Micro-nutritional, Endocrine, and Metabolic Complications in Bariatric Surgery-Case Capsules

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Knowing is better than wondering, waking is better than sleeping, and even the biggest failure, even the worst, beats the hell out of never trying.

—Grey's Anatomy

23.1 Post-RYGB Cardiomyopathy

A 56-year-old male had undergone bariatric surgery 11 months back. He was readmitted to the hospital with exertional dyspnea and bilateral lower extremity pitting edema. His preoperative BMI reduced from 43 kg/m^2 to a current BMI of 33.7 kg/m^2 (weight 112 kg to 87 kg). He had no cardiovascular risk factors. Physical examination revealed normal blood pressure and pulse rate, normal heart sounds, no jugular venous distension, no hepatojugular reflux, and no lower limb venous disease. Complete blood count, C reactive protein, renal function test, liver function tests were normal, and no proteinuria was detected. CXR and ECG were normal. N-Terminal pro-brain Natriuretic Peptide (NT pro-BNP) value was elevated at 1417 ng/l (normal value <300 ng/ml).

CT of thorax and abdomen scan revealed no features suggestive of complications post-surgery. There was no abdominal or pelvic mass, venous thrombosis, pulmonary embolism, or evidence of Budd-Chiari syndrome. A bilateral venous doppler was done to rule out any peripheral signs of deep vein thrombosis. Transthoracic echocardiography (2-D Echo) showed a reduced left ventricular ejection fraction to 50% from preoperative value of 62%. 2-D Echo also showed normal size and volume of the cardiac chambers and no pericardial disease. There was an impairment

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of percentage left ventricular (LV) global longitudinal strain (GLS) (−12.4%). We found a "pseudo-normal" trans-mitral flow pattern in the echocardiography. Diastolic dysfunction was also noted. The right ventricular function and pulmonary artery pressure were normal. Computed tomography (CT) coronary angiogram was normal. Impaired left ventricular (LV) global longitudinal strain with evidence of increased LV-filling pressures, the diagnosis of cardiomyopathy was made. The various reasons for cardiomyopathy were evaluated. It was noted that the serum selenium concentration was low at 61 g/l (normal values range from 89 to 150 g/l). The blood levels were normal for the other micro-nutrients: vitamins A, B1, B9, B12, C, D, E, and K, iron, calcium, zinc, copper. The possible association of selenium-deficient cardiomyopathy was made. Oral supplementation with a dosage of 2 g/kg/day was initiated and was continued for three months. Congestive heart failure treatment with ACE inhibitor and furosemide was started along with the supplementation of selenium. Dyspnea and the pedal edema were reduced with 2 weeks of treatment, and the patient symptomatically improved. On follow-up of the patient after 6 months, the patient remained asymptomatic. Serum selenium and NT pro-BNP (121 ng/l) had returned to normal levels. Echocardiography findings were normal on the follow-up of the patient.

Selenium is an essential trace element and a vital constituent of antioxidant enzymes that participate in various physiological activities, protecting the cells against the harmful effects of free radicals by modulating the cell response [1]. The role of selenium has been explored in normal thyroid functioning, immune system enhancement, carcinogenesis, cardiovascular diseases, in the prevention of pre-eclampsia, diabetes mellitus, and also male reproduction. It has been documented that a significant percentage of obese individuals have pre-existing lower serum selenium levels [2, 3]. A recent study by Papamargaritis et al. showed, a reduction in selenium concentration was observed in the early postoperative period following bariatric surgery, even after adequate multivitamin and mineral supplementation [4]. The deficiency appears within 3 months post-surgery [5]. Interestingly, no specific recommendation exists for selenium replacement in the post-bariatric setting.

23.2 Causes of Selenium Deficiency After RYGB

Several mechanisms relating to selenium deficiency may occur concurrently after RYGB, which are as follows:

Pre-existing deficiency is one of the most common reasons for clinical manifestation post-surgery (2–58%). Reduced dietary intake of selenium that may further be reduced following surgery due to the predominant restrictive nature of the operation. RYGB results in bypass of the proximal intestines (duodenum and upper jejunum), with failure to absorb the micro-nutrients, precipitating deficiencies. There is no absorption from the stomach or the remaining parts of the intestine. Therefore, malabsorption of selenium following RYGB is a possible cause of deficiencies. Discontinuation of postoperative selenium supplementation could lead to decreased

levels of serum selenium. Some types of multivitamin/mineral supplements may not contain sufficient amounts of minerals, which need to look for appropriately.

