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The use of parenteral nutrition for the management of PKU patient undergoing chemotherapy for lymphoma: A case report

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ABSTRACT

The metabolic control of phenylalanine levels is a challenge during illness. We present the metabolic management of a 6 year old boy with classical PKU who was diagnosed with stage III intraabdominal Burkit's lymphoma and underwent surgical resection and chemotherapy. The metabolic control during chemotherapy was achieved by the use of parenteral custom made amino acid solution and pro-active adjustment of intake. From the 94 obtained plasma phenylalanine (Phe) levels, 18.4% were above our clinic's recommended upper limit (360 μmol/L, 6 mg/dL) while 52.7% of Phe levels were below the recommended lower limit (120 μmol/L, 2 mg/dL). Phe levels above recommended range were associated with low caloric/protein intake, while levels below recommended range reflected the difficulty in achieving the full prescribed Phe intake. We recommend early institution of custom made amino acid solution with maximum amino acid content and caloric intake to provide optimal phenylalanine control. Administration of phenylalanine via regular intravenous amino acid solution may assist in avoiding low Phe levels when prescribed intake is compromised due to vomiting and other disease related illnesses.

Use of custom made, phenylalanine free amino acid solution proved beneficial in the management of blood phenylalanine levels in a PKU patient during chemotherapy for Burkitt lymphoma.

1. Introduction

Phenylketonuria (McKusick 261600, PKU) is an inborn error of the phenylalanine hydroxylase resulting in deficient degradation and accumulation of phenylalanine (Phe) in blood and tissues [1]. Untreated PKU leads to intellectual disability and behavioral defects. Newborn screening and early institution of treatment based on diet restricted in Phe widely prevents the clinical phenotype.

Currently, the metabolic control of Phe levels by a Phe restricted diet is the biochemical management strategy necessary to provide the best potential for optimum outcome [2]. The metabolic control of blood Phe levels is a challenge during catabolic states. Malignant diseases are particularly challenging, but reported experience in metabolic management if PKU patients with concommittant malignant diseases is limited. Increased Phe levels have been observed during chemotherapy in two PKU patients with skin T-lymphoma mycosis fungoides and B cell non-Hodgkin lymphoma [3] and nasogastric tube feeding and parenteral nutrition has been reported in a patient with acute lymphoblastic leukemia (ALL) [4]. Our own review of the Metab-l data base, an international list server used by metabolic physicians worldwide for reports on malignancy in PKU patients, revealed only seven recorded cases between 1999 and 2009, including three cases of PKU patients with ALL, one case with Non-Hodgkin Lymphoma, one case with testicular cancer, and one case with an unspecified malignant condition. No details on PKU management during chemotherapy treatment were given in these reports. Indeed, there is virtually no information in the literature on the management and optimization of Phe control in cases where oral or nasogastric route is not possible. We attempt to address this short-coming with a report of a six year-old PKU patient with Burkitt's lymphoma and metabolic management using a custom made Phe free amino acid solution supplemented with tyrosine.

2. Case report

This male patient was diagnosed with classical PKU through newborn screening, with a pretreatment Phe level of 1225 μmol/L (20.4 mg/dL) on day 7 of life. His estimated Phe tolerance was 275 mg (34 mg/kg/day) at the age of 4 months. Mutation analysis of PHA gene was not performed. The patient had excellent dietary Phe control with 75% of his lifetime Phe levels within the clinic's

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Table 1
Cycles of chemotherapy and recovery periods (denoted as "a"), mean and median Phe levels, Phe intake, amino acids, protein and caloric intake by source. * denotes use of regular TPN during IIa for period of seven days.

Cycle	Day of hospital stay	Phe level Mean/median	Phe intake	Amino acids from TPN	Amino acids from NG/PO	Natural protein	Total protein	Calories from lipids	Calories from TPN	Calories from IV dextrose	Calories from NG/PO	Total calories	Cycle treatments and complications
I	9–15	4.1/4.0	322/342	13.2/17.3	39.7/38.1	6.5/7.1	59.4/59.6	541/522	218.5/274	14/0	1254/1063	2125/2184	• Cylophosphamide • Vinristine • Prednisone.
II	16–21	2.62/1.6	215/215.5	25.4/24.5	36.3/35.7	4.3/4.1	66.1/66.1	498.6/458	314.6/302.5	287.8/306	1609.8/1556	2263.8/2603.5	• Cylophosphamide • Vinristine • Prednisone • Methotrexate • Doxorubicin
*IIa	22–35	7.2/6.4	167.5/172	26.6/25	11.6/2.3	3.3/3.25	41.6/39.2	450.8/450	281.2/276	29.6/7.5	411.5/384.5	1193/1139.5	• Mucositis • C. dificile infection • Febrile neutropenia • Pneumonia • Vomiting • SIADH
III	36–41	2.6/2.05	157.5/152	32.3/36.3	18.9/10.4	3.2/3.2	54.5/58.3	418.3/418	275/308.5	340.2/400	706.5/602.5	1743.3/1635	• Cylophosphamide • Vinristine • Prednisone • Methotrexate • Doxorubicin
IIIa	42–55	5.9/5.1	150.5/133.5	30/28.6	21.3/21.65	3.1/2.75	54.6/56.9	377.7/452	262.8/194	157.5/146.5	540.8/502.5	1320/1314.5	• Febrile neutropenia • Vomiting • Urosepsis • Thick bowels on ultrasound • Feeding intolerance
IV	56–62	0.67/0.4	198.2/186	23.6/22.8	32.2/34.1	4.1/3.9	60/66.9	365.4/378	160.5/155	486.7/438	799.5/669	1886/1886	• AraC • Methotrexate
IVa	63–90	0.9/0.5	317.5/317.5	22.6/22.9	33.3/34.5	6.6/6.6	62.6/64.25	390.2/436	154/155.5	79.5/73	957.4/917.5	1609.1/1490	• Febrile neutropenia • Vomiting
V	91–97	1.1/0.5	343.8/396	23.8/20	28.8/34.9	6.7/8.1	59.3/65.4	474.8/589	163.5/154	555.7/518	970.7/986	2125/1768	• AraC • Methotrexate
Va	98–109	1.9/1.75	423.3/410	9.57/9.05	44.5/46.2	8.7/8.5	62.0/55	298.7/284	111.5/103	45.5/38	1239.4/1260	1753.5/1629.5	• Febrile neutropenia