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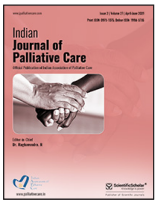

Case Report

Palliative Care Aspects of Acute Intermittent Porphyria – A Case Report

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ABSTRACT

Acute intermitttent porphyria belongs to a rare group of diseases hallmarked by deficient biosynthesis of heme. It carries a significant symptom burden, both physical and emotional,and therefore palliative care has emerged as an essential tool in the armamentarium of porphyria management . It takes care of the patient as a whole and caters to all aspects that the disease process demands. There are many lacunae in the literature regarding the palliative management of porphyria. We are reporting a case of a 16-year-old female who presented with severe abdominal pain, lower backache and symmetrical bilateral lower limb pain to the palliative ward referred by the neurology department for supportive care. This case describes the palliative care aspects of porphyria management which was successfully provided in the palliative care unit right from referral till the last. A multidisciplinary palliative care team managed the patient, and the necessary interventions were provided to the patient and family. Palliative acre in AIP needs to be emphasized, and palliative care services need to be utilized in these cases. The unavailability of specific treatment measure, heme, in countries like India further emphasizes the need for long-term supportive care for the patient and family. The case shows the importance of palliative care throughout the disease course as it is a chronic disease with significant morbidity and carries a heavy symptom burden. This case provides the insight that rather than conventional management alone for such chronic diseases, palliative care should be incorporated. Early integration with palliative care helps in exploring all the domains of disease. This is one of the first cases reported highlighting palliative care in porphyria , bridging the gap in the literature.

Keywords: Acute intermittent porphyria, Heme, Porphobilinogen deaminase, Neuropsychiatric manifestations, Palliative care

INTRODUCTION

Acute intermittent porphyria (AIP) is the most common and most severe variety of acute hepatic porphyria, a rare metabolic disorder caused by defective heme biosynthetic pathways. It encompasses genetic defects in the synthesis of heme, resulting in subnormal levels of porphobilinogen (PBG) deaminase, which, in turn, causes the accumulation of upstream metabolites, delta-aminolevulinic acid (ALA) and PBG.[1-4]

AIP hallmarks various physical and psychological symptoms. The physical symptoms are abdominal pain (in 85–95% of patients), pain in the limbs, chest, head and neck (50–52%), vomiting (43–88%), constipation (48–84%), muscle weakness (42–60%), hypertension (36–54%), tachycardia (28–80%), seizure (10–20%), sensory loss (9–38%), fever (9–37%), respiratory paralysis (5–12%) and diarrhoea (5–12%). The psychological manifestations are disorientation, confusion, restlessness and hallucinations (40–58%).[5-7]

Pain is one of the chief complaints which can be debilitating to patients and families. Various mechanisms result in peripheral and central sensitisation and neuronal plasticity, leading to the transmission of nociceptive information and causing pain perception. Accumulation of porphyrin metabolites can result in vasospasm, causing acute attacks of pain. Peripheral neuropathy can irritate nerves, causing pain, hyperesthesia, paraesthesia, etc. In general, pain is managed according to the severity and the mechanism of the pain. The WHO analgesic ladder can be employed.[8-11]

AIP can be confused with other acute medical conditions as they may result in recurrent or persistent acute neurovisceral life-threatening attacks, posing diagnostic and treatment challenges. Strong suspicion and timely treatment are

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needed.[12] The treatment options available are heme and other supportive measures. There is unavailability of heme in countries like India, and patients may need multiple admissions and lifestyle modifications like dietary changes for symptom control.[13]

As it is a chronic disease with significant morbidity, generally affecting adolescents, and carries a huge symptom burden, a multidisciplinary approach is required to deal with the multifaceted disease. The lack of a specific treatment measure, heme, underlines the requirement for supportive care in these patients. Palliative care is needed throughout the illness to cover the various aspects of the disease trajectory. This is one of the first cases reported highlighting the importance of palliative care in porphyria.

CASE REPORT

A 16-year-old female patient with a known case of porphyria for 2½ years presented to the palliative care ward and was referred by the neurology department for supportive care. She had a history of recurrent, approximately 10–15 episodes of sensory-motor symmetrical quadriparesis relapses. The patient presented with chief complaints of abdominal pain, lower backache and symmetrical bilateral lower limb pain. The intensity of pain was severe, with a numerical rating scale of 8–9/10; the patient described her pain as continuous baseline pain with acute shooting episodes, which were debilitating in nature. Furthermore, she had a history of intermittent, non-bilious vomiting and occasional palpitations. There was significantly decreased appetite and poor quality. She had a cachexic body structure and stable vitals. On central nervous system examination, motor examination showed reduced bulk and tone in all the upper and lower limb muscles. She had contractures at multiple joints, along with reduced motor power and graded sensory loss. Among the investigations, the porphyria screen was detected at 550 nm wavelength, and urine for PBG came positive. The electrocardiogram revealed sinus tachycardia. All other investigations were unremarkable.

In the palliative care ward, the palliative care team had aimed for a multidisciplinary holistic care approach. Her medications were revised. She was started with morphine infusion for severe pain at 6 mg/h as the patient was already opioid-tolerant (she was taking a total of 70 mg of intermittent release morphine 4 hourly) and later went up to 16 mg/h without any sedation. She was also given paracetamol 500 mg thrice daily and gabapentin 300 mg thrice daily as adjuvants. Antiemetics like metoclopramide were used for vomiting episodes. She was given haematology consultation and neurology consultations in the palliative care ward. She was given dextrose round the clock (bolus of 50% dextrose, 6 hourly 25% dextrose infusions and continuous 5% dextrose infusions). The patient was also advised to have a regular, very high oral carbohydrate diet after consulting the dietician, which she complied with. For autonomic symptoms such as palpitations, metoprolol was added to her medications. Furthermore, she was advised regular physiotherapy for contractures in conjunction with the physiotherapy team. The palliative team also had daily interactions with the patient and had conversations about her symptoms, both physical and emotional. All the issues regarding education, job, body image, self-esteem, family dynamics, sexuality, peer pressure, financial and future plans and social acceptance were explored in detail. She was assessed for any significant psychological issues that needed referral and pharmacological treatment but did not qualify for psychotherapy. Her family was given detailed information regarding her disease and symptoms. Family meetings were conducted, and all the information was conveyed at regular intervals. Her family consisted of her father, mother, brothers and sisters. Her brothers and sisters were her bystanders throughout her multiple admissions in the palliative care ward. Psychological support was provided to her family members in the form of listening to their concerns and providing reassurance. They were provided with utmost tender care. They were calmed and convinced by the recurrent conversations, and they understood the prognosis and the anticipated terminal event. They did not seem to be in psychological distress for any consultative intervention. They were allowed to make their prayers in the ward as they were strong believers in God. She was discharged from the palliative care ward on oral morphine 60 mg immediate release 3.5 tablets 4 hourly and breakthrough doses along with adjuvants. She was advised to do regular physiotherapy at home. After the last discharge, she was on home-based care with frequent outpatient department visits. She passed away at home peacefully 2 months after the last admission. Post her death, the family was called a few times, and bereavement support was given.

DISCUSSION

Our case is one of the first cases that describe the role and significance of palliative care in porphyria. Symptomatic management remains the cornerstone in the management of AIP, as patients will have varied physical as well as psychological symptoms. Our case describes the palliative aspects of dealing with a case of AIP, which involves holistic care, that is, the management of physical as well as psychological symptoms, rehabilitation, caregiver support and counselling. The diagnosis is established by random urine samples for qualitative screening tests for PBG followed by quantitative testing of ALA and PBG.[14-17]

The management of AIP can be summarised under specific management and general measures. In case of an acute attack, early administration of heme preparations, 3–4 mg/kg/day for 3 or 4 consecutive days, is the specific therapy.[18] The general management of AIP in the hospital is getting good

symptomatic relief, avoidance of unsafe medications and achieving proper fluid and electrolyte balance. Carbohydrate loading helps in ameliorating acute attacks with per day administration of at least 300–500 g.[19] Using syringe pumps, continuous high-dose glucose should be infused around the clock under sugar monitoring to avoid neurological complications due to hypo or hyperglycaemia. In patients who take it orally, the diet should be rich in carbohydrates.[20]

Palliative management involves a multidisciplinary approach to patient care with the involvement of a palliative physician, psychiatrist, psychologist, dietician, physiatrist, physiotherapist, counsellor, occupational therapist, etc., apart from conventional medical management, which generally focuses on the specific treatment and on the physical symptoms, where psychosocial and caregiver support is generally ignored. Pain is the most important clinical manifestation. It may be highly variable with regard to both intensity and presentation. Acute attacks may be associated with somatic, visceral and neuropathic pain. Prompt assessment of pain, stepwise pain management approach with safe nonopioid and opioid medications with emotional support from the fundamentals of pain management in them. In our case, we had to use higher doses of opioids to optimise the pain.[11] The patient was already using a higher dosage of oral morphine when she came to us to the palliative care unit. Therefore, she was titrated at higher doses of intravenous morphine. There is no high-quality evidence regarding the use of high-dose opioids in chronic non-cancer pain, their efficacy or adverse effects. Hence, there is a lack of evidence to either support or refute the use of high-dose opioids in non-cancer pain. In clinical practice, evidence-based statements cannot be made on the use of higher doses of opioids.[21]

For symptoms of autonomic neuropathy, such as tachycardia, hypertension, constipation, vomiting and urinary retention, symptomatic management is required. Beta-blockers may be used for tachycardia and arrhythmia, and antiemetics can be used for vomiting. If urinary retention is present, catheterisation may be done. Acute encephalopathic symptoms such as mental changes, insomnia, hallucinations, anxiety and convulsions require electrolyte correction, benzodiazepines, and anti-seizure drugs such as diazepam, gabapentin, levetiracetam or propofol in case of status epilepticus. Acute renal failure or hyponatremia may require fluid management, sodium correction or sometimes haemodialysis.[19] Bulbar weakness, muscle weakness and arrhythmias can be warning signs of a worsening acute attack and should be dealt with carefully. The patient may need intensive care. Respiratory difficulties can indicate motor neuropathy and can lead to pneumonia, and early mechanical ventilation may be warranted. In such cases, early rehabilitation is imperative. Furthermore, there may be long-term complications, such as chronic kidney disease, chronic hypertension, pain syndromes or hepatocellular cancers, which need attention.[18]

Palliative care also advocates the proper assessment of emotional psychosocial needs followed by its prompt addressal. Various validated screening tools may be employed bedside, such as Edmonton Symptom Assessment Scale(ESAS) or Depression Anxiety Stress Scale-21 (DASS 21) scales for symptom assessment. If screening generates moderate, severe grades of emotional or psychological distress, pharmacological interventions are to be considered, along with psychotherapy and counselling in mild to moderate distress. Family support during the entire trajectory of the disease, as well as during the end of life, is the hallmark of palliative care. Family counselling sessions are conducted, and members are explained regarding disease process, outcomes and the associated prognosis. Any queries and suggestions are carefully dealt with, and care is extended to end-of-life and bereavement.[22]

Since our patient comes in the adolescent age group, there is the added burden of integration of patient identity into this already complex phase of life. Their palliative care concerns may be different from adults. They may have many social and emotional concerns. Tender care and counselling are required in them. Palliative care is different compared to other specialties, which may concentrate on the physical aspects of care alone.[23-25]

Palliative care also aims at rehabilitation involving a physiatrist or physiotherapist as a part of a multidisciplinary approach to care, which consists of speech therapy involving stimulation of phonation and swallowing, psychological rehabilitation involving the provision of emotional support for patients and families and respiratory rehabilitation therapy with respiratory muscle training. Occupational therapy incorporates passive mobilisation of limbs, limb muscle strengthening, dynamic trunk control exercises, prescription of assistive devices and education on prevention measures. Physical therapy includes general muscle strengthening, joint mobilisation and stretching dynamic trunk control exercises, training of rolling and transitions and gait training with partial body weight support.[23]

CONCLUSION

Palliative care in AIP may be less described, but it is one of the hereditary metabolic disorders that carries a high scope for palliative interventions. AIP currently has a good prognosis but may be fatal and carries high morbidity. There is a lack of availability of specific therapy heme in countries like India that may result in more symptomatic burden. Palliative care is much different from conventional management of AIP as it involves the total care of the patient and the family, including the management of symptoms, such as pain and contractures, that are troublesome and sometimes intractable. Young adults may have innumerable psychological and social

concerns which need special attention which is also provided by the palliative care team. As this disease may result in a high caregiver burden, the family also needs careful attention and counselling, which is one of the hallmarks of palliative care. End-of-life care and advanced care planning are also important requirements in AIP during the terminal stages, which are provided by the palliative care team. There should be changes in the personal attitudes of physicians and the generation of new policies for the early integration of chronic diseases with palliative care for optimal outcomes in clinical practice. Palliative care in AIP needs further exploration, and palliative care services need to be utilised in all cases worldwide.

Authors' contributions

(I) Conception and design: Dr. Seema Mishra. (II) Administrative support: Dr. Seema Mishra. (III) Provision of study materials or patients: Dr. Saurabh Vig. (IV) Collection and assembly of data: Dr. Neethu Susan Abraham. (V) Data analysis and interpretation: Dr. Seema Mishra. (VI) Manuscript writing: Dr. Neethu Susan Abraham. (VII) Final approval of manuscript: All authors.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author confirms that there was use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing, images of the manuscript and no images were manipulated using AI.

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