Anesthetic Management of the Child with Homocystinuria: Case Report

Homosistinürili Bır Çocukta Anestezi Uygulaması

Türkay ÇAKAN, MD,[a]
Aynur DEMIR, MD,[a]
Bülent BALTACI, MD[a]

[a]Department of Anesthesiology, Ministry of Health Ankara Training and Research Hospital, Ankara

Geliş Tarihi/*Received:* 17.04.2009
Kabul Tarihi/*Accepted:* 24.09.2009

Yazışma Adresi/*Correspondence:*
Türkay ÇAKAN, MD
Ministry of Health Ankara Training and Research Hospital, Department of Anesthesiology, Ankara,
TÜRKİYE/TURKEY
turkaycakan@ yahoo.com

ABSTRACT Homocystinuria, an autosomal recessive disorder, is characterized by excretion of large amounts of urinary homocystein and accumulation of methionine and homocystine. Dislocation of the lens, osteoporosis of long bones, lax ligaments, lengthened extremities, kyphoscoliosis, genu valgum, light coloured hair, flat feet and mental retardation are clinical appearance of this syndrome. Anaesthesiologist faced to high anaesthetic hazards due to arterial and venous thrombotic episodes. Maintenance of high cardiac output, reduction of blood viscosity, good venous return, rapid recovery from anaesthesia and early ambulation are the goals of anaesthetic management. In this case, general anaesthesia was performed to a five years old girl with homocystinuria who underwent an operation due to right lens dislocation to the anterior chamber and increased intraocular pressure. Any complication was not observed during the perioperative period with an anaesthetic management taking care to the pathophysiology of the illness and the patient was discharged from the hospital without any problem.

Key Words: Amino acid metabolism, inborn errors; homocystinuria; anesthesia, general

ÖZET Homosistinüri otozomal resesif bir bozukluk olup, idrarla büyük miktarlarda homosistein atılımı ve vücutta metiyonin ve homosistin birikimi ile karakterizedir. Bu sendromda lens dislokasyonu, uzun kemiklerde osteoporoz, bağlarda gevşeklik, uzamış extremiteler, kifoskolyoz, genu valgum, açık renk saç, düzleşmiş ayak tabanı ve mental gerilik görülebilmektedir. Anestezistler arteriyal ve venöz trombotik olaylardan ötürü yüksek anestezik risklerle karşı karşıyadırlar. Yüksek kardiyak outputun sağlanması, kan viskozitesinin azaltılması, iyi venöz dönüş, anestezi sonrası hızla derlenme ve erken ambulasyon anestezi yönetiminin hedefleridir. Bu olguda, beş yaşında homosistinürili bir kız çocuğuna sağ gözde ön kamaraya lens dislokasyonu ve göz içi basınç artışı nedeni ile uygulanacak olan ameliyat için genel anestezi verildi. Hastalığın patofizyolojisine dikkat edilerek uygulanan anestezi sonrası hastada perioperatif herhangi bir komplikasyonla karşılaşılmadı ve hasta hiçbir sorun çıkmadan taburcu edildi.

Anahtar Kelimeler: Amino asid metabolizması, kalıtsal hatalar; homosistinüri; anestezi, genel

Turkiye Klinikleri J Anest Reanim 2010;8(2):150-3

Homocystinuria, an autosomal recessive disorder, is the second most common inborn error of amino acid metabolism after phenylketonuria. Its' incidence is approximately 1/200 000.[1] Homocystinuria is associated with defect in genes encoding for methionine metabolism enzymes. Deficiency of cystathionine beta-synthase is the usual biochemical defect. It is characterized by excretion of large amounts of urinary homocystein and accumulation of methionine and homocystine. The affected

person's weak collagen explains the clinical manifestation; dislocation of the lens, osteoporosis of long bones, lax ligaments, lengthened extremities, kyphoscoliosis, genu valgum, light colored hair, flat feet and malar flush.[2] Mental retardation is also seen in this disorder and it may be prevented by early diagnosis, dietary management (low methionine diet) and pyridoxine administration.[3]

CASE REPORT

The patient was 5 years old girl with photofobia, blephorospasm and high intraocüler pressure on the right considering due to acute dislocation of lens into the anterior chamber. She scheduled for emergency surgery for lens manipulation.

Five months before she was diagnosed as homocystinuria during the evaluation of her symptoms including mental retardation, and skeletal deformities like Marfan syndrome. In addition to blepharospasm, physical examination revealed lengthened extremities without hyperflexibility of joints. Her parents mentioned that they were first cousins and their two other daughters had the similar symptoms. Our patient began to use some drugs for her illness five months ago after diagnose, but medication was stopped 4 weeks ago and parents were not able to define the names of the medications.

