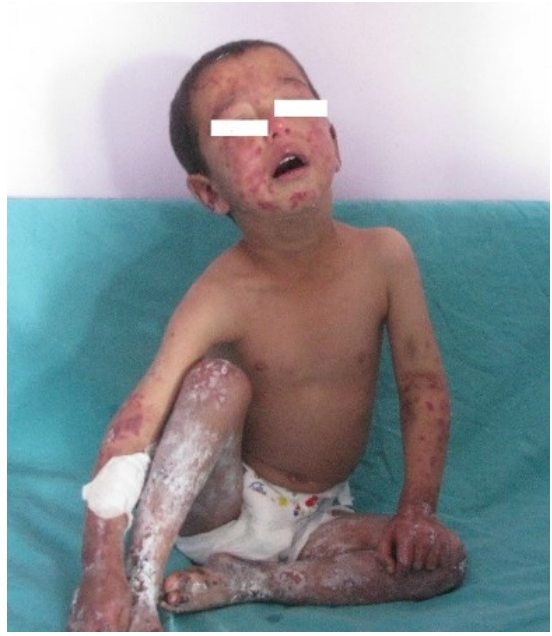
This case report was presented as a poster presentation in the 25th Turkish National Congress of Dermatology, 21-25 October 2015, Rixos Sungate Hotel, Antalya



**Picture 1:** Widespread skin lesions and edema were mainly distributed over the face and the lower extremities

Our patient was referred to us from a first-step health clinic due to acute tonsillopharyngitis and purpuric skin lesions. Throat cultures were positive for fast antigens. The antibiotic, steroid, and antihistamine treatment provided dramatic relief of symptoms.

## Conclusion

We conclude that AIHE should be suspected in the differential diagnosis of the children presenting to first-step health clinics, with Henoch-Schönlein purpura, since these diseases require different approaches for examination, treatment, and follow-up

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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# Adult nasopharyngeal hairy polyp presenting with middle ear effusion

Yunus Kaplan[1], Burak Ulkumen[2], Serkan Gokpınar[3], Zeynep Senel[4]

**Abstract**
Hairy polyp is a relatively uncommon congenital mass mainly seen in naso-oropharynx. It has been also called as choristoma owing to its bigerminal composition and unexpected location. It is almost always seen at birth and in the early infancy period. Adult presentation is very exceptional and only 5 adult cases have been reported as far as we know. We present a rare case of nasopharyngeal hairy polyp in a 69 year old woman admitted with hearing impairment due to middle ear effusion. We also review the relevant literature. The lesion was totally removed via combined naso-endoscopic and trans-oral approach. After 1 year of follow up there was no sign of recurrence neither in the endoscopic evaluation nor in the magnetic resonance imaging. Although nasopharyngeal hairy polyp frequently leads ear problems exclusively in the infancy period, the presented case is the 1'st adult hairy polyp case with middle ear effusion. Also it is the 2'nd oldest one so far

**Key words:** Choristoma, Eustachian tube, Nasopharynx**,** Hairy polyp, Adult

## Introduction

Hairy polyp (HP) is a congenital benign mass which was first described by Brown-Kelly in 1918 [1]. It typically consists of mature ectodermal and mesodermal elements [2]. Due to this composition and improbable location it also has been named as choristoma [3]. It is mainly seen at birth or in the infancy period and may originate from any sub-region of naso-orofarenks [4,5]. HP of infancy commonly present with respiratory distress, feeding difficulties and less frequently with middle ear effusion. Intensity of the symptoms depends on the site of the involvement and size of the lesion [5,6]. Adult presentation of HP is very rare and according to our knowledge only 5 cases has been reported so far. In adults main reported symptoms were epistaxis, nasal obstruction and dysphagia [3]. Middle ear effusion was not reported in any of the adult HP cases up to now. We present the 6$^{th}$ adult case in which the main symptom was hearing impairment due to middle ear effusion

## Case

A 69 year old woman was referred with a history of hearing loss. She also reported that she had fullness sensation in her left ear for 2 weeks. Oral amoxicillin had prescribed by a general practitioner with the diagnosis of acute otitis media. However, her symptoms worsened and hearing loss with pain in the left ear during swallowing has begun 5-days prior to admission. When thoroughly questioned, the patient was also complained about snoring and left sided nasal obstruction. She stated that snoring had started 6 months ago and had been progressed up to the time of referral. She was otherwise healthy, with no other major medical problems. On oropharyngeal examination a pale, smooth and pedunculated mass hanging from the nasopharynx just posterosuperior to the left palatopharyngeal arch and uvula was detected (Fig. 1).