Selenium deficiency is rare, but if present, it may cause myopathy, cardiomyopathy, decreased immunity, low thyroid function, skin loss, pigmentation of hair, and progressive encephalopathy [6, 7]. Selenium deficiency has also been shown to contribute to the progression of viral infections. Cardiomyopathy results from the depletion of selenium-associated enzymes, which aid in the protection of cell membranes from damage by free radicals hence exposing it to myocardial necrosis and sudden death. The time duration for the development of congestive heart failure varies from several days or weeks in patients who develop a deficiency of selenium following malabsorptive bariatric procedures. The prompt correction of the gap by selenium treatment becomes necessary to reverse the harmful effects on the myocardium.

Selenium is more effectively absorbed from plant food than animal products. Other dietary components like vitamin C and E, zinc, copper, magnesium, vitamin B, and some amino acids such as methionine, cysteine, and glutamine may play a role that affects the serum selenium levels. Selenium deficiency can be assessed by measuring plasma erythrocyte ad whole blood selenium, plasma selenoproteins P, and overall blood glutathione activity. Selenoenzyme methionine sulfoxide reductase B1 (MsrB1) assessment is considered to be the most sensitive protein marker of selenium status [8]. Plant origin food products are the primary source of selenium, and the concentration varies tremendously according to its levels in the soil. A high concentration of selenium is found in food products like walnuts, brazil nuts, peanuts, almonds, cashew nuts, hazelnuts, pistachios, grains, saltwater and freshwater fish, poultry, eggs, and mushroom. A prospective study by Freeth et al. has shown that RYGB increased the risk of selenium deficiency, leading to deranged GTP homeostasis. The study recommended supplementation of selenium at a higher dosage than the current RDA (i.e., 55 μg) during the first 3 months post-surgery [5].

A multidisciplinary team managing the increasing number of bariatric patients needs to be aware of possible micro-nutrient deficiencies, their symptoms, diagnosis, and prevention [9]. Stress should be placed on the need for lifelong supplementation and annual monitoring of nutritional laboratory values. Selenium can be supplemented as a part of a vitamin-mineral supplement regime following metabolic surgery.

23.3 Postprandial Fainting

A morbidly obese diabetic female (BMI −45.6 kg/m^2; HbA1c-8.7%) who underwent laparoscopic sleeve followed by Roux-en-Y gastric bypass for inadequate weight loss was referred with frequent episodes of lightheadedness, flushing, abdominal pain, loose stools, and frequent fainting episodes 20–30 min after meals. The symptoms began 2 months following surgery. Her BMI dropped from 45.6 kg/m^2 to 31 kg/m^2, with aa %EWL of 78%, 16 months post revisional RYGB. A multidisciplinary bariatric team comprising of a surgeon, medical gastroenterologist,

endocrinologist, psychiatrist, and dietician analyzed the patient. The possible differential diagnoses were dumping syndrome, nesidioblastosis, and neuroendocrine tumors. The patient was evaluated for insulin, C-peptide, chromogranin, which were normal. Computerized tomography (CT scan), upper GI endoscopy was also normal. With a provisional diagnosis of dumping syndrome, pharmacotherapy in the form of acarbose and octreotide was initiated with dietary modifications, but there was no alleviation of the symptoms. The provocative test in the way of oral glucose tolerance test (OGTT) was done to confirm the diagnosis. The Sigstad's score was 21.

