Fetal Alcohol Syndrome Characteristics and Clinical Features

Fetal Alcohol Syndrome (FAS) is a condition caused by maternal alcohol use during pregnancy, especially during the first trimester. As such, this is a teratogenic disease. FAS is the most common preventable cause of intellectual disability in the United States. The range and severity of associated abnormalities may vary greatly from case to case. Clinical features include midline craniofacial abnormalities like holoprosencephaly, a thin upper lip, a smooth philtrum, and short palpebral fissures. Cardiopulmonary, musculoskeletal, and genitourinary abnormalities may also be seen.

PLAY PICMONIC

Characteristics

Teratogenic Disease

Tarantula-gem

Alcohol is a teratogen that disrupts neuronal and glial cell migration. Maternal exposure to alcohol results in a decreased expression of the sonic hedgehog (*SHH*) gene and *SHH* transcription factors. In addition, alcohol (ethanol) is attributed to mammalian alcohol dehydrogenase (ADH), an enzyme that uses both retinol and ethanol as substrates. This causes a build-up of excess retinoic acid.

Intellectual Disability

Book Covered in Tar

Fetal alcohol syndrome is the most common preventable cause, and most common overall cause, of intellectual disability in the United States. Compare this to Down Syndrome, which is the most common genetic cause. Prenatal alcohol exposure can result in pre- and postnatal developmental retardation, by disrupting the retinoic acid and Sonic Hedgehog developmental pathways, and impairing neuronal and glial migration. This, in turn, may damage the CNS during fetal development and lead to intellectual disability, as well as other clinical findings.

Clinical Features

Midline Craniofacial Abnormalities

Middle-Line Crane-Face

Neonates exposed to alcohol in utero may present with characteristic facial abnormalities of the midline features of the face. These can include a thin upper lip, epicanthal folds, micrognathia, down-slanting, short palpebral fissures, and/or a smooth, indistinct philtrum. A short, upturned nose with a broad nasal bridge, midfacial hypoplasia, and eye abnormalities may also be seen. Other manifestations can include cyclopia and a cleft lip/palate associated with holoprosencephaly. Facial defects occur as a result of alcohol-induced damage to cranial neural crest cells, which are responsible for the formation of the frontonasal process that gives rise to facial features.

Holoprosencephaly

Halo-brain

Holoprosencephaly is caused by a failure of the forebrain to divide properly into two hemispheres and may be observed in severe cases of Fetal Alcohol Syndrome.

Thin Upper Lip

Thin Upper Lip

A thin upper lip can be seen in FAS patients. It is also associated with Prader Willi Syndrome. The upper lip thinness refers to the area demarcated by the vermilion border.

Smooth Philtrum

Smoothie Phil-Drum

The philtrum is the vertical groove between the nose and upper lip. In patients with Fetal Alcohol Syndrome, a common facial manifestation is an abnormally long, smooth philtrum in the center of the upper lip.

Short Palpebral Fissures

Short-ruler Pulp Fissures

Palpebral fissures are openings between the upper and lower eyelid; the elliptic space between the medial and lateral canthi of the two open eyelids. These can be characteristically shortened in FAS.

Cardiopulmonary Abnormalities

Abnormal Heart and Lungs

Heart defects associated with Fetal Alcohol Syndrome include ventricular septal defect, atrial septal defect, patent ductus arteriosus, and Tetralogy of Fallot. In severe cases, heart-lung fistulas may be seen. The primordial heart begins to beat during the fourth week of gestation and arises from mesoderm. Prenatal alcohol exposure can impact cardiogenesis by altering the retinoic acid pathway. Retinoic acid is critical to early cardiac development, aiding in the specification of cardiac progenitor cells.

Musculoskeletal Abnormalities

Muscle-skeleton with Abnormalities

Growth retardation is a characteristic of Fetal Alcohol Syndrome, associated with height, weight, and head circumference deficiencies. Clinically, this can present as a small body size, microcephaly, midface hypoplasia or micrognathia (a receding chin), and/or decreased muscle tone. Additionally, other orthopedic manifestations may be present, such as limb abnormalities or dislocations, joint contractures, scoliosis, hip dislocations, or pectus excavatum.

Genitourinary Abnormalities

Abnormal Genital-gentleman-Urinal

Prenatal alcohol exposure has been linked to urinary and kidney anomalies, such as aplastic / hypoplastic / dysplastic kidneys, urethropelvic junction obstruction, and functional abnormalities. These functional abnormalities can include impaired potassium excretion, impaired urinary concentrating ability, or impaired renal acidification, even in the absence of structural changes.