Right otoscopic examination was normal. In left otoscopic examination tympanic membrane was hyperemic with effusion in the cavum tympani. Transnasal rigid endoscopic nasopharyngeal evaluation revealed the pedunculated skin-covered mass originating from the lateral nasopharyngeal wall. Both nasal passages were otherwise normal. Pure tone audiogram confirmed a mild conductive hearing loss on the ipsilateral ear.

Tympanometry was Type-B for the left and Type-A for the right ear which was compatible with the otoscopic findings. Magnetic resonans imaging (MRI) with intravenous gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA) was done. It revealed a well circumscribed mass extending from inside the left eustachian tube to the nasopharynx and oropharynx measuring 30x7x18 milimeters (Fig. 2).

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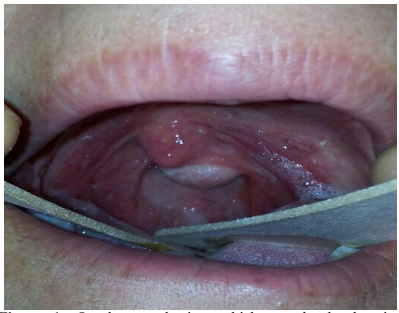

**Figure 1:** Oropharyngeal view which reveals the hanging polypoid mass just behind the uvula and the palatopharyngeal arch

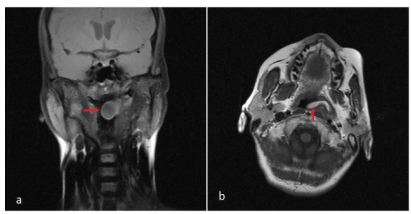


**Figure 2:** MRI with intravenous contrast. (a) Coronal view revealing a well-circumscribed mass (arrow) which is peripherally enhanced after intravenous contrast. (b) The same lesion (arrow) in axial view in which dilatation in the orifice of the left eusthacian tube can be noticed

Surgical excision was done under endoscopic view by dissecting the peduncle from the orifice of the eustachian tube under general anesthesia. After freeing the peduncle the mass was taken out transorally. A concomitant paracentesis to the left ear was also done. There was no major bleeding.

Histopathology demonstrated a 35X15X10 mm polypoid lesion covered by stratified squamous epithelium with associated seromucinous glands and lenfoid folicules which was compatible with the diagnosis of HP.

After 1 year of follow up there was no sign of recurrence neither in the endoscopic evaluation nor in the MRI. The middle ear effusion was also totally resolved

## Discussion

Although the classification of germinal-cell originated tumors of naso-oropharynx was first done by Arnold in 1870 [7], the term of "hairy polyp" was first used by Brown-Kelly in 1918 for a benign nasopharyngeal congenital mass having both ectodermal and mesodermal components [1,2]. It was called as hairy because of its outer layer which composed of mature epidermis that frequently has a hairy appearance. In Arnold's classification; HP had defined as "choristoma" which describes a lesion mistakenly separated from its mother tissue [3,7]. He also had described it as a type of dermoid due to its mature bigerminal composition [7].

HP is relatively rare and has an incidence of 1 in 40,000 live births and have a tendency to occur in female newborns [8,9]. Due to this presentation, HP is typically defined as a disease of early infancy and is very exceptional after the first year of life [10]. Only 5 adult cases have been reported up to now, the oldest being 71 years [4, 11]. We believe that our case is the 6$^{th}$ adult HP and also the 2$^{nd}$ oldest one so far.

HP of naso-oropharynx mostly originates from lateral nasal wall followed by the tonsils, palatal arches and soft palate [4,5]. Almost two-thirds of lateral pharyngeal wall HPs originate from the eusthachian tube [3]. In our case it was also originated from the eusthachian tube resulting with middle ear effusion. HP of infancy usually presents with feeding difficulties, drooling, respiratory distress, hemoptysis, coughing, otorrhea, hearing loss, vomiting and recurrent ear infections [5] while in adults it commonly presents with snoring, recurrent epistaxis, dysphagia and cough [3]. In our case the main symptoms were hearing loss and otalgia which were presumably caused by middle ear effusion. Considering the adult cases, middle ear involvement has not been reported before. In the literature the adult HPs were presented mainly with symptoms associated to nasal obstruction and swallowing difficulties [3].