Dumping syndrome post-RYGB was made as a diagnosis. With dietary and medical options exhausted, a decision for the reversal of RYGB to sleeve gastrectomy was made. The proximal and the distal pouches were mobilized after clearing all the dense adhesions to the liver. The gastrojejunostomy complex was mobilized and divided. The biliopancreatic limb proximal to the jejunostomy was divided and anastomosed to the divided end of the roux limb. Gastro-gastrostomy was done between the proximal and the distal pouches using a linear stapler technique. The patient improved drastically with complete resolution of symptoms and Sigstad's score of 1. The patient had a minimal weight regain of 3 kg, with the static status of diabetes.

Dumping syndrome (DS) is a frequent complication observed after Roux-en-Y gastric bypass (RYGB) found in around 40–50% cases [10]. The mechanisms which lead to dumping syndrome after RYGB are numerous and remain to be fully elucidated. Early DS is observed 10–30 min after a rapid passage of hyperosmolar food into the proximal bowel, which facilitates the fast movement of fluids into the bowel lumen, causing an increased sympathetic response [11]. Hyperosmolar nutrients in the proximal gut cause a shift of fluid from the plasma to the intestinal lumen. This results in a reduction in plasma volume, tachycardia, and rarely syncope. These events are manifested by hypotension, tachycardia, dizziness, fatigue, nausea, pallor, flushing, headache, diaphoresis, crampy abdominal pain, bloating, diarrhea, and syncope. Late DS occurs 1–3 h after the passage of a highly loaded carbohydrate meal into the jejunum, causing an incretin-driven hyper-insulinemic response. A couple of GI hormones are believed to play an essential role in the incretin effect: glucose-dependent insulinotropic polypeptide or gastric inhibitory polypeptide (GIP) and GLP-1. An elevated GLP-1 response has been reported in patients following RYGB, and a positive correlation has been observed between increasing GLP-1 levels and insulin release. Therefore, an exaggerated GLP-1 response appears to be pivotal in mediating the hyper-insulinemic and hypoglycemic effect that is characteristic of late dumping syndrome [12]. Late DS is characterized by diaphoresis, weakness, tremors, dizziness, fatigue, and altered consciousness [11].

Scores such as Sigstad's score and the Arts' dumping questionnaire can be used to identify patients with clinically significant dumping symptoms. The Sigstad's scoring system allocates points to each dumping symptom, and the cumulative points are used to calculate a diagnostic index, which helps in diagnostic

confirmation of DS. A score value of >7 confirms DS, while patients with score <4, another differential diagnosis should be considered [13]. Art's questionnaire is used to differentiate early, and late DS [14]. Provocative tests such as the oral glucose tolerance test (OGTT) or mixed-meal tolerance test can be used to confirm clinically suspicious DS [15]. The OGTT is considered confirmatory for early dumping syndrome based on the presence of an early (30 min) increase in hematocrit greater than 3% or an increment in pulse rate more than 10 beats/min after 30 min, the latter being regarded as the most sensitive indicator of early dumping syndrome. Test results are conclusive for late dumping based on the development of late (60–180 min post-ingestion) hypoglycemia [11].

Most (around 95%) of the DS can be treated by adequate counseling and dietary therapy [16]. Fluid intake should be delayed until at least 30 min after meals. Rapidly absorbable carbohydrates should be excluded from the diet to prevent late dumping symptoms. High fiber, protein-rich foods, consumption of fruit and vegetable should be encouraged, whereas alcoholic beverages are better avoided. Meals should be eaten slowly and chewed well. Dietary supplements which increase the viscosity of food (e.g., pectin, guar gum, and glucomannan) delays the rate of gastric emptying and inhibits glucose absorption. The above dietary modifications result in slowing gastric emptying, reducing the release of GI hormones, improving hyperglycemia, and thereby controlling dumping symptoms. [17]. Few (3–5%) need medical therapy in the form of acarbose, octreotide for the treatment [16]. Acarbose is an α-glycosidase hydrolase inhibitor. It delays carbohydrate digestion in the proximal bowel, thus blunting postprandial hyperglycemia and subsequent hypoglycemia. Acarbose usage is best suited for patients with late dumping syndrome and is associated with abdominal bloating, excessive flatulence, and loose stools [18]. Somatostatin analogs (octreotide, pasireotide) are an effective treatment option for patients with dumping syndrome who fail to respond to or do not tolerate dietary modification and acarbose management. Somatostatin analogs inhibit gastric emptying time. They also inhibit the release of GI hormones and insulin and also inhibit postprandial vasodilatation. Both short-acting and long-acting formulations of somatostatin analogs are efficient in reducing early and late dumping symptoms [18]. Other pharmacologic interventions, such as diazoxide, nifedipine, and exendin 9–39, have also been investigated for the management of dumping syndrome. However, the data supporting the efficacy of the above is limited. Intractable cases (<1%) may require endoscopic or surgical revisions for its treatment [19, 20]. Multiple surgical options have been proposed ranging from reduction of gastrojejunal anastomosis, jejunal interposition, partial pancreatectomy to the reversal of RYGB [20–24]. Weight regain, and relapse of comorbidities remain the prime cause of concern in patients undergoing reversal to normal anatomy. Reversal of RYGB to LSG, however, provides a dynamic equilibrium concerning the resolution of symptoms of DS as well as decreasing the possibility of weight regain and recurrence of obesity-associated comorbidities. However, in the case described, a reversal to sleeve was the only option available.