On laboratory examination hemotocrit 34,8%, platelet count 361,000/mm^3, protrombin time 13,3 seconds, partial tromboplastin time 33,3 seconds and INR 1,16 were found. Chest X-ray, electrocardiogram, serum electrolyte levels and other routine laboratory data were within normal limits.

According to the consultation of paediatricians 15 mg/kg acetylsalicylic acid was administered to the patient preoperatively. 5-7 mg/kg Na-tiopental and 0,1 mg/kg vecuronyum bromür were given in the induction of anaesthesia. Any narcotic analgesic was not given in induction for preventing the delay in postoperative recovery. Sevoflurane and 100% oxygen were used in maintenance of anaesthesia. The patient was entubated with 5 mm noncuffed orotracheal tube. Blood pressure, heart rate, SpO_2, Et CO_2 were recorded every 5 minutes and serum glucose levels were also measured during the operation. Dextrose/saline solution (izomix Eczacıbası Baxter®) and dextran 40 (Rheomacrodex 10% Eczacıbası Baxter®) were infused. Her lower extremities were wrapped with elastic bandages for preventing blood pooling (Figure 1). She was mechanically ventilated and $EtCO_2$ was kept on 30-35 mmHg. Ophthalmic surgeons performed lens extraction to her and the procedure uneventfully continued 55 minutes. Blood pressure, heart rate, SpO_2 and $EtCO_2$ were in normal limits during the operation. Serum glucose levels were measured as 130 mg/dl, 166 mg/dl and 172 mg/dl. The total amount of fluid infusion during the operation was 425 ml (225 ml dextran 40 and 200 ml dextrose/saline solution). After the antagonization of residual neuromuscular blockade with neostigmine patient was extubated and transferred to post anaesthesia care unit (PACU). The signs of pulmonary embolism and her vital signs were observed in PACU and when she was fully awake (45 minutes after the operation) she transferred to ophthalmology clinic. She was given 3 doses of acetylsalicylic acid 15 mg/kg in the operation day after surgery and her lower extremities continued to wrap with bandages and massaged. On the first post operative day dipyridamole 50 mg orally 3 times a day, pridoxin 500 mg orally 4 times a day and folic acid were given to the patient. She was discharged from hospital on the third postoperative day.

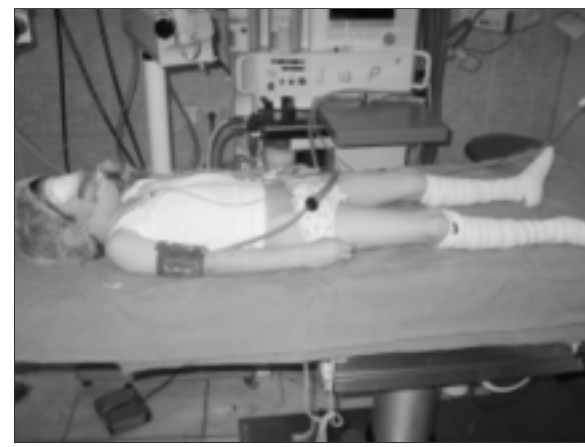

FIGURE 1: The appearance of our patient at the end of the operation.

DISCUSSION

The most common procedure performed in homocystinüric patients is manipulation of the ectopic lentis.

Hyperhomocysteinemia is frequent cause of thrombothic episodes in juveniles. Hyper homocysteinemic patients have high risk for repeated venous trombosis and the first attack of thrombosis is seen before forties. The risk of venous thrombosis is higher in hyperhomocystinemia patients than in hyperhomocystinüric patients.[4] Arterial and venous thrombothic episodes are associated with high anaesthetic and surgical hazards. Anaesthetic hazards may be avoided by careful consideration of its pathophysiology. Maintenance of high cardiac output, reduction of blood viscosity and platelet adhesiveness, reduction of vascular resistance, good venous return, avoidance of dehydration, rapid recovery from anaesthesia and early ambulation are the goals of anaesthetic management.[5]

It was postulated before that homocystine increased velocity of coagulation, firmness of the formed coagulum and prolonged initiation phase of the coagulation; it also increased platelet activation, impaired fibrinolysis and function of the contact activation pathway of coagulation, by genetic regulation of blood cells and reduced functional activities of single coagulation factors FXII, FX and FII.[6] The most frightened complication in homocystinuric patient was sudden occlusion of cerebral, renal, pulmonary and myocardial vessels in perioperative period. For that reason we administered excessive amounts of Dextran 40 to decrease platelet adhesiveness and blood viscosity. We also used acetylsalicylic acid preoperatively and dipyridamole postoperatively to inhibited platelet utilization. Lower extremities of the patient were wrapped with elastic bandages and calf muscles were massaged against venous stasis and to facilitate peripheral venous return during the operation and on the postoperative period. Early ambulation and oral fluid intake was supplied to prevent thromboembolic episodes.

