INTRODUCTION: Hyperphenylalaninemia (HPA) may be caused by either a deficiency in phenylalanine hydroxylase or in tetrahydrobiopterin (BH4), the essential cofactor required for the hydroxylation of aromatic amino acids. The most common forms of BH4 deficiency are 6-pyruvoyl-tetrahydropterin synthase deficiency and dihydropteridine reductase deficiency, which require a different treatment from classical HPA. Tetrahydrobiopterin-deficient HPA is an autosomal recessive disorder characterized by mild transient hyperphenylalaninemia often detected by newborn screening. Patients also show increased excretion of 7-biopterin. Affected individuals are asymptomatic and show normal psychomotor development, although transient neurologic deficits in infancy have been reported. Patients may also develop hypomagnesemia and nonautoimmune diabetes mellitus during puberty. CASE PRESENTATION: We present a one year old boy with diagnosis of hyperphenylalaninemia due to tetrahydrobiopterin (BH4) deficiency. He presented positive newborn screening for Phenylketonuria. In successive controls Phenylalanine levels were within 1-6 mg/dl (60-360 mmol/l) without protein restriction or phenylalanine restricted formula. Biopterin and neopterin in dried blood spot were normal. Hyperphenylalaninemia associated genes were sequenced finding an homozygous pathogenic variant in PCBD1 gene (c.292C>T, p.Gln98Ter), compatible with tetrahydrobiopterin-deficient hyperphenylalaninemia. Determination of urinary pterins was performed, resulting in neopterin 4398.0 nmol/mmol of creatinine (range 300-1600) biopterin 982.5 nmol/mmol creatinine (range 500-3500) Percentage of biopterin in urine 18.3% (range 50-75); ratifying the diagnosis. Follow up with phenylalanine levels was performed monthly. At 7 months of age, after the introduction of meat in the diet his phenylalanine level climbed to 10.9 mg/dl Treatment with sapropterin was started without protein restriction, normalizing phenylalanine levels. At age 12 months all developmental milestones were attained. The patient presents to date no neurologic symptoms. Further follow-up monitoring development, neurologic symptoms and blood glucose will be assured. CONCLUSION: Further evaluation of cases of hyperphenylalaninemia found in newborn screening, including molecular genetic analysis and/or urinary pterins, is useful in providing a definitive diagnosis for the patient and eventual specific treatment.