23.4 Liver Decompensation

A 42-year-old hypertensive female with weight and height of 141 kg and 151 cm, suffering from super-super-obese and metabolic syndrome with a BMI of 61.8 kg/m^2, had been admitted to the hospital with complaints of gradual increase in weight past 15 years. She had limited physical activity. Her lipid parameters were deranged (cholesterol-230 mg/dl, triglyceride-264 mg/dl, VLDL-180 mg/dl, LDL-180 mg/dl). She was a known case of diabetes and hypertensive past 20 years on treatment. Her glycosylated hemoglobin preoperatively was 9.3%. The liver function tests during the preoperative period were normal. Ultrasonogram (USG) of the abdomen showed grade 2 fatty liver. Upper GI endoscopy showed reflux esophagitis (Los-Angeles grade-A). The patient had a history of open hernioplasty with abdominoplasty in the year 2012. The patient had tried weight reduction measures but was not able to achieve the same. After a thorough evaluation, the patient underwent laparoscopic Roux-en-Y gastric bypass (RYGB). The patient was put on calcium (1000 g/day), multivitamin, proton pump inhibitors, Vit B-12, and ursodeoxycholic acid (UDCA) supplements for 6 months and was on regular follow-up.

Following 6 months, the patient lost 36 kg of weight and BMI change of 15 (62 kg/m^2 to 47.1 kg/m^2). Seven months post-surgery, the patient was readmitted to our hospital with decreased appetite, jaundice, and persistent vomiting. On evaluation, her total bilirubin was 10.2 mg/dl, with the direct component being 8.2 mg/dl. AST levels were abnormally high at 213 U/l? (N-up-to 40 U/l). She had a low albumin level of 1.9 g/dl. USG showed severe hepatomegaly with fatty liver. Magnetic resonance cholangiography (MRCP) abdomen showed severe fatty infiltration of the liver with hepatomegaly.

There was no evidence of gall stone disease or common bile duct stones, ruling out the possibility of cholangitis. INR was raised to 2.64. The same was corrected using fresh frozen plasma. The patient developed features of hepatic encephalopathy. Serum ammonia levels were elevated to 171.9 μg/dl (N-18.7-86.9 μg/dl). Liver biopsy to rule out any autoimmune etiology was done, which showed features suggestive of non-alcoholic steatohepatitis (NAFLD activity score-6) with periportal and perisinusoidal fibrosis (stage 2). Over time, the patient's conscious level decreased with increased stupor and drowsiness. Her serum creatinine increased to 4.2 mg/dl, with a subsequent decrease in the urine output. Hemodialysis was started because of the failing renal parameters as well as anuria. The patient developed features of sepsis and multi-organ dysfunction syndrome over the next 4 days and expired after that. The cause of the death was acute liver failure, hepatorenal syndrome post-RYGB.