Pancreatic islet cells are sensitive to the balance of sulfur amino acids. When hypermethioninemia occurs it causes hyperinsulinemia and secondary to hyperinsulinemia hypoglycemia is seen.[7] In our case dextrose/saline solution was infused to avoid hypoglycaemia. We were also careful about the quantity of fluid administration to maintain sufficient cardiac output.

In our case, inhalation anaesthetics were preferred to prevent the early recovery. For the same reason we avoided to use narcotic analgesics. In an editorial Koblin D[8] suggested exclusion of N_2O from the anaesthetic technique as nitrous oxide 50-70% inactivated the enzyme methionine synthase and impaired the conversion of homocystein to methionine. Increase in serum homocystein level was the result of that inactivation. Selzer et al reported neurological deterioration and death of a child anesthetized twice with nitrous oxide, who was later diagnosed with type III homocystinuria.[9] They also warned that patients with type III homocystinuria should not receive nitrous oxide. The use of nitrous oxide in a patient with type III homocystinuria could result in functional disorder of the nervous system because of extreme deficiency of methionine in the brain. Similar to Selzer, Yamada et al[10] reported that use of nitrous oxide prevents methionine synthesis from homocystein and resulting in further decrease in methionine especially in Type III homocystinüria. Because the use of nitrous oxide in patients with type III homocystinüri could result in functional disorder of nervous system, they did not use nitrous oxide in their patient with type III homocystinuria. Although we did not know the type of homocytinuria of our patient we did not use nitrous oxide in our case like the authors.

We did not have any measurement of her serum homocystein level preoperatively but her postoperative homocystein level was measured as 187 mmol/L (normal laboratory range 8-10 mmol/L). Therefore we were not able to make any comparison if any change occurred after anaesthetic management or not. Although the homocystein level was too high, any complication did not occur in the perioperative period. Anaesthetic mortality and morbidity of homocystinüria could be reduced if its pathophysiology is known well and the necessary controls are made strictly during the anaesthetic management.

REFERENCES

1. Mc Goldrick KE. Eye, ear, nose and throat diseases. In: Flesher LA, ed. Anesthesia and Uncommon Disease. 5th ed. Philadelphia, PA: Saunders Elsevier; 2006. p.1-27.
2. Rosenberg LE .Disorders of amino acid metabolism: the homocystinüria. In: Isselfacher KH, Adams Braunweld E, Pedersdorf RG, Wilson JD, eds. Harrison's Principal of Internal Medicine. 9th ed. New York: McGraw-Hill Co; 1980. p.463-8.
3. Grieco AJ. Homocystinüria: Pathogenic mechanism. Am J Med Sci 1977;273(2):120-32.
4. Baykal Y, Özet G, Kocabalkan F. [The risk factors related to venous thrombosis]. Turkiye Klinikleri J Med Sci 1999;19(4):236-41.
5. Parris WC, Quimby CW Jr. Anesthetic considerations for the patient with homocystinüria. Anesth Analg 1982;61(8):708-10.
6. Ebbesen LS. Hyperhomocysteinemia, thrombosis and vascular biology. Cell Mol Biol (Noisy-le-grand) 2004;50(8):917-30.
7. Abu-Lebdeh HS, Barazzoni R, Meek SE, Bigelow ML, Persson XM, Nair KS. Effects of insulin deprivation and treatment on homocysteine metabolism in people with type 1 diabetes. J Clin Endocrinol Metab 2006;91(9):3344-8.
8. Koblin DD. Homocystinüria and administration of nitrous oxide. J Clin Anesth 1995;7(2):176.
9. Selzer RR, Rosenblatt DS, Laxova R, Hogan K. Adverse effect of nitrous oxide in a child with 5,10-methylenetetrahydrofolate reductase deficiency. N Engl J Med 2003;349(1):45-50.
10. Yamada T, Hamada H, Mochizuki S, Tsuji M, Kawamoto M, Yuge O. General anesthesia for patient with type III homocystinüria (tetrahydrofolate reductase). J Clin Anesth 2005;17(7):565-7.