ACUTE PAINFUL VASO-OCCLUSIVE SICKLE CELL CRISIS IN AN OPIOID TOLERANT PATIENT

Azmat Riaz, Waqas Ahmad Kazi*, Nadeem Fazal, Hamid Saeed Malik

Armed Forces Hospital Najran, Saudi Araibia, *CMH Rawalpindi

INTRODUCTION

The clinical phenotype of sickle cell disease (SCD) is characterized by repeated vaso-occlusive events that can result in acute pain crisis, acute chest syndrome, priapism, skin ulceration, stroke, and in children splenic sequestration. Pain is by far the most common indication for hospital admission in these patients[1]. Sickle cell disease is prevalent in eastern and southern provinces of Saudi Arabia[2]. Vaso-occlusion is the single most important patho-physiological process that results in most of the acute complications of SCD. Haemoglobin polymerization significantly increases whole blood viscosity and leads to microvascular occlusion[3]. Once microvascular occlusion has occurred, the resultant hypoxia causes further sickling and the start of a vicious cycle that result in tissue infarction, the release of inflammatory cytokines and severe pain. The acute clinical problems of SCD, need expert management by a multidisciplinary team[4]. As a result of recent developments in the administration of analgesia, anaesthetists have become involved in the management of these patients. In addition, the anaesthetists play an important role in the treatment of patients with sickle cell crisis perioperatively and in the intensive care unit[5]. Patients presenting with frequent painful conditions are usually prescribed opioids. Repeated and frequent opioid consumption can lead to tolerance and sometimes addiction to opioids.

CASE REPORT

A 21 years old local Saudi lady with documented history of sickle cell disease presented to emergency room (ER) with sudden onset severe pain in her lower back and lower extremity joints. There was no history of any trauma. She was initially treated in ER with intramuscular diclofenac sodium but there was little pain relief. She was referred to surgeon who admitted her. Her past history revealed that she had multiple admissions in hospital with similar painful episodes in last few years. Last admission was 2 months back and she remained in hospital for 10 days. Physical examination showed a young lady in severe agony due to pain. She had tachycardia, sweating and pallor. Systemic examination was insignificant. Laboratory values revealed haemoglobin 7.8 gm/dl, a haematocrit of 24.5%, WBC count 11×10^9. Platelet count, Prothrombin time and Partial thromboplastin times were within normal limits. Alkaline phosphatase, lactic dehydrogenase, bilirubin, BUN, creatinine and electrolytes were also normal. Radiological evidence was insignificant. A diagnosis of acute painful vaso-occlusive sickle cell crisis was made. The anaesthesia department was requested to assess and treat the patient. The detailed history from close relatives of the patient revealed that in the last few months she had frequent admissions in hospital due to pain and each time pain intensity was increasingly severe. She used to get satisfactory pain relief with opioids but in her last admission she showed very little pain relief with morphine. The lady was shifted to intensive care unit and treated with bed rest, intravenous hydration, oxygen via face mask at rate 3 L min–1, antibiotics and intravenous morphine 0.1 mg kg–1 stat and then continuous infusion of 1 mg/hr and inj diclofenac sodium 75 mg IM 8 hourly. Pain intensity was measured on 10 point visual analogue scale (VAS). It was 9/10 before the start of treatment and after above treatment it was 8/10. After 4 hours patient was reassessed. VAS was found to be unchanged. Morphine dosage was increased to 1.5 mg/hr and then after 2 hours at rate of 2 mg/hr, but satisfactory pain relief was not achieved. The possible explanation of this little pain relief was that due to repeated comsumption of opioids she had developed tolerance to them.