Non-alcoholic fatty liver disease (NAFLD) is among the most common causes of chronic liver disease in India and worldwide and is strongly associated with obesity and metabolic syndrome [25]. NAFLD comprises a wide spectrum of conditions, characterized by macro-vesicular hepatic steatosis, prevalent in patients who are non-alcoholic [26]. The histopathological NAFLD findings varied. It ranged from

steatosis, non-alcoholic steatohepatitis (NASH) to advanced fibrosis, and cirrhosis. NAFLD represents the hepatic component of the metabolic syndrome [27]. Steatohepatitis is now considered as an important cause of end-stage liver disease. It is also a predisposing cause of an unknown number of cases of cryptogenic cirrhosis. Cryptogenic liver cirrhosis has been found in around 1.4% of patients with morbid obesity [28]. In the majority of patients, metabolic surgery improves liver steatosis, inflammation, and fibrosis in NAFLD patients with obesity, the exact mechanism of the worsening is unclear. Although rare, the progression of NAFLD to liver cirrhosis and further liver damage has been reported, based upon the severity of steatosis [29]. A possible explanation of liver function worsening could be due to rapid weight loss resulting in increased free fatty acid levels due to extensive fat mobilization, thus causing liver injury.

Varying degrees of fibrosis and also cases of de novo fibrosis are seen in a few cases, which is mild, without the development of cirrhosis or liver function alteration, seen in around 16% cases. Deterioration of liver function was attributed to the type of the metabolic procedure and the extent of malnutrition and malabsorption [30]. Progressive fibrosis during the long term (>5 years follow-up) was seen in spite of the improvement of hepatic steatosis and ballooning, which occurred during the first year post-RYGB. Worsening of liver function was seen as patients with higher BMI and higher insulin resistance [30]. Only a few reports of severe liver deterioration following RYGB have been seen [31]. A recent RCT by Kalinowski et al. reported that patients with NASH undergoing RYGB were more likely to develop early transient deterioration of liver function compared to Sleeve gastrectomy (LSG) [32]. Preoperatively diagnosed liver cirrhosis, alcohol abuse, and the presence of intraoperative complications contributed to negative events after RYGB [33]. Extended excluded limbs or distal versions of RYGB also contribute to the negative impact on liver function after RYGB [34]. A systemic review by Jan et al. also highlighted the increased incidence of morbidity and mortality, post-bariatric surgery, leading to decompensatory liver disease and also fulminating acute liver failure, in Child A group of patients [33]. A "second hit," post rapid weight loss after malabsorptive procedures, that is caused due to exposure of toxins from bacterial overgrowth from intestinal mobilization, nutritional, and protein deficiencies, maybe the cause for liver injury [35]. According to a study by Sasaki et al., around 5% of the patients with morbid obesity had a component of undiagnosed cirrhosis at the time of bariatric surgery [36]. Such patients have non-specific symptoms during the preoperative period, and even intraoperative macroscopic liver disease may be easily overlooked [37]. Hence it is of utmost importance to exclude advanced liver disease before bariatric surgery. Meticulous postoperative follow-up with close monitoring of liver function tests, especially in patients with super obesity, impaired insulin resistance, and preoperative liver pathologies, have been established. Improvement or even cessation of symptoms could be achieved by elongation of the common limb or biliopancreatic limb reversal in patients who underwent RYGB.

23.5 Neuropathy

A 48-year-old woman underwent laparoscopic RYGB for morbid obesity (body mass index [BMI] of 43.7 kg/m^2) in 2017. Medical history consisted of type 2 diabetes mellitus (T2DM) and hypothyroidism and was on regular medications with HB1Ac being 6.4% and TSH being 3.9 μIU/l. Previous surgical history comprised of a classical cesarean section. She had no history of intestinal problems, coeliac disease, malabsorption, or neurological symptoms. The patient was a non-alcoholic and a non-smoker. Her nutritional intake was incongruity with the international guidelines and recommendations following bariatric surgery (BS). The patient was on over-the-counter multivitamin and mineral supplement with a calcium dosage of 1000 mg calcium-carbonate consumption every day. The patient was on a regular follow-up as per the institutional protocol. Two years after surgery, she presented for a standard follow-up review, including the required blood investigations. Her weight was stable (BMI of 26.2 kg/m^2).

