**Table II. PBD differential diagnosis:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Age** | **Disease** | **PBD** | **Clinical similarities** | **Distinguishing PBD features** |
| **Neonate** |  |  |  |  |
| **Dysmorphic syndromes** | Down syndrome, Prader-Willi syndrome | ZS, NALD | Dysmorphism, single transverse palmar creases, hypotonia | Cataract, CDP, neuronal migration defects, liver disease, laboratory, molecular findings |
| **Neuromuscular disorders** | Spinal muscular atrophy, congenital myotonic dystrophy, congenital polyneuropathy,  congenital myopathies, muscle-eye-brain syndromes | ZS, NALD | Hypotonia | Dysmorphic features, liver disease, deafness, laboratory, molecular findings |
| **CDP affecting multiple epiphyses** | CDPX1, CDPX2, warfarin embryopathy, maternal vitamin K deficiency or maternal autoimmune disease | RCDP | Limb shortening, cataract | Rhizomelia, psychomotor retardation, laboratory, molecular findings |
| **Inborn errors of metabolism** | Nonketotic hyperglycinemia, molybdenum cofactor/sulfite oxidase deficiency, multiple acyl-CoA dehydrogenase deficiency, severe CPTII, mitochondrial respiratory chain defects, CDG, SLO, hepatorenal tyrosinemia, galactosemia | ZS, NALD | Hypotonia, seizures, dysmorphic features, liver disease | Cataract, deafness, CDP, neuronal migration disorders, laboratory, molecular findings |
| **1-6 months** | **Disease** | **PBD** | **Clinical similarities** | **Distinguishing PBD features** |
| **Cholestatic jaundice** | α1 antitrypsin deficiency, disorders of bile acid metabolism | ZS, NALD, IRD | Failure to thrive, jaundice, liver failure | Psychomotor delay, sensory deficits, laboratory, molecular findings |
| **Inborn errors of metabolism** | Organic acidurias, Niemann-Pick type C, CDG, respiratory chain defects | ZS, NALD, IRD | Seizures, hypotonia, liver disease | Neuronal migration disorders, cataract, CDP, sensory deficits, laboratory, molecular findings |
| **6 months-4 years** | **Disease** | **PBD** | **Clinical similarities** | **Distinguishing PBD features** |
| **Sensorineural hearing loss and retinitis pigmentosa** | Usher syndrome, Leber congenital amaurosis, Alstrom syndrome, Bardet-Biedl syndrome  | NALD, IRD | psychomoter retardation | Laboratory, molecular findings |
| **Leukodystrophy** | Canavan disease, Krabbe disease, MLD, mitochondrial respiratory chain defects, X-ALD | NALD, IRD | Failure to thrive, seizures, neurologic dysfunction | Laboratory, molecular findings |
| **Ataxia** | Abetalipoproteinemia, vitamin E deficiency, neuronal ceroid-lipofuscinosis, CDG, Friedreich’s ataxia, spinocerebellar ataxias | IRD, atypical | Ataxia, peripheral neuropathy | Laboratory, molecular findings |

Abbreviations used-CDG: congenital disorders of glycosylation, CDP: chondrodysplasia punctata, X-ALD: X-linked adrenoleukodystrophy, CDPX1: X linked dominant Conradi Hunermann syndrome, CDPX2: X-linked recessive brachytelephalangic CDP, SLO: Smith Lemli Opitz syndrome, MLD: metachromatic leukodystrophy, CPTII: carnitine palmitoyltransferase II deficiency