Differential diagnosis of HP; including teratoma, hamartoma and dermoid cyst can sometimes be challenging due to similar histopathological findings. Teratomas can be differentiated by trigerminal origin and the observation of endodermal derivatives while hamartomas can be identified by the presence of single germ cell layer [11]. When regarding the dermoid cysts; they have the typical keratin flakes. In this presented case none of these above mentioned findings were seen, instead there was a bigerminal structure consisting of ectodermal and mesodermal components with an epidermal lining which was compatible with HP. The mesodermal inner core which mainly composed of fat can also be noticed in the MRI (Fig. 2). Whereas teratomas exhibit more blended appearance of germ cell layers and may sometimes have bone or teeth fragments which may be hyperdense in MRI unlike in our case.

Main treatment modality for HP is total surgical excision. Malignant potential, metastasis or recurrence after complete removal has not been reported so far [8]. Although it can be removed trans-nasally or trans-orally; in our opinion the best approach is combined naso-endoscopic and trans-oral approach which provides better visualization and control [12]. Thus, we used the combined endoscopic approach in which we first excise the peduncule from the eusthacian tube under

endoscopic view followed by removal of the mass transorally.

Naso-oropharyngeal HPs typically seen in female neonates with left sided predominancy while they are extremely rare in adult population [10,13]. We present the 6th case of adult nasopharyngeal HP with an uncommon presentation. We achieved total removal of the lesion by a combined naso-endoscopic and trans-oral approach. We believe that endoscopic guidance is essential for total removal to prevent recurrence in adult HPs

**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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# Bell's palsy together with scarlet fever in a child: A rare case

Veysel Kars[1], Ahmet Yilmaz[1], Tahsin Celepkolu[1], Hamza Aslanhan[1], Necmi Arslan[1], Vasfiye Demir[1], Abdullah Cim[2]

**Abstract**
Scarlet fever is an infectious disease caused by the erythrogenic toxin produced by β-hemolytic streptococci. The prodrome phase is 12-24 hours with fever, emesis, sore throat, and headache. If not treated, the fever rises up to 39.5 °C and may last up to 5-7 days. Complications may occur in case of a prolonged prodrome. We report a five-year-old child who presented with Bell's paralysis together with scarlet fever. We emphasize that facial paralysis should be take into consideration in the treatment and follow-up of the patients presenting with scarlet fever

**Key words:** Scarlet fever, Bell's palsy, Petechiae

## Introduction

Scarlet fever (SF), caused by the erythrogenic toxin produced by Group A β-hemolytic streptococci, is an infectious disease characterized by widespread erythematous rash. Once the patient has been exposed to this toxin, protective antibodies are developed and the toxin is neutralized. Therefore, erythematous rash is seen when no protective antibodies are present. SF has an average incubation period of 1-7 days. The prodrome phase of SF is 12-24 hours of fever, emesis, sore throat, and headache. If not treated, the fever rises up to 39.5 °C and may last up to 5-7 days. The use of penicillin can bring down the fever in 12-24 h. SF leads to erythematous rash which includes enanthema and exanthema. It may also represent with tonsillar exudate or palatal petechia. At first two days white strawberry tongue is represent because of hyperceratotic membrane. On the 4 $^{th}$ and 5 $^{th}$ day membrane sheds to reveal a bright red mucosa and red strawberry tongue shows up. On the proximal part of body, scarlanitiform shaped punctiform papules that resemble sandpaper occur whereon erythroderma and then these papules spread to the whole body in 4-5 days. These papules, particularly the ones on the hands and feet, are resolved via desquamation. Also, Pastia's lines become visible, which are brighter red than the rest of the rash.

The anatomy and function of the facial nerve (FN) was first described by Sir Charles Bell in early 1800s. The facial nerve is a complex nerve which includes the motor fibers innervating the facial muscles; the parasympathetic fibers innervating lacrimal, submandibular, and sublingual salivary glands; the afferent fibers from taste receptors from the anterior two thirds of the tongue; and the somatic afferents from the external auditory canal and pinna. Bell's paralysis (BP) is mostly seen among 15-45 year old patients, and the incidence rate is 10-40/100.000 with no obvious sexual predominance. Upper respiratory tract infections such as influenza and common cold, tooth extraction, and long-term exposure to cold air and wind are reported as the history of BP [1, 2]. Moreover, two-thirds of facial nerve paralysis (FNP) cases are diagnosed as idiopathic since they represent no clear etiology [3]. Clinical presentation of FNP is characterized by unilateral facial paralysis, impaired platysma muscle, drooping of the corner of the mouth and the forehead, and difficulty in closing the eye or the mouth [4]. BP is generally diagnosed via patient's history and the findings of physical examination, without any need for diagnostic imaging and routine laboratory testing [7]. BP is the most common cause of unilateral facial paralysis and constitutes 60-75% of all cases of FNP [5,6]. Although the incidence of BP in children remains unknown, Peitersen reviewed 2,500 BP cases and reported the incidence for children below 15 years of age as 14% [6]. BP has a better prognosis for the patients below 20 years of age; however, the rate of complete recovery decreases by age [7]. There are several theories for the cause of peripheral facial nerve paralysis (PFP); some studies argue that PFP results from the local ischemia in the nerve cause by the

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vasoconstriction in the fallopian canal, whereas the others claim that PFP is a result of direct invasion of the nerve by the toxins that are produced by the infectious agents [8].

Facial nerve consists of intracranial, intra temporal, and extra temporal segments [9]. In central facial palsy, the function of the fibers innervating the forehead is normal due to the supra nuclear fibers that are connected with ipsi lateral cortex. However, nuclear and peripheral facial paralyses are often accompanied by loss of function fibers function in the affected side of the face [10]. Various facial grading systems have been developed by House-Breckmann, Sunnybrook, Burres-Fisch, MoReSS, Sydney, and Yanagihara. Of these, the one developed by Yana gihara is the most commonly used [11].

## Case

A five-year-old girl presented to the family physician with fever, sore throat, and discomfort, and then she was orally administered amoxicillin, decongestant and antipyretic. On the following days, the parents failed to administer the drugs due to the child's continuous discomfort. On the 5$^{th}$ day of treatment, the body temperature suddenly increased to 40 °C and thereafter the patient represented to our clinic with fever, abdominal pain, rash in groins and darkening of urine. During the physical examination, the tonsils were hyperaemic and hypertrophic; the tongue had a strawberry appearance. 5x5 cm squamous lesion was detected on the left armpit and a bright red macula papullar rash had been spread whole body - predominantly to the groins. The ear examination was uneventful, except for mild hyperaemia in the outer ear canal. The patient was extremely sensitive to the slightest noise. When she cried, the left side of her mouth drooped and her right eye remained open. The sclera was slightly pale, but no jaundice was detected in any part of the body. Temperature was 39.6 °C, ALT and AST levels were normal, leukocyte count was 8.900/mm3, and thrombocyte count was 180.000. The patient had no family history of BP, and her weight and height were in the 50$^{th}$ percentile (Figure 1). Streptococcus pyogenes reproduced in patient's throat cultures. The patient who has had both scarlet fever and FNP was administered a course of steroid and antibiotic therapy. Clinical improvement was seen within the first week and the facial paralysis completely resolved on day 14 $^{th}$

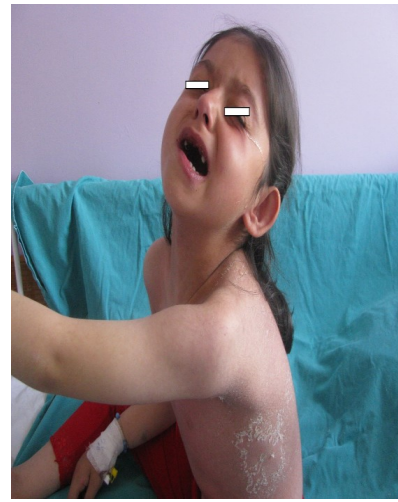

**Figure 1:** Distinctive desquamative lesions and facial palsy in the patient

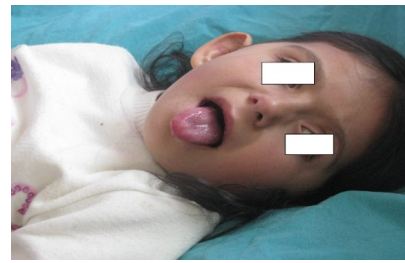

**Figure 2:** Marked improvement of the patient on the 14$^{th}$ day of treatment

## Discussion

Facial nerve paralysis may resolve within one year. While spontaneous or complete recovery can be seen in 80-85% of the patients, mild nerve damage can be seen in 15-20% and severe nerve damage can be seen in 5% of the patients [3,12]. The infections caused by Group A β-hemolytic streptococci (GABHS) may be accompanied by otitis, sinusitis, meningitis, hepatitis, and scarlet fever [13]. Prompt treatment of scarlet fever decreases the infection and facilitates the recovery process. The ideal treatment includes amoxicillin for 10 days or intramuscular penicillin administration. With prompt treatment, the symptoms can resolve quicker and also the neurological complications can be prevented. Our patients presented to us with PFP on the 5$^{th}$ day after the onset of fever. The patient was administered parenteral ampicillin and antipyretic. The patient clinically improved within the first

week, and the facial paralysis completely resolved on day 14 (Figure 2).

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**Conflict of Interest:** The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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