She returned to our center, around 5 months later, as she started to develop multiple complaints. Her complaints included blurred vision, concentration problems, confusion, irritability, tinnitus, palpitations, tingling in the fingers and toes, behavioral changes, mood swings, decreased muscle strength, muscle weakness, ataxia, aphasia, and glossitis. A clinical diagnosis of anemia based on deficiencies of iron, folate, and vitamin B12 and also deficiency of vitamin B1, B 6, B11, B12, E, or copper a vitamin D deficiency was kept in mind owing to the peculiar clinical features of the patient. The patient was admitted and evaluated. Her blood parameters were normal except for the following deranged parameters hemoglobin (7.9 mmol/l) (N-8.5–11.0 mmol/l); borderline low hematocrit (0.35) (N-0.35–0.45); Vit D (34 nmol/l) (N > 75 nmol/l); iron (4.0 μmol/l) (N-10–25 μmol/l); ferritin (6.0 μg/l) (N-13–200 μg/l); Vit B12 (170 pmol/l) (N > 200 pmol/l); methylmalonic acid (MMA) (155 nmol/l) (N < 430 nmol/l). MCV was normal. Other vitamins like B1, B6, B11, E, and trace minerals like selenium, copper, and zinc were normal. Serum folic acid level was 11.8 nmol/l (N > 10 nmol/l).

A differential diagnosis of polyneuropathy associated with neuropsychiatric symptoms was made. Management was streamlined, taking deficiency of vitamin B12 deficiency and folic acid into the aspect. As the cause of these problems could be identified, no electromyogram was performed. The patient received an intramuscular injection directly (1000 μg hydroxocobalamin per dose). The same was repeated weekly for the next 6 weeks. Improvements were seen within 1 week of commencing the therapy. Glossitis, tingling in fingers and toes, and neuropsychiatric symptoms (irritability, mood swings, and behavioral changes) symptoms started to get alleviated with treatment. Concentration issues, confusion, blurred vision, palpitations, reduced muscle strength, weakness, aphasia, ataxia, and tinnitus improved; however, they were still present in a milder form. After 2–3 weeks of treatment, weakness, confusion, aphasia, and ataxia were entirely resolved. However, within 4–5 days of the follow-up injection, she reported improvement in the above symptoms. After that, the intramuscular injection therapy of Vit B12 was adjusted to two doses per week. Tinnitus, palpitations, and concentration problems

were cured, and overall weakness had disappeared after 4 weeks of treatment. Only the blurred vision was persistent in a subtle form. All laboratory blood results mentioned in this scenario came to normalcy, while all the complaints had resolved the following 6 weeks of therapy entirely.

Laparoscopic RYGB has been the most commonly reported procedure that is associated with anemia and other nutritional deficiencies. Following RYGB, anemia can be microcytic (which is because of iron deficiency), or macrocytic (due to Vit B12 or folic acid deficiency). A recent meta-analysis by Kwon et al. have shown the high prevalence of Vit B12 deficiency following RYGB [38]. Vitamin B12 plays a pivotal role in erythropoiesis and is a key vitamin essential for proper brain development. Deficiency of Vit B12 causes leads to megaloblastic anemia and developmental disorders of the nervous system with dementia and mood disorders [39]. Vitamin B12 is essential for the initial myelination and development of the central nervous system and also for the maintenance of its normal function. Demyelination of the cervical, thoracic dorsal, and lateral columns of the spinal cord are seen in patients with cobalamin deficiency. Occasionally it is also associated with demyelination of cranial, peripheral nerves and white matter in the brain. Histopathological analysis reveals a "spongy degeneration" owing to the loss of and swelling of the myelin sheath [40].

The most frequently associated neurological symptoms encountered are symmetric paraesthesia with altered sensation over the skin and gait problems [41]. Physical examination may reveal pallor, jaundice, pigmentary changes in the skin, edema, or neurological defects such as altered proprio-reception, ataxia, and weakness. Personality changes, amnesia, psychosis, and, rarely, delirium neuropsychiatric manifestations are encountered [40]. Less prevalent conditions associated with Vit B12 deficiency include glossitis, malabsorption, and rarely thrombosis. Hematological abnormalities usually precede the onset of neurological disease [42].

