**Supplemental Table 1:** All patients with pyrroline-5-carboxylate reductase 2 deficiency are summarized in Supplemental Table 1 for their clinical features, neuroimaging and molecular genetic test results.

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| --- | --- | --- | --- | --- | --- | --- |
|  | **Nakayama *et al* 2015** **(n=4)** | **Zaki *et al* 2016****(n=14)** | **Meng *et al* 2017****(n=5)** | **Brick et al** **(n=1)** | **Current patient****(n=1)** | **Number of patients** |
| **Age at the time of publication (year)** | 7.5-11.5 | <10 | 2- 16.5 | 9.5 | 1.5 | 25 |
| **Gender** | Male (n=1)Female (n=3) | Male (n=8)Female (n=6) | Male (n=2)Female (n=3) | Male(n=1) | Female | Male(n=12)Female (n=13) |
| **Ethnicity** | Omani (n=2)Palestinian (n=2) | Egyptian (n=13)Pakistani (n=1) | Indian (n=2)Spanish (n=2)Moroccan (n=1) | NA | Egyptian |  |
| **Consanguinity**  | Yes (n=4) | Yes (n=13) | Yes (n=3) | NA | Yes | n=21 |
| **Birth History** |
| **Gestation** | Full-term (n=4) | Full-term (n=14) | Full-term (n=3) | NA | Full-term | n=22 |
| **Postnatal** | Normal (n=3)Transient fetal distress (n=1) | Normal (n=14) | Normal (n=3) | NA | Normal | n=21 |
| **Excessive vomiting/ Feeding** | NA/G-tube (n=2) | Yes (n=4) / NA | Yes (n=4)/ G-tube (n=3) | NA | Yes/no | Excessive vomiting (n=19)/G-tube feeding (n=5) |
| **Facial features** |
| **Eyes** | Down slanting (n=2), up-slanting (n=1), prominent eyelashes (n=2) | Normal (n=14) | Widely spaced (n=1) | NA | Up slanting, prominent eye lashes | Eye dysmorphic features (n=7) |
| **Nose** | Bulbous nasal tip (n=1), bunted nasal tip (n=1) | Bulbous nasal tip (n=14) | Convex nasal ridge (n=1) | NA | Bulbous nasal tip | Nasal dysmorphic features (n=18) |
| **Lips** | Thin vermillion of lips (n=2) | Normal (n=14) | Normal | NA | Normal | Lip dysmorphic features (n=2) |
| **Ears** | Hypoplastic antihelix (n=1) | Prominent ears (n=14) | Prominent ear (n=1) | NA | Hypoplastic antihelix | Ear dysmorphic features (n=17)  |
| **Facial shape & bones** | Triangular face (n=2) | Triangular face (n=14)Malar hypoplasia (n=14) | Normal | NA | Normal | Facial shape dysmorphic features (n=16)  |
| **Other clinical features** |
| **Failure to thrive** | Yes (n=4) | Yes (n=14) | Yes (n=5) | Yes(n=1)  | Yes | n=25 |
| **Acquired Microcephaly** | Yes (n=4) | Yes (n=14) | Yes (n=5) | NA | Yes |  n=24 |
| **Global developmental delay** | Yes (n=4) | Yes (n=14) | Yes (n=5) | Yes (n=1) | Yes | n=25 |
| **Seizures** | No | Yes (n=8) | Yes (n=3) | No | Yes | n=12 |
| **Hyperkinetic movements** | NA | Yes (n=14) | NA | Yes (n=1) | No | n=15 |
| **Muscle wasting** | Yes (n=4) | Yes (n=13) | NA | NA | Yes | n=18 |
| **Muscle tone** | Hypertonia (n=2) | Hypertonia (n=8) | Hypertonia (n=2)Hypertonia (n=3) | Hypertonia (n=1) | Hypotonia | Hypertonia (n=13)Hypotonia (n=4) |
| **Upper motor neuron signs** | Yes (n=4) | Yes (n=14) | NA | NA | Yes |  n=19 |
| **Non-ambulatory** | Yes (n=4) | Yes (n=14) | Yes (n=3) | NA | Yes |  n=22 |
| **Ophthalmological features** | NA | Nystagmus (n=3) | Cortical blindness (n=1), esotropia (n=1) | NA | Normal | n=5 |
| **Skeletal Features** | Hyperextensible joints (n=2) | Normal | High arched palate, broad thumb (n=1)Kyphoscoliosis (n=1) | NA | Normal | n=4 |
| **Brain MRI features** |
| **Delayed myelination** | Yes (n=4) | Yes (n=13) | Yes (n=1) | NA | Yes | n=19 |
| **Decreased white matter volume** | Yes (n=4) | Yes (n=13) | Yes (n=1) | NA | Yes | n=19 |
| **Thin corpus callosum** | Yes (n=4) | Yes (n=8) | Yes (n=2) | NA | Yes | n=15 |
| **Thin brain stem** | Yes (n=4) | Yes (n=2)No (n=12) | Yes (n=1)No (n=4) | NA | No (n=1) | n=7 |
| **Molecular genetic test results** |
| **Variant****(alleles)** | Hmz c.355C>T (p.Arg119Cys) (n=4)Hmz c.751C>T (p.Arg251Cys) (n=4) | Hmzc.796G>A (p.Arg266\*)(n=12)Hmzc.595G>A (p.Arg199Trp)(n=4)Hmzc.773T>C (p.Val184Ala)(n=4)Hmzc.139-3C>G (p.?)(n=4)Hmzc.694A>C(p.Cys232Gly)(n=2)Hmzc.394C>T(p.Gly159Arg)(n=2) | Hmzc.28C>T (p.Glu10\*) (n=4)Hmzc.796C>T (p.Arg266\*) (n=2)Hmzc.577G>A (p.Val193Met) (n=4) | Cmp Htzc.784-delCCT(p.261delSer) andc.138+1G > T (p?) | Hmzc.796C>T(p.Arg266\*)(n=2) | Missense (n=7)Truncating (n=5) |

**Abbreviations (listed alphabetically)**: Cmp=compound; Htz=heterozygous; Hmz=homozygous; MRI=magnetic resonance imaging; NA= not available.