Correspondence: Maj Azmat Riaz, Anaesthetist, PO Box 3217, Najran, Kingdom of Saudi Arabia
Email: azmatrt@yahoo.com
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Intravenous cyclizine 50 mg 8 hourly was started to counter nausea. One unit packed red cells was transfused to improve the oxygen carrying capacity of blood. Room temperature was kept optimum to prevent shivering.12 hours after the admission patient was still in pain and VAS was 7/10. Midazolam infusion 50 µg kg–1 hr–1 was started for sedation and anxiolysis. Sedation score was continuously monitored. In the evening patient became excessively drowsy and her respiratory rate dropped to less than 7. Arterial oxygen saturation also dropped below 90%. Auscultation of chest revealed clear chest with bilateral air entry. Arterial blood gases (ABGs) showed hypoxia with respiratory acidosis. Her respiratory functions were supported with bag-mask ventilation. Midazolam infusion was stopped. Intubation was performed to secure the airway and ventilatory support was started. Naloxone 400µg was administered which improved her respiratory functions. She was removed from ventilator and extubated when she became fully awake and had satisfactory respiratory functions but at the same time she started complaining of severe pain. Epidural analgesia was planned and an epidural catheter was placed at L2-L3 interspace without difficulty. After a test dose of 3 ml lignocaine 2% with adrenaline 1:200000, 15 ml bupivacaine 0.25% with 25µg fentanyl was given. An analgesic level to the sixth thoracic dermatome was achieved. Patient started having improvement in pain and after one hour her VAS was 3/10. Symptoms of nausea also improved. Intravenous morphine was omitted. Epidural bupivacaine 0.125% with 25µg fentanyl was continued every 8 hourly. Other supportive treatment was also continued. Patient was virtually pain free and VAS was only 1/10. No adverse effects like respiratory depression, drowsiness, nausea, vomiting, itching or urinary retention were observed. ABGs showed normal values. Epidural catheter was removed on fifth day and patient was discharged very much satisfied with her pain management.

DISCUSSION

The painful vaso-occlusive crisis is one of the major acute complications of SCD that is likely to involve the anaesthetist. Acute pain in SCD is thought to be caused by vascular occlusion and, in the case of bone pain, the consequent release of inflammatory mediators that result in raised intramedullary pressure and stimulation of nociceptors. Pain is the commonest manifestation of SCD after the age of 2 years and painful episodes are most frequent from 20–40 years of age[6]. The average rate of painful episodes is 0.8 per patient-year in sickle cell anaemia; however, 1% of these patients have more than six episodes per year, whereas some experience none. The extreme variability in severity of the clinical phenotype is largely unexplained[7]. Patients with more than three pain episodes per year are at a significantly increased risk of early death[8]. A few patients with repeated painful episodes develop a chronic pain syndrome that results in restricted activity, fear of further pain and a high risk of depression[9]. Numerous precipitating factors have been identified for acute pain crises. Pain is more likely to start at night, perhaps because of nocturnal desaturation or relative dehydration. Other potential precipitants are exposure to cold, dehydration, alcohol intake, stress, menstruation and intercurrent infections[10]. However, 57% of episodes have no identifiable precipitant. The lumbar spine, femur, knee, sternum and abdomen are the most commonly affected sites. It is uncommon for pain to affect only one area and usually two or three sites are involved. An intriguing observation is the high frequency of symmetrical, bilateral bony pain. This observation has prompted the hypothesis that marrow ischemia might result from a centrally mediated reflex that shunts blood flow away from the medullary cavity. The acute pain crisis of SCD results from the cumulative effects of HbS polymerization, red cell sickling, sickle cell adhesion to vascular endothelium and fibrin deposition; all of these act together to cause microvascular occlusion .