Various factors have been implicated in the occurrence of anemia post metabolic surgery.

1. Existing preoperative deficiency of Vit B12 (around 13%), which is considered to be a major predictive factor for postoperative deficiency, leading to secondary anemia [43]
2. Inadequate food intake during the postoperative period, as the patients tend to avoid consumption of red meat, which acts as a good source of heme iron [44]
3. Deranged absorption following RYGB
4. Altered bioavailability of drugs
5. Increased hepcidin levels due to obesity-related inflammation [45]
6. Altered metabolism and absorption of other micro-nutrients [46]

Most (99%) of the active absorption of cobalamin is dependent on the cobalamin-binding protein intrinsic factor (IF), while only 1% of the absorption is carried out through non-specific passive absorption [40, 41]. Following RYGB, there is a loss of acid secretion and IF in the stomach. There is an exclusion of the remnant stomach, while the proximal small bowel is bypassed [47]. Altered anatomy has an influence on the absorption of cobalamin.

Serum Vit. B12 serves as a poor predictor of functional Vit B12 deficiency, as the intracellular level deficiencies are not taken into account. Increased methylmalonic acid (MMA) and total homocysteine levels are considered to be sensitive markers for Vit B12 deficiencies [48, 49]. More intense follow-up and management of Vit B12 deficiency become necessary as these deficiencies have been reported in spite of regular supplementations according to the existing guidelines. Studies have proven that oral supplementation of postoperative Vit B-12 deficiencies was successful in greater than 80% of the patients. Intramuscular injection of Vit B12 remains the gold standard in symptomatic Vit B12 deficient patients [43]. A high dose of oral cyanocobalamin can be considered in selected asymptomatic patients [50]. Dosage of 1000 μg oral Vit B12 daily or a 500 μg weekly administration of Vit B12 through the intranasal route can also be considered. Intramuscular or subcutaneous of B12 supplementation, with a dose of 1000–3000 μg every 6–12 months to 1000 μg/month is indicated if cobalamin sufficiency cannot be maintained through oral or intranasal routes [51].

23.6 Adrenal Insufficiency

A 54-year post-menopausal female, with class 3 morbid obesity (BMI 45.6 kg/m^2) was consulted and counseled for abdominoplasty along with weight loss surgery. Comorbidities included T2DM, hypertension, and was on medications. She was also a known case of bronchial asthma on treatment. Previous surgical history included an open hysterectomy for dysfunctional uterine bleeding. She had a wound infection during the hospital stay and was subsequently hospitalized for a month and a half. She had a history of osteoarthritis and used to take intra-articular steroid injection for joint pain occasionally. On examination, she had exertional dyspnea, pendulous hanging abdomen wall, which hindered her day to day activity along with severely restricted mobility. She had multiple bruises with thinned out atrophic skin with striae at numerous points all over the abdominal wall. She was assessed, evaluated, and underwent laparoscopic RYGB with concomitant abdominoplasty. Postoperatively she had wound infection, which was managed with culture-specific antibiotics. The patient was discharged on postoperative day 07. The patient was not on proper follow-up and came just once, 2 weeks following the surgery. Three months following discharge, the patient came to the hospital with dyspnea at rest, pain at the wound line with recurrent episodes of vomiting with reduced intake. She had fainting episodes on and off, past 2 weeks, and was clinically dehydrated. The patient had frequent bouts of hypotension, weakness, and inability to carry day to day activities. On examination, she was dyspneic, hypotensive along with tachycardia and tachypnea. There was an acute exacerbation of asthma. Bilateral wheeze was present, and she had wound site induration with cellulitis with wound gaping at few points of the suture line.

Transthoracic echocardiography and serum electrolytes were in normal range except for hyponatremia. Other blood parameters were in the normal range, except for mildly increased total counts and serum sodium levels being 130 mEq/l

(N-135–145 mEq/l). Serum renin and aldosterone were normal. The patient's clinical picture raised the suspicion for adrenal insufficiency. She had orthostatic hypotension, inappropriately low cortisol of 1.9 μg/dl (N-3–18 μg/dl). On performing dynamic testing with 1 μg cosyntropin (low dose ACTH stimulation test), which aided in the stimulation of the hypothalamic-pituitary-adrenal (HPA) axis, 30 min after stimulation, the values of serum cortisol increased to 10.8 μg/dl, hence confirming the AI diagnosis. Serum ACTH measured 22.8 pg/ml, confirming the diagnosis of adrenal insufficiency. MRI brain showed no abnormality of pituitary glands. Anti-adrenal antibodies were negative. Computed tomography of the abdomen revealed no mass lesions in the pancreas or the adrenals. Injectable hydrocortisone therapy (100 mg/day thrice daily) was initiated and given for a week. The patient was discharged on tablet prednisolone 40 mg continued for 10 months and was gradually weaned off later to 20 mg/day prednisolone. A 250 μg cosyntropin stimulation test was done during the follow-up. The analysis revealed an adequate serum cortisol response following which hydrocortisone therapy was discontinued. The patient has remained clinically stable to date.

BS, like many major abdominal surgeries, is surgical stress to the body [52, 53]. Adrenal insufficiency has been noted after major surgery as a consequence of surgical stress or blood loss affecting the pituitary gland [53]. Adequate absorption of oral corticosteroids plays a key role in survival in patients who have primary or secondary adrenal insufficiency. RYGB creates altered anatomy, reduced gastrointestinal transit time, which is further associated with changes in the absorption surface hence compromising the medication bioavailability [54]. Enhanced absorption following rapid gastric emptying results in excess plasma peak cortisol levels and could cause intermittent overexposure to corticosteroids, with possibly harmful long-term effects [55]. There is malabsorption of bile following RYGB, which affects cholesterol absorption. Altered absorption leads to a decreased precursor for steroid synthesis, causing adrenal insufficiency [56]. Malabsorption of trace elements and vitamins (especially selenium and vitamin B5), which are considered to be steroid biosynthesis cofactors, also leads to the reduction of the same. There is weight loss following RYGB, which causes the re-setting of the hypothalamic-pituitary-adrenal axis (HPA). Similar conditions causing adrenal insufficiency are seen in anorexia nervosa and perioperative complications such as blood loss causing pituitary/adrenal infarct or apoplexy [57–59].

The HPA axis is a major factor that determines the patient's responses to surgical trauma, and cortisol plays an important role in regulating humoral mediators during those conditions [60]. Postoperative complications are thought to be caused due to an uncontrolled inflammatory response. The increased stress leads to the overproduction of proinflammatory cytokines like TNF and IL-6 [61]. Literature suggests that severe sepsis and severe surgical stress may be associated with relative adrenal insufficiency, which may contribute to a fatal outcome [62]. Literature has also shown, that there is a direct correlation between the increase in serum cortisol levels postoperatively with the degree of surgical stress. There is a hypersecretion of IL-6 and CRP in scenarios of severe surgical stress, such as in our case. Furthermore, these variables could be directly linked to the serious postoperative complications

and hence the prolonged hospitalization. Several studies have concluded that corticosteroid replacement therapy is useful in patients with relative adrenal insufficiency [63]. It has been shown that the preoperative administration of corticosteroids has been found beneficial in attenuating surgery-induced inflammatory responses and in preventing postoperative complications. A short ACTH stimulation test performed in the preoperative period helps to determine a patient's maximal cortisol response to surgical trauma.

Daily cortisol requirements are more in patients who are morbidly obese because of a higher volume distribution and accelerated clearance [64]. Literature shows that the cortisol clearance is inversely related to insulin sensitivity and that fatty liver disease is associated with enhanced cortisol clearance, possibly through alterations in the activity of the 5α-, 5β-reductase, and also 11β-hydroxysteroid dehydrogenase type 1 in the liver [65]. Since the majority of the patients who are morbidly obese have fatty liver disease as well as decreased insulin sensitivity, there are at least two factors that lead to cortisol clearance. Hence dose adjustments of serum cortisol, individualized according to the daily profiles, before as well as after surgery, in morbidly obese patients is recommended.

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