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Sleeve Gastrectomy in a Severe Hemophilia A Patient: One of the Very Rare Cases

Ağır Hemofili A Hastasında Sleeve Gastrektomi Operasyonu: Çok Nadir Olgulardan Biri

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To the Editor,

Obesity is becoming a problem for aging hemophilia patients. The estimated prevalence of overweight and obesity in European and North American hemophilia patients is 31% [1]. Similarly to non-hemophiliacs, excessive weight has an adverse effect on the cardiovascular system and the psychological and musculoskeletal health of hemophilia patients. Bariatric surgery is advised to be considered for patients from the general population with a body mass index (BMI) of ≥ 40 kg/m² or BMI of ≥ 35 kg/m² with comorbidities [2]. Although it is not contraindicated, there are limited data on bariatric surgery among hemophilia patients. There are only two hemophilia A patients reported in the literature who had bariatric surgery. The first one underwent a successful sleeve gastrectomy [3] and the other had mini-gastric bypass surgery [4].

A 55-year-old severe hemophilia A patient with arterial hypertension, diabetes mellitus, hyperlipidemia, obstructive sleep apnea, and morbid obesity (BMI of 42.45 kg/m²) decided to have obesity surgery because of inconclusive efforts at losing weight and obesity-related comorbidities. He had been receiving factor VIII prophylaxis at 6000 units/week for the last few years because conventional treatment at 4500 units/week was not sufficient for his frequent joint bleedings.

According to the Hemophilia Diagnosis and Treatment Guidelines of the Turkish Society of Hematology [5], the perioperative factor VIII target was calculated as 100%. Three days before surgery, his factor VIII level was 2.3% and factor VIII inhibitor was negative. He received factor VIII at 42 units/kg preoperatively and we planned to administer 23 units/kg at the postoperative 12th hour (weight: 130 kg). At the postoperative 7th hour he had hypotension, loss of consciousness, oliguria, 13% decline in hematocrit level, and increase in creatinine and transaminase levels. At that time, activated partial thromboplastin time (aPTT) was 26.8 s (normal range: 22.5-31.3). During explorative laparotomy, approximately 500 mL of blood was drained from the abdominal cavity, but a surgical bleeding focus could not be found. Packing was performed according to damage control surgery principles. After 48 h the abdominal cavity was reopened for unpacking and no bleeding was observed. He was followed in the intensive care unit for the following 8 days with mechanical ventilation. He needed intermittent hemodialysis because of hemorrhage-related acute kidney injury. During this period, he had thrombocytopenia and prolonged prothrombin time. He had multiple erythrocyte, platelet, and fresh frozen plasma replacements due to probable disseminated intravascular coagulation. Hemorrhage from the surgical drains lessened and finally stopped. Perioperative laboratory results are summarized in Table 1.

Table 1. Perioperative laboratory results.

	Preop, 3 days	Postop 7 th hour	Postop 1 st day	Postop 2 nd day	Postop 4 th day	Postop 8 th day	Postop 14 th day	Postop 21 st day	Postop 1 st month	Postop 2 nd month	Postop 3.5 th month	Postop 7 th month
aPTT	36.7	26.8	33.7	33.6	29.5	28.5	28.6	31.8	-	-	29.5	-
PT	10.5	11.7	20.4	19.5	12	10.4	-	12	-	-	10.7	-
HCT	44.1	29.4	36.3	25.2	22.7	22.8	23.3	25.4	24.2	31	38.1	38.6
PLT	206000	314000	145000	96000	43000	136000	408000	275000	245000	209000	228000	146000
Urea	38	-	39	74	47	64	78	82	156	16	28	-
Cr	0.63	-	2.06	4.94	2.48	2.2	6.32	8.04	4.2	1.11	0.76	-
AST	26	-	1649	1467	690	172	172	19	13	-	13	-
ALT	68	-	2125	1714	1416	214	214	6	<5	-	13	-
Fibr	-	-	215	291	-	-	-	-	-	-	-	-
T.bil	0.58	-	1.09	1.11	2.27	1.29	0.66	0.61	-	-	-	-
D.bil	0.25	-	0.81	0.9	2.07	1.19	0.28	0.41	-	-	-	-

aPTT: Activated partial thromboplastin time (22.5-31.3 s), PT: prothrombin time (10.9-14.7 s), HCT: hematocrit (39%-50%), PLT: platelets (150-450 103/ μ L), urea (10-50 mg/dL), Cr: creatinine (0.7-1.3 mg/dL), AST: aspartate aminotransferase (<35 U/L), ALT: alanine aminotransferase (<35 U/L), Fibr: fibrinogen (175-400 mg/dL), T.bil: total bilirubin (0.1-1 mg/dL), D.bil: direct bilirubin (<0.25 mg/dL), Preop: preoperative, Postop: postoperative.

Factor VIII replacement was performed at 100% level (42 units/kg/day) until bleeding ceased for 8 days after surgery. The factor threshold was decreased to 60% (30 units/kg/day) during the next 8 days and to 40% (20 units/kg/day) the next 5 days, and then the patient was switched to prophylactic treatment (6000 units/week).

During follow-up in the inpatient clinic for the next 30 days, his need for high doses of factor VIII replacement diminished, his urine output increased, cytopenia and hemostatic problems resolved, and kidney and liver functions normalized.

At 7 months after surgery, he had lost 42 kg and his BMI was 28.7 kg/m². His blood pressure and glucose are now well controlled. We intend to reduce factor VIII prophylaxis to 4500 units/week when the ideal body mass is achieved.

To the best of our knowledge, we are reporting the second hemophilia A patient to have a sleeve gastrectomy operation. The course of the procedure was challenging but the patient survived without any permanent damage and has even already begun to see the benefits of losing weight. His unexpected bleeding a couple of hours after the operation could not be attributed to any manifest surgical reasons or hemostatic defects. However, we think that there were likely some microvascular and hemostatic deficiencies. Since it was not possible to measure the factor VIII level just before the operation, we did not know the factor level precisely. Although aPTT was in the

normal range, the factor concentration may be below the target level during this procedure. Our experience shows that major surgical operations such as bariatric surgery can be complicated in hemophilia patients; therefore, it is necessary that all parts of the team providing hemophilia care cooperate together.

Keywords: Hemophilia A, Obesity, Bariatric surgery

Anahtar Sözcükler: Hemofili A, Obezite, Bariatrik cerrahi

Informed Consent: Obtained.

Authorship Contributions

Design: E.D.A., Z.D., F.Ş.; Data collection and processing: E.D.A., Z.D., Ö.F., G.S., F.Ş.; Writing: E.D.A.

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A Novel Coincidence: Essential Thrombocythemia with Facioscapulohumeral Muscular Dystrophy

Yeni Bir Birliktelik: Esansiyel Trombositemi ve Fasioskapulohumeral Musküler Distrofi

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To the Editor,

Essential thrombocythemia (ET) is a myeloproliferative disorder with elevated numbers of thrombocytes and facioscapulohumeral muscular dystrophy (FSHD) is the third most common dystrophy among all dystrophies. In this paper, we report a novel case of FSHD coinciding with ET.

The male FSHD patient was diagnosed at the age of 17 with difficulty of raising his arms. He had 4q35 D4Z4 repeat contraction. A neurological examination revealed positive facial involvement and scapula alata; right and left shoulder flexion 4+; right forearm flexion 4+; left forearm flexion 3+; right and left hip flexion 4+; remaining muscle strengths 5+. Mild involvement and loss of power were seen in the extensor indicis, peroneal muscles, and abdominal muscles. When the patient was 67 years old, he was admitted to the hematology clinic with facial redness and increased platelet count (1,200,000/mm³) without hepatosplenomegaly.

Since myeloproliferative neoplasms (MPNs) are frequently related to somatic mutations of the *JAK2*, *MPL*, and *CALR* genes, the patient's blood sample was analyzed for the hot-spot mutations of these genes. The exon 10 region of the *MPL* gene was analyzed for p.W515K/L mutation and the exon 9 region of the *CALR* gene was analyzed for insertion/deletion mutations

with PCR/sequencing methods. The exon 14 region of the *JAK2* (Janus kinase 2) gene was investigated for p.V617F (c.1849G>T) mutation by quantitative real-time PCR using plasmids of wild type and mutant alleles. There was no mutation in the target regions of the *MPL* and *CALR* genes. In the exon 14 region of the *JAK2* gene, p.V617F (c.1849G>T) mutation was detected with 28% allele burden (Figure 1).

His child was also investigated for the *JAK2* p.V617F (c.1849G>T) mutation and was found to be negative. Finally, the patient was diagnosed with high-risk ET because of being aged >60 years with *JAK2* mutation, and hydroxyurea and low-dose aspirin were started.

In this case, the presence of the *JAK2* p.V617F mutation confirmed the diagnosis of ET. There has been no report on the co-occurrence of FSHD with MPNs including ET and *JAK2* p.V617F mutation, and this is the first such case in the literature. Recently, a number of reports indicated that some germ-line DNA variants may predispose to MPNs with *JAK2* p.V617F mutation [1].

FSHD patients are prone to develop other systemic diseases, especially malignancies [2], via re-expression of the *DUX4* gene that allows cancer cells to escape immune surveillance [3]. In addition, myeloid cells (including thrombocytes) and skeletal