The mainstays of management of painful crisis are analgesia and fluid replacement. Oral or intravenous fluids are required to prevent dehydration, which results in a raised haematocrit and increased sickling[11]. Although

fever may be a simple consequence of sickling, the presence of fever should prompt a search for an infective focus and cultures of blood, urine and sputum should be taken as indicated. As there is a high risk of bacterial infection in patients with SCD, most clinicians would recommend the use of broad-spectrum antibiotics in the presence of fever. Blood transfusion has a place in acute crisis only in the presence of the acute chest syndrome or stroke, or when a pain crisis is refractory to standard therapy or relapses quickly. Episodes of crisis may last from a few minutes to weeks and the severity and location of the pain may vary from time to time or involve the whole body. Accident and emergency staff with limited experience of SCD may underestimate the severity of pain, because no objective criteria accurately quantify it. The result may be unnecessary suffering, inadequate pain control or misinterpretation of the patient's demands. The pain of sickle cell crisis is probably one of the most severe forms of pain[12]. The intensity and description of pain during crisis have been studied and the average pain severity score was 9.5 on a 10 cm visual analogue scale. Most patients with sickle cell crisis requiring prolonged treatment with opioids will develop tolerance, and on discontinuing opioids exhibit some signs of withdrawal. The latter can be minimized by a gradual withdrawal of opioids[13]. Clinicians who are relatively inexperienced in the management of sickle cell crisis may interpret evidence of tolerance or withdrawal as being indicative of a state of addiction, and understandably this may cause considerable patient distress. Tolerance to a drug is defined as the failure of a steady dose of the drug over time, to sustain the desired pharmacological effect, i.e., the need to increase the drug dosage to maintain the original pharmacological effect. But it is vital to realize that many episodes of pain are under treated. This under treatment will lead to an increased fear of future episodes and may well contribute to the development of a chronic pain syndrome[14]. The patient's ability to cope with the present painful situation depends on his or her previous experience of pain relief and the treatment received in hospital, as well as family relationships and social circumstances.

REFERENCES

1. Sergeant GR, Ceulaer CD, Lethbridge R, Morris J, Singhal A, Thomas PW. The painful crisis of homozygous sickle cell disease: clinical features. British Journal of Haematology 1994; 87: 586-91.
2. Padmos MA, Roberts GT, Sackey K, et al. Two different forms of homozygous sickle cell disease occur in Saudi Arabia. Br J Haematology 1991; 79: 93-8.
3. Vichinsky EP, Lubin BH. Sickle cell anaemia and related haemaglobinopathies. Pediatric Clinics of North America 1980; 27: 429-47.
4. Sergeant GR. Sickle Cell Disease; 2nd Edn. Oxford: Oxford Medical Publications, 1992.
5. Firth PG, Head CA. Sickle cell disease and anesthesia. Anesthesiology 2004; 101: 766–85.
6. Waters J, Thomas V. Pain from sickle cell crisis. Nursing Times 1995; 91: 16: 29-31.
7. Ballas SK, Rubin RN, Gabuzda TC. Treating sickle cell pain like cancer pain. Annals of Internal Medicine 1992; 117: 263.
8. Platt OS, Thorington BD, Brambilla DJ, et al. Pain in sickle cell disease. Rates and risk factors. N Engl J Med 1991; 325: 11–6.
9. Baum KF, Dunn DT, Maude GH, Serjeant GR. The painful crisis of sickle cell disease. A study of risk factors. Arch Intern Med 1987; 147: 1231-4.
10. Morgan SA, Jackson J. Psychological and social concomitants of sickle cell anaemia in adolescents. Journal of Pediatric Psychology 1986; 11: 429-40.
11. Marchant WA, Walker I. Anaesthetic management of the child with sickle cell disease. Paed Anaesth 2003; 13: 473–89.
12. Ballas SK, Delengowski A. Pain measurement in hospitalized adults with sickle cell painful episodes. Annals of Clinical Laboratory Science.1993; 23: 358-61.
13. Galton JS, Mark WC, Naser B. Postoperative opioid consumption in sickle cell disease. Can J Anesth 2004; 51: A94.
14. Gil KM. Coping with sickle cell disease pain. Annals of Behavioural Medicine 1989; 11: 49-57. Rodgers GP. Recent approaches to the treatment of sickle cell anaemia. Journal of the American Medical Association 1991; 265: 2097-101.