Figure 1. 2-Ketoglutarate (2-Kg) is normally processed in the citric acid cycle of mitochondria to produce usable energy for the cell. 2-Kg is metabolized via 2-ketoglutarate dehydrogenase in a reaction that requires thiamine pyrophosphate that is transported into the mitochondria from the cytoplasm. This transport into the mitochondria requires a special transporter (A) (left). In microcephaly Amish-type, thiamine pyrophosphate transporter is deficient (X) that in turn lowers the activity of 2-ketoglutarate dehydrogenase (X) (right). Low activity of 2-ketoglutarate dehydrogenase leads to decreased energy and accumulation of 2-Kg that is excreted in the urine. In rare instances patients can benefit from B vitamins to boost the amount of thiamine pyrophosphate that